Title
Risk Factors for a Higher Symptom Burden in Patients With Cancer During the COVID-19 Pandemic

Author
Kwak, Ji Hun

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Risk Factors for a Higher Symptom Burden in Patients With Cancer During the COVID-19 Pandemic

by
Ji Hun Kwak

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Approved:

DocuSigned by:
Christine Miaskowski
4058DA2CA6554BB...

Christine Miaskowski
Chair

DocuSigned by:
Astrid Block
DocuSigned by:
Lynda Mackin
DocuSigned by:
Sueann Mark
942CF42139A744C...

Astrid Block
Lynda Mackin
Sueann Mark

Committee Members

CONTRIBUTIONS

Lynda Mackin, RN, PhD[1]

Astrid Block, RN, MS[1]

Sueann Mark, RN, PhD[1]

Steven M. Paul, PhD[1]

Bruce A. Cooper, PhD[1]

Maura Abbott, RN, PhD[2]

Susan Chang, MD[3]

Marilyn J. Hammer, RN, PhD[4]

Kord M. Kober, PhD[1]

Jon D. Levine, MD, PhD[3]

Rachel Pozzar, RN, PhD[4]

Kim F. Rhoads, MD, MS, MPH[3]

Karin Snowberg, MA[1]

Katy Tsai, MD[3]

Erin Van Blarigan, ScD[3]

Katherine Van Loon, MD, MPH[3]

Christine Miaskowski, RN, PhD[1,3]

[1]School of Nursing, University of California, San Francisco, CA

[2]Columbia University Medical Center, New York, NY

[3]School of Medicine, University of California, San Francisco, CA

[4]Dana Farber Cancer Institute, Boston, MA

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ABSTRACT

Objectives: Evaluate for subgroups of patients with distinct symptom profiles and for differences in demographic and clinical characteristics and stress and resilience among these subgroups.

Sample and setting: Patients were ≥18 years of age; had a diagnosis of cancer; and completed a survey online. Data were collected between May 2020 and February 2021.

Methods and variables: Patients (n = 1145) completed measures for depression, state anxiety, cognitive function, morning fatigue, evening fatigue, morning energy, evening energy, sleep disturbance and worst pain and measures of stress and resilience. Latent class profile analysis was used to identify subgroups of patients with distinct symptom profiles. Differences among the subgroups in study measures were evaluated using parametric and non-parametric tests.

Results: Four distinct profiles were identified (i.e., None (28.5%), Low 37.7%), High (25.9%), Very High (7.9%)). Patients in the High and Very High classes reported clinically meaningful levels of all nine symptoms. Differences among the four profiles for stress and resilience exhibited a dose response effect (i.e., as symptom burden increased ratings of stress, loneliness, and social isolation increased and ratings of resilience decreased.

Implications for Nursing: Findings can serve as “benchmark data” of the symptom burden of patients with cancer following the pandemic.

Key words: anxiety; cancer; COVID-19; depression; fatigue; loneliness; oncology; pain; sleep disturbance; social isolation

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INTRODUCTION

As a result of the COVID 19 pandemic that began in March of 2020, cancer care underwent a dramatic transformation (Ashbury, 2021). With the imposed isolation and mitigation procedures and limited access to inpatient and outpatient services, many patients with cancer received care using telehealth approaches (Ashbury, 2021; Singh et al., 2021). On an individual level, patients experienced significant stress associated with fears of contracting COVID-19; disruptions in cancer treatments and follow-up; financial concerns associated with job losses and decreases in income; as well as social isolation and loneliness (Ashbury, 2021).

Equally important, the COVID-19 pandemic created changes in individuals' health care behaviors to accommodate the fears associated with contracting COVID-19 and the enforced social distancing (Moraliyage et al., 2021). For example, in a population-based study in the United Kingdom (Quinn-Scoggins et al., 2021), of the 40.1% of participants who experienced a symptom suggestive of cancer, 44.8% did not contact their primary care provider. The major reasons for not seeking care included: fear of going to the hospital; worries about wasting clinicians' time; and concerns about putting strain on healthcare services. For patients with cancer and survivors, inconsistent guidelines from public health officials and professional organizations on cancer care created an atmosphere of uncertainty regarding treatment decisions (Mauri et al., 2020; Saini et al., 2020). In addition, delays in cancer screening, suspension of clinical trials, and postponements in ongoing or planned therapy added to patients' stress (Mauri et al., 2020; Moraliyage et al., 2021; Saini et al., 2020; Venkatesulu et al., 2021). Furthermore, patients with cancer experienced significant reductions in access to social services and supportive care, that worsened feelings of stress and loneliness (Aapro et al., 2021; Gallagher et al., 2021).

Prior to the COVID-19 pandemic, patients with cancer reported an average of nine unrelieved symptoms (Mazor et al., 2019). The most common symptoms included fatigue, sleep disturbance, depression, anxiety, and pain. Of note, a higher symptom burden was associated with higher levels of perceived stress. In our previous study that evaluated symptom burden

during the COVID-19 pandemic (Miaskowski et al., 2020), patients with cancer in the stressed group reported clinically meaningful levels of depression, anxiety, fatigue, and sleep disturbance, and significant decrements in energy and cognitive function. However, a large amount of inter-individual variability existed in the scores for all of the symptoms. More recently, in a qualitative study of patients who had access to online cancer forums (Colomer-Lahiguera et al., 2021), an analysis of 230 posts identified the most common emotions associated with the COVID-19 pandemic to be: *fear/panic, feeling lost, being stressed/anxious, being sad/depressed, feeling ignored/discarded, being upset, or feeling alone.* However, in a longitudinal study of older patients with breast cancer and noncancer controls (Rentscher et al., 2021), no between group differences were found in depression, anxiety, and loneliness scores. Of note, in both groups, as loneliness increased depression and anxiety levels increased.

As noted in our previous studies of patients with cancer (Allemann-Su et al., 2022; Calvo-Schimmel et al., 2022; Hammer et al., 2022; Huang et al., 2022; Lin et al., 2022; Shin et al., 2022), a large amount of inter-individual variability exists in their symptom experiences. Person-centered analytic approaches, like latent variable modeling (Muthen, 2002), allow for the identification of subgroups of patients with distinct symptom profiles. Once these subgroups are identified, risk factors associated with a worse symptom profile can be determined.

It is abundantly clear that during the COVID-19 pandemic, patients with cancer experienced clinically meaningful levels of fatigue, sleep disturbance, depression, anxiety, cognitive impairment, and pain (Miaskowski et al., 2020). However, no studies were identified that evaluated for inter-individual variability in patients' symptom experiences and associated risk factors during the COVID-19 pandemic. Therefore, in a sample of patients with cancer (n=1145), who were assessed from May of 2020 to February of 2021, the purposes of this study were to use latent class profile analysis (LCPA) to evaluate for subgroups of patients with distinct symptom profiles and to evaluate for differences in demographic and clinical characteristics and stress scores among these subgroups. We hypothesized that patients with a worse symptom

profile will report higher levels of global and cancer-specific stress, as well as higher levels of social isolation and loneliness and lower levels of resilience.

METHODS

Sample and settings

Patients were recruited from a registry of individuals who participated in our previous symptom management studies (CA187160, CA212064, CA151692); from electronic health record searches for patients with oncology diagnoses at University of California, San Francisco (UCSF) and Mount Sinai Medical Center and Columbia University Medical Center in New York City; and from the Dr. Susan Love Foundation for Breast Cancer Research. Potential patients received an email with a brief explanation of the study and a link that directed them to the study's enrollment page. This page explained the purpose of the study; the time frame for survey completion; and information about participating in research. This study was exempt from requiring written informed consent by the Institutional Review Board at the UCSF and from each of the participating institutions.

Patients were included if they were ≥18 years of age; were able to read, write, and understand English; had a diagnosis of cancer; were able to complete the study questionnaires online; and by completing the survey consented to participate. Of the 1908 patients who began the survey, 1145 completed the information that is presented in this paper (60.0% completion rate).

Recruitment and survey administration

Emails were sent to potential patients beginning May 27, 2020. Responses up to February 22, 2021 are presented in this paper. Patients who received the survey link were asked to complete the survey within two weeks. After 14 days, one reminder was sent to the patients who did not respond to the initial request to complete the survey.

Study measures

Patients were asked to answer all of the survey questions in relationship to their experiences in the past 14 days. The entire survey took approximately 60 minutes to complete. Patients were advised that doing the survey in one sitting was preferable but to take as many breaks as needed. All of the instruments were completed online using REDCap (Harris et al., 2019).

Instruments

Demographic and clinical characteristics

Patients completed a demographic questionnaire, Karnofsky Performance Status (KPS) scale (Karnofsky, 1977), Self-Administered Comorbidity Questionnaire (SCQ) (Sangha et al., 2003), and International Physical Activity Questionnaire (Craig et al., 2003; Hallal & Victora, 2004). In addition, patients responded to questions about their height and weight, cancer diagnosis, previous and current cancer treatments, presence of metastatic disease, and occurrence of COVID-19 infection.

Symptom measures

The 20-item Center for Epidemiological Studies-Depression scale (CES-D) evaluates the major symptoms in the clinical syndrome of depression. A total score can range from 0 to 60, with scores of $\geq$16 indicating the need for individuals to seek clinical evaluation for major depression (Radloff, 1977). Its Cronbach's alpha was 0.92.

The 20 items on the Spielberger State-Trait Anxiety Inventories (STAI-T and STAI-S) were summed for each scale to create a score that ranges from 20 to 80. The STAI-S measures a person's temporary anxiety response or how anxious or tense a person is "right now" in a specific situation. The STAI-T measures a person's predisposition to anxiety as part of one's personality. Cutoff scores of $\geq$31.8 and $\geq$32.2 indicate high levels of trait and state anxiety, respectively (Spielberger et al., 1983). Cronbach's alphas for the STAI-T and STAI-S were 0.94 and 0.97, respectively. State anxiety scores were used in the LCPA.

The 13-item Attentional Function Index (AFI) was designed to measure an individual's perceived effectiveness in performing daily activities that are supported by attention, working memory, and executive functions (Cimprich et al., 2011). A higher total mean score on a 0 to 10 numeric rating scale (NRS) indicates greater capacity to direct attention (Cimprich et al., 2011). Total scores are grouped into categories of attentional function (i.e., <5.0 low function, 5.0 to 7.5 moderate function, >7.5 high function) (Cimprich et al., 2005). Its Cronbach's alpha was 0.93.

The 18-item Lee Fatigue Scale (LFS) was designed to assess physical fatigue and energy (Lee et al., 1991). Each item was rated on a 0 to 10 NRS. Total fatigue and energy scores are calculated as the mean of the 13 fatigue items and the 5 energy items, respectively. Higher scores indicate greater fatigue severity and higher levels of energy. Using separate LFS questionaries, patients were asked to rate each item based on how they felt within 30 minutes of awakening (i.e., morning fatigue, morning energy) and prior to going to bed (i.e., evening fatigue, evening energy). The LFS has established cut-off scores for clinically meaningful levels of fatigue (i.e., ≥3.2 for morning fatigue, ≥5.6 for evening fatigue) (Fletcher et al., 2008) and energy (i.e., ≤6.2 for morning energy, ≤3.5 for evening energy) (Fletcher et al., 2008). Cronbach's alphas were 0.97 for morning and 0.94 for evening fatigue and 0.96 for morning and 0.93 for evening energy.

The 21-item General Sleep Disturbance Scale (GSDS) was designed to assess the quality of sleep. Each item was rated on a 0 (never) to 7 (everyday) NRS. The GSDS total score is the sum of the seven subscale scores that can range from 0 (no disturbance) to 147 (extreme sleep disturbance) and a score of ≥43 indicates a clinically meaningful level of sleep disturbance (Fletcher et al., 2008). Its Cronbach's alpha was 0.86.

Occurrence of pain was evaluated using the Brief Pain Inventory (Daut et al., 1983). Patients who responded yes to the question about having pain were rate the intensity of their worst pain using a 0 (none) to 10 (excruciating) NRS.

Stress and resilience measures

The 22-item Impact of Event Scale-Revised (IES-R) was used to measure distress associated with cancer and its treatment and the COVID-19 pandemic (Weiss & Marmar, 1997). 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”. A total IES-R score was created by summing the responses to the 22 items. For the IES-R total score, sum scores of $\geq$24 indicates clinically meaningful post-traumatic symptomatology and scores of $\geq$33 indicate probable post-traumatic stress disorder (PTSD) (Creamer et al., 2003; Morina et al., 2013). Its Cronbach’s alpha was 0.93

The 10-item Perceived Stress Scale (PSS) was used as a measure of global perceived stress according to the degree that life circumstances are appraised as stressful over the course of the previous 14 days (Cohen et al., 1983). Total PSS scores can range from 0 to 40. Its Cronbach’s alpha was 0.91.

The 6-item Social Isolation Scale (SIS) evaluates an individual’s perceptions of connectedness and belonginess (Nicholson et al., 2020). 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. Its Cronbach’s alpha was 0.71.

The 20-item UCLA Loneliness Scale was designed to measure an individual’s subjective feelings of loneliness as well as feelings of social isolation (Russell et al., 1980; Russell et al., 1978; Russell, 1996). A score of 36 represents a normative value for the general population (Knight et al., 1988). Its Cronbach’s alpha was 0.95.

The 10-item Connor-Davidson Resilience Scale (CDRS) evaluates a patient's personal ability to handle adversity (e.g., "I am able to adapt when changes occur") (Campbell-Sills & Stein, 2007). Total scores range from 0 to 40, with higher scores indicative of higher self-perceived resilience. The normative adult mean score in the United States is 31.8 ($\pm$5.4) (Campbell-Sills et al., 2009). Its Cronbach's alpha was 0.91.

Data analysis

Survey responses reside on a UCSF secure server. Data were downloaded from REDCap (Harris et al., 2019) into the Statistical Package for the Social Sciences (SPSS) Version 28 (IBM Corporation, Armonk, NY) for subsequent analyses.

Latent class profile analysis (LCPA) was used to identify subgroups of patients (i.e., latent classes) with similar experiences for nine symptoms (i.e., depression, state anxiety, cognitive function, morning fatigue, evening fatigue, morning energy, evening energy, sleep disturbance, worst pain) (Vermunt & Magidson, 2002). Latent class models often use categorical variables (Lanza, 2003). As in this study, when continuous variables are analyzed, LCA is called LCPA. However, one of the continuous variables in this study, namely ‘‘worst pain,’’ that was reported on a 0 to 10 NRS, had a large number of 0s because a number of the patients did not report pain. We accommodated this large number of 0s by modeling worst pain as a ‘‘two-part’’ variable. In this type of model, the variable is examined with one part representing the difference between those who did and did not report and with the second part differentiating among those who reported any pain on the remaining portion of the NRS (i.e., the 1 to 10 part of the NRS) (Muthen, 1989-2010b).

The LCPA was performed using Mplus Version 8.5 (Muthen, 1989-2010b). The final number of latent classes was identified by evaluating the Bayesian information criterion (BIC), Vuong-Lo-Mendell-Rubin Likelihood Ratio test (VLMR), and entropy. With this analysis, the model that fits the data best has the lowest BIC and/or VLMR (Nylund et al., 2007). In addition, better fitting models should produce higher entropy values (Celeux & Soromenho, 1996). Finally, well-fitting models ‘‘make sense’’ conceptually and the estimated classes differ as might be expected on variables not used in the generation of the model (Nylund et al., 2007). Estimation was carried out with robust maximum likelihood and missingness was accommodated for with the use of the expectation maximization algorithm (Muthen & Shedden, 1999). Due to the inclusion of a

categorical variable (i.e., the binary variable for the occurrence of pain versus no pain), rectangular numeric integration with 15 integration points was employed for logit estimation.

Differences among the latent classes in demographic, clinical, stress, and resilience characteristics were evaluated using parametric and nonparametric tests. A p-value of <.05 was considered statistically significant. Post hoc contrasts were done using a Bonferroni corrected p-value of 0.008 (0.05/6 possible pairwise contrasts).

RESULTS

A four class solution was selected because the BIC for that solution was lower than the BIC for the 3-class solution (Table 1). In addition, the VLMR was significant for the 4-class solution, indicating that four classes fit the data better than three classes. While the BIC was smaller for the 5-class than for the 4-class solution, the VLMR for 5-classes was not significant, indicating that too many classes were extracted. Using clinically meaningful cut-off scores for the symptom measures to name the classes (Table 2), of the 1145 survivors in this study, 28.5% were in the None class; 37.7% were in the Low class, 25.9% were in the High class; and 7.9% were in the Very High class.

Demographic and clinical characteristics

As shown in Table 3, compared to the None lass, the other three classes were more likely to be female, reported a lower level of exercise, and were more likely to report back pain. Compared to the other three classes, the Very High class was younger, had a lower level of education, had a lower annual household income, had a higher body mass index (BMI), and had a higher number of metastatic sites. Differences among the four classes in KPS scores (i.e., None > Low > High > Very High), number of comorbidities, SCQ scores, and occurrence rates for self-reported depression (i.e., None < Low < High < Very High) followed similar patterns.

Stress and Resilience

As shown in Table 4, differences among the four classes in IES-R, PSS, and UCLA Loneliness scale scores followed similar patterns (i.e., None < Low < High < Very High).

Differences among the four classes in SIS and CDRS scores followed similar patterns (i.e., None > Low > High > Very High).

DISCUSSION

This study is the first to use LCPA to evaluate for distinct symptom profiles using severity scores for nine common symptoms reported by patients with cancer during the height of the COVID-19 pandemic when vaccines and anti-viral medications were not available. These findings can be used as "benchmark data" of the symptom burden of patients with cancer for comparative purposes following the broad availability of vaccines and the lifting of social distancing and shelter in place orders, as well as to evaluate patients with cancer who have long COVID (Mafi et al., 2022; Montani et al., 2022). It is interesting to note that compared to previous studies that found 3 (Doong et al., 2015; Hammer et al., 2022) to 4 (Miaskowski et al., 2006; Pud et al., 2008) distinct symptom profiles using the prespecified symptom cluster of pain, fatigue, sleep disturbance, and depression, the current study identified four distinct symptom profiles. While none of the previous studies identified a Very High class (7.9% of the current sample), all of them found a High class whose sizes were relatively consistent with the current study (i.e., 6.6% (Pud et al., 2008), 7.1% (Doong et al., 2015), 10.8% (Hammer et al., 2022), and 15.0% (Miaskowski et al., 2006)). These consistent findings suggest that approximately 10% of patients with cancer experience a high to very high symptom burden.

While, in the current study, the classes were named based on the distribution of clinically meaningful cutpoint scores across the nine symptoms, it is worth noting that 66.7% of the symptoms in the Low class and 100% of the symptoms in both the High and Very High classes exceed these cutpoints. The remainder of the Discussion compares our findings regarding symptom severity and modifiable and non-modifiable risk factors with the extant literature prior to and during the COVID-19 pandemic.

Symptoms

In terms of depression and state anxiety, 33.8% of our sample (i.e., High and Very High classes) reported clinically meaningful levels of both symptoms. These prevalence rates are consistent with a recent systematic review and meta-analysis that found that during COVID-19, overall prevalence rates for depression and anxiety in the general population were 33.7% and 31.9%, respectively (Salari et al., 2020). While the CES-D scores for our two highest classes (23.3 and 37.6) were comparable to outpatients receiving chemotherapy (Oppegaard et al., 2022), they were significantly higher than scores for survivors with (13.5) and without (6.7) chemotherapy-induced peripheral neuropathy (CIPN) (Miaskowski et al., 2018) obtained prior to COVID-19. A similar pattern was observed for state anxiety scores in the two highest classes (i.e., 45.9 and 61.3) that were comparable to scores for outpatients receiving chemotherapy (Oppegaard et al., 2021) but higher than scores for survivors with (35.5) and without (28.4) CIPN (Miaskowski et al., 2018). Of note, consistent with a systematic review that showed that having a stable, high monthly income was a protective factor for both depression and anxiety in older adults during the pandemic (Ciuffreda et al., 2021), patients in our None class had a higher annual household income and lower rates of depression than patients in our Very High class (i.e., 6.3 versus 77.5%, respectively).

In terms of cognitive function, 71.5% of our sample reported moderate to high levels of cognitive impairment. This percentage is slightly higher than 43.0% to 66.6% reported in a systematic review of cognitive impairment in patients who were hospitalized for COVID-19 (Alnefeesi et al., 2020). However, it is comparable to the 75% occurrence rate reported for patients with cancer prior to the pandemic (Janelsins et al., 2014). In terms of the AFI scores for our two highest classes (i.e., 5.4 and 3.5), they are comparable to scores reported by outpatients receiving chemotherapy (Atallah et al., 2020), but significantly lower than scores for survivors with (6.2) and without (7.5) CIPN (Miaskowski et al., 2018).

Similar to the 60.7% prevalence rate for sleep problems in patients with cancer reported in a meta-analysis (Al Maqbali et al., 2022), 71.5% of the current sample reported clinically meaningful levels of sleep disturbance. However, in a study that compared breast cancer survivors to healthy women during COVID-19 (Bethea et al., 2022), only 10.0% and 13.5% reported sleep disturbances, respectively. One potential reason for these disparate findings is that in the study of breast cancer survivors (Bethea et al., 2022), sleep disturbance was evaluated using a single item from the CES-D rather than a multidimensional sleep disturbance measure like the GSDS. Equally important, the GSDS scores for our two highest classes were significantly higher than scores reported by survivors with (51.4) and without (39.2) CIPN (Miaskowski et al., 2018).

Similar to sleep disturbance and most likely linked with this symptom, 71.5% of our patients reported clinically meaningful levels of morning fatigue and decrements in morning and evening energy. In addition, the High and the Very High classes had clinically meaningful levels of evening fatigue. These findings are consistent with our previous work that demonstrated positive associations between both evening fatigue (Wright et al., 2017) and decrements in energy (Abid et al., 2017) and sleep disturbance in patients receiving chemotherapy prior to COVID-19. Compared to cancer survivors with and without CIPN, the morning (3.5 and 2.5) and evening (5.4 and 5.3) were significantly higher in the current sample. In addition, the decrements in morning (4.4 and 5.4) and evening (3.4 and 4.1) energy were worse in the current sample compared to survivors with and without CIPN (Miaskowski et al., 2018).

Moderate to severe pain was reported by all four classes (i.e., 100% of the patients). Of note, this prevalence rate is significantly higher than the 38.0% reported in a meta-analysis that considered a pain rating of $\geq$5 to equate with moderate or severe pain in patients with cancer (van den Beuken-van Everdingen et al., 2016). While the specific causes of pain in our sample were not assessed, the prevalence of osteoarthritis ranged from 26.0% to 33.3% and the prevalence of back pain ranged from 19.8% to 57.8%. As noted by Paice (2022), managing pain in patients

with cancer during both the opioid epidemic and the contemporaneous pandemic posed significant challenges. While trying to mitigate opioid misuse, the shelter in place orders severely limited patients' ability to access non-pharmacologic interventions (e.g., physical therapy, acupuncture) and mental health services that could contribute to exacerbations in pain.

Demographic and Clinical Risk Factors

As shown in Table 5, compared to the None class, several common and distinct risk factors were associated with a higher symptom burden. Consistent with previous reports of patients with cancer, younger age (Doong et al., 2015; Hammer et al., 2022; Miaskowski et al., 2006) and being female (Hammer et al., 2022; Miaskowski et al., 2014) were associated with a higher symptom burden. The age-related differences in symptom burden are often attributed to a response shift in older adults' ability to adapt to their changing health status (Sprangers & Schwartz, 1999). In the context of the loneliness and social isolation associated with the COVID-19 pandemic, older patients with cancer, who may be more accustomed to a home bound lifestyle, may experience less disruption in their daily routines that younger adults of working age and an associated decrease in symptoms (Clifton et al., 2022). In terms of gender differences, our results may be influenced by the high percentage of patients with breast cancer in the current sample and warrant additional investigation.

Compared to the other three classes, in addition to younger age and female gender, the Very High class had a lower level of education, was more likely to identify as non-white, and had a lower annual household income. While associations between these characteristics and a higher symptom burden were reported in previous studies of patients with cancer (Hammer et al., 2022; Miaskowski et al., 2014), in the context of the inequities in health care unearthed during the COVID-19 pandemic (Boserup et al., 2020; Hawkins et al., 2020; Llanos et al., 2023), increased attention needs to be paid to these social determinants of health (SDOH) in the context of cancer care. Clinicians need to assess for associations between a higher symptom burden and all of

these SDOH, as well as others that were not assessed in this study (e.g., food insecurity, discrimination).

A higher BMI and comorbidity burden and lower level of exercise and functional status were the common clinical characteristics associated with membership in the High and Very High classes. Of note, patients in the two highest classes had BMIs that were in the overweight and obese ranges (Centers for Disease Control and Prevention, 2016). While the pre-COVID-19 weights of our patients are not known, the results of a systematic review suggest that during the first year of the pandemic, both children and adults incurred potentially clinically significant increases in weight and BMI (Anderson et al., 2023). Equally important, the extremely low level of exercise in our two highest symptom burden classes may have existed or were exacerbated by the COVID-19 pandemic's mitigation procedures (Hilbold et al., 2023). Given the benefits of exercise to decrease symptom burden in patients with cancer (Larson et al., 2023; Matthews et al., 2018; Zhang et al., 2023; Zhu et al., 2022), clinicians need to assess for post COVID-19 weight gain and changes in exercise behaviors and counsel patients to start or maintain a regular exercise routine and make appropriate referrals to enhance their functional status.

A dose response effect was seen among the symptom classes in the number of comorbidities and comorbidity burden. This linkage between a higher symptom burden and higher comorbidity burden was highlighted in a recent review (George et al., 2021). These authors noted that between 37.9% and 74.3% of colorectal and 12.6% to 49.0% of patients with breast cancer have one or more comorbidities. In addition, the presence of comorbidities was associated with less optimal cancer treatment and associated decreases in survival. Therefore, oncology clinicians need to work collaboratively with patients' primary care providers to effectively manage these conditions and associated symptoms.

Stress and Resilience

As noted in Table 4, all of the stress and resilience measures exhibited a dose response effect (i.e., as symptom burden increased cancer- and COVID-19-specific stress, global stress,

and loneliness scores increased and social isolation (i.e., lower scores on SIS indicate higher levels of social isolation) and resilience scores decreased). While not linked definitively to a higher symptom burden, as noted in one review (Aknin et al., 2022), during the early months of the COVID-19 pandemic, psychologic distress increased in the general population. Moreover, psychological distress was particularly pronounced among individuals who were female, young, and had children under 5 years of age.

While evidence suggests that the prevalence of PTSD in the general population during the pandemic was approximately 22% (Cenat et al., 2021), a total of 33.8% of the patients in the High and Very High classes had IES-R total scores that were suggestive of partial or probable PTSD. This measure specifically assessed cancer- and COVID-19- related stress. In addition, this same percentage of patients had global stress scores (i.e., PSS-10) that exceeded normative scores for the United States population in 2006 (12.73 ($\pm$7.34)) and during the 2009 economic downturn (15.21 ($\pm$7.28)) (Cohen & Janicki-Deverts, 2012). These high levels of both types of stress may be related to cancer patients' concerns about being at increased risk for more severe disease and complications, as well as increased mortality if they contracted the virus (Colomer-Lahiguera et al., 2021; Dhada et al., 2021; Jammu et al., 2021). While increased stress is associated with a higher symptom burden in patients with cancer (Langford et al., 2022; Shin et al., 2022; Stacker et al., 2023), our findings suggest that the added stress associated with the pandemic markedly increased the severity of nine common symptoms in 33.8% of our sample.

Social isolation and loneliness can be considered somewhat "unique types of stress" imposed by the COVID-19 pandemic (Harden et al., 2020; Killgore et al., 2020; Pietrabissa & Simpson, 2020). While none of the classes had SIS scores indicative of being socially isolated, 71.5% of our sample had moderate to moderately high scores on the UCLA Loneliness Scale. The absence of a correlation between social isolation and loneliness is consistent with a population-based study of older adults in their last years of life (Kotwal et al., 2021), that found that 19% experienced social isolation, 18% experienced loneliness, and only 5% experienced

both types of stress. However, the occurrence rate for loneliness in our sample is higher than the 28% reported in a review of studies of older adults during the pandemic (Su et al., 2022). While most of the research on the impact of loneliness on symptom burden during the pandemic focused on mental health problems (Aknin et al., 2022; Giacco, 2023; Jamil et al., 2023), our findings suggest that these added types of stress were associated with clinically meaningful levels of both physical AND psychological symptoms in over a third of the patient in the current sample.

Research on associations between symptom burden and resilience in patients with cancer has focused primarily on psychological symptoms (Aizpurua-Perez & Perez-Tejada, 2020; Oppegaard et al., 2021; Shin et al., 2022; Tamura, 2021; Tamura et al., 2021) and quality of life outcomes (Franjic et al., 2021; Macia et al., 2020; Zhang et al., 2017). In general, patients with cancer with higher levels of resilience report lower levels of psychological distress (Aizpurua-Perez & Perez-Tejada, 2020; Oppegaard et al., 2021; Shin et al., 2022; Tamura, 2021; Tamura et al., 2021) and better quality of life (Franjic et al., 2021; Macia et al., 2020; Zhang et al., 2017). While no studies were identified that evaluated for associations between symptom burden in patients with cancer and their levels of resilience during the COVID-19 pandemic, the resilience scores for our three classes with the highest symptom were below the normative score for the general population of the United States (Campbell-Sills et al., 2009). Given that a variety of interventions (e.g., cognitive behavioral therapy, mindfulness training) are known to enhance resilience (Joyce et al., 2018; Ludolph et al., 2019), clinicians need to refer patients for these types of interventions and assess their efficacy in reducing symptom burden, particularly in high risk patients.

LIMITATIONS

Several limitations warrant consideration. Given that a majority of our patients were women with breast cancer, our findings may not generalize to males and patients with other types of cancer. In our study, the patients were well educated and had a household income that was greater than the median household income of $70,784 reported by the Census Bureau for citizens

of the United States in 2021. Therefore, our findings may not generalize to patients with lower levels of education or socioeconomic status. Because patients were recruited through an online survey, sampling bias may be present, skewing the sample to individuals who were technology literate and had access to emails and the internet. Given the study's cross-sectional design, causal relationships between symptom burden and various risk factors cannot be determined.

IMPLICATIONS FOR CLINICAL PRACTICE AND RESEARCH

Despite these limitations, many of the risk factors associated with a higher symptom burden profile are amenable to interventions. For example, weight management and exercise interventions can be prescribed to decrease many of the common symptoms associated with cancer and its treatments (Larson et al., 2023; Matthews et al., 2018; Zhang et al., 2023; Zhu et al., 2022). In addition, stress reduction interventions and resilience training, along with targeted pharmacologic interventions, should be prescribed to decrease the extremely high symptom burden of these high risk patients. One of the major unanswered questions is whether the symptom burden of patients with cancer has decreased in the post-pandemic era. Future research, that administers the same measures used in this study, can use our findings as "benchmark" data for comparative purposes and for the development of individualized symptom management interventions.

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REFERENCES

Aapro, M., Lyman, G. H., Bokemeyer, C., Rapoport, B. L., Mathieson, N., Koptelova, N., Cornes, P., Anderson, R., Gascon, P., & Kuderer, N. M. (2021). Supportive care in patients with cancer during the COVID-19 pandemic. *ESMO Open*, *6*(1), 100038. https://doi.org/10.1016/j.esmoop.2020.100038

Abid, H., Kober, K. M., Smoot, B., Paul, S. M., Hammer, M., Levine, J. D., Lee, K., Wright, F., Cooper, B. A., Conley, Y. P., & Miaskowski, C. (2017). Common and distinct characteristics associated with trajectories of morning and evening energy in oncology patients receiving chemotherapy. *Journal of Pain and Symptom Management*, *53*(5), 887-900 e882. https://doi.org/10.1016/j.jpainsymman.2016.12.339

Aizpurua-Perez, I., & Perez-Tejada, J. (2020). Resilience in women with breast cancer: A systematic review. *European Journal of Oncology Nursing*, *49*, 101854. https://doi.org/10.1016/j.ejon.2020.101854

Aknin, L. B., De Neve, J. E., Dunn, E. W., Fancourt, D. E., Goldberg, E., Helliwell, J. F., Jones, S. P., Karam, E., Layard, R., Lyubomirsky, S., Rzepa, A., Saxena, S., Thornton, E. M., VanderWeele, T. J., Whillans, A. V., Zaki, J., Karadag, O., & Ben Amor, Y. (2022). Mental health during the first year of the COVID-19 pandemic: A review and recommendations for moving rorward. *Perspectives in Psychological Sciences*, *17*(4), 915-936. https://doi.org/10.1177/17456916211029964

Al Maqbali, M., Al Sinani, M., Alsayed, A., & Gleason, A. M. (2022). Prevalence of sleep disturbance in patients with cancer: A systematic review and meta-analysis. *Clinical Nursing Research*, *31*(6), 1107-1123. https://doi.org/10.1177/10547738221092146

Allemann-Su, Y. Y., Vetter, M., Koechlin, H., Conley, Y., Paul, S. M., Cooper, B. A., Kober, K. M., Levine, J. D., Miaskowski, C., & Katapodi, M. C. (2022). Distinct cognitive function profiles are associated with a higher presurgery symptom burden in patients with breast cancer. *Cancer Nursing*. https://doi.org/10.1097/NCC.0000000000001114

Alnefeesi, Y., Siegel, A., Lui, L. M. W., Teopiz, K. M., Ho, R. C. M., Lee, Y., Nasri, F., Gill, H., Lin, K., Cao, B., Rosenblat, J. D., & McIntyre, R. S. (2020). Impact of SARS-CoV-2 infection on cognitive function: A systematic teview. *Frontiers in Psychiatry*, *11*, 621773. https://doi.org/10.3389/fpsyt.2020.621773

Anderson, L. N., Yoshida-Montezuma, Y., Dewart, N., Jalil, E., Khattar, J., De Rubeis, V., Carsley, S., Griffith, L. E., & Mbuagbaw, L. (2023). Obesity and weight change during the COVID-19 pandemic in children and adults: A systematic review and meta-analysis. *Obesity Reviews*, e13550. https://doi.org/10.1111/obr.13550

Ashbury, F. D. (2021). COVID-19 and supportive cancer care: key issues and opportunities. *Current Opinions in Oncology*, *33*(4), 295-300. https://doi.org/10.1097/CCO.0000000000000729

Atallah, M., Cooper, B., Munoz, R. F., Paul, S. M., Anguera, J., Levine, J. D., Hammer, M., Wright, F., Chen, L. M., Melisko, M., Conley, Y. P., Miaskowski, C., & Dunn, L. B. (2020). Psychological symptoms and stress are associated with decrements in attentional function in cancer patients undergoing chemotherapy. *Cancer Nursing*, *43*(5), 402-410. https://doi.org/10.1097/NCC.0000000000000713

Bethea, T. N., Zhai, W., Zhou, X., Ahles, T. A., Ahn, J., Cohen, H. J., Dilawari, A. A., Graham, D. M. A., Jim, H. S. L., McDonald, B. C., Nakamura, Z. M., Patel, S. K., Rentscher, K. E., Root, J., Saykin, A. J., Small, B. J., Van Dyk, K. M., Mandelblatt, J. S., & Carroll, J. E. (2022). Associations between longitudinal changes in sleep disturbance and depressive and anxiety symptoms during the COVID-19 virus pandemic among older women with and without breast cancer in the thinking and living with breast cancer study. *Cancer Medicine*, *11*(17), 3352-3363. https://doi.org/10.1002/cam4.4682

Boserup, B., McKenney, M., & Elkbuli, A. (2020). Disproportionate impact of COVID-19 pandemic on racial and ethnic minorities. *American Surgeon*, *86*(12), 1615-1622. https://doi.org/10.1177/0003134820973356

Calvo-Schimmel, A., Paul, S. M., Cooper, B. A., Shin, J., Harris, C., Oppegaard, K., Hammer, M. J., Cartwright, F., Conley, Y. P., Kober, K. M., Levine, J. D., & Miaskowski, C. (2022). Oncology outpatients with worse anxiety and sleep disturbance profiles are at increased risk for a higher symptom burden and poorer quality of life. *Cancer Nursing*. https://doi.org/10.1097/ncc.0000000000001139

Campbell-Sills, L., Forde, D. R., & Stein, M. B. (2009). Demographic and childhood environmental predictors of resilience in a community sample. *Journal of Psychiatric Research*, *43*(12), 1007-1012. https://doi.org/10.1016/j.jpsychires.2009.01.013

Campbell-Sills, L., & Stein, M. B. (2007). Psychometric analysis and refinement of the Connor-davidson Resilience Scale (CD-RISC): Validation of a 10-item measure of resilience. *Journal of Trauma and Stress*, *20*(6), 1019-1028. https://doi.org/10.1002/jts.20271

Celeux, G., & Soromenho, G. (1996). An entropy criterion for assessing the number of clusters in a mixture model. *Journal of Classification*, *13*(2), 195-212. https://doi.org/10.1007/BF01246098

Cenat, J. M., Blais-Rochette, C., Kokou-Kpolou, C. K., Noorishad, P. G., Mukunzi, J. N., McIntee, S. E., Dalexis, R. D., Goulet, M. A., & Labelle, P. R. (2021). Prevalence of symptoms of depression, anxiety, insomnia, posttraumatic stress disorder, and psychological distress among populations affected by the COVID-19 pandemic: A systematic review and meta-analysis. *Psychiatry Research*, *295*, 113599. https://doi.org/10.1016/j.psychres.2020.113599

Centers for Disease Control and Prevention. (2016). *About adult BMI, healthy weight*. Retrieved May 15, 2015 from http://www.cdc.gov/healthyweight/assing/bmi/adult_bmi/index.html

Cimprich, B., So, H., Ronis, D. L., & Trask, C. (2005). Pre-treatment factors related to cognitive functioning in women newly diagnosed with breast cancer. *Psychooncology*, *14*(1), 70-78. https://doi.org/10.1002/pon.821

Cimprich, B., Visovatti, M., & Ronis, D. L. (2011). The Attentional Function Index--a self-report cognitive measure. *Psychooncology*, *20*(2), 194-202. https://doi.org/10.1002/pon.1729

Ciuffreda, G., Cabanillas-Barea, S., Carrasco-Uribarren, A., Albarova-Corral, M. I., Arguello-Espinosa, M. I., & Marcen-Roman, Y. (2021). Factors associated with depression and anxiety in adults >/=60 years old during the COVID-19 pandemic: A systematic review. *International Journal of Environmental Research and Public Health*, *18*(22). https://doi.org/10.3390/ijerph182211859

Clifton, K., Gao, F., Jabbari, J., Van Aman, M., Dulle, P., Hanson, J., & Wildes, T. M. (2022). Loneliness, social isolation, and social support in older adults with active cancer during the COVID-19 pandemic. *Journal of Geriatric Oncology*, *13*(8), 1122-1131. https://doi.org/10.1016/j.jgo.2022.08.003

Cohen, S., & Janicki-Deverts, D. (2012). Who's stressed? Distributions of psychological stress in the United States in probability samples from 1983, . *Journal of Applied Social Psychology*, *42*(6), 1320-1334.

Cohen, S., Kamarck, T., & Mermelstein, R. (1983). A global measure of perceived stress. *Journal of Health and Social Behavior*, *24*(4), 385-396. https://www.ncbi.nlm.nih.gov/pubmed/6668417

Colomer-Lahiguera, S., Ribi, K., Dunnack, H. J., Cooley, M. E., Hammer, M. J., Miaskowski, C., & Eicher, M. (2021). Experiences of people affected by cancer during the outbreak of the COVID-19 pandemic: an exploratory qualitative analysis of public online forums. *Supportive Care in Cancer*, *29*(9), 4979-4985. https://doi.org/10.1007/s00520-021-06041-y

Craig, C. L., Marshall, A. L., Sjostrom, M., Bauman, A. E., Booth, M. L., Ainsworth, B. E., Pratt, M., Ekelund, U., Yngve, A., Sallis, J. F., & Oja, P. (2003). International physical activity questionnaire: 12-country reliability and validity. *Medicine & Science in Sports & Exercise*, *35*(8), 1381-1395. https://doi.org/10.1249/01.MSS.0000078924.61453.FB

Creamer, M., Bell, R., & Failla, S. (2003). Psychometric properties of the Impact of Event Scale - Revised. *Behavioral Research and Therapy*, *41*(12), 1489-1496. https://doi.org/10.1016/j.brat.2003.07.010

Daut, R. L., Cleeland, C. S., & Flanery, R. C. (1983). Development of the Wisconsin Brief Pain Questionnaire to assess pain in cancer and other diseases. *Pain*, *17*(2), 197-210. https://doi.org/10.1016/0304-3959(83)90143-4

Dhada, S., Stewart, D., Cheema, E., Hadi, M. A., & Paudyal, V. (2021). Cancer services during the COVID-19 pandemic: Systematic review of patient's and caregiver's experiences. *Cancer Management Research*, *13*, 5875-5887. https://doi.org/10.2147/CMAR.S318115

Doong, S. H., Dhruva, A., Dunn, L. B., West, C., Paul, S. M., Cooper, B. A., Elboim, C., Abrams, G., Merriman, J. D., Langford, D. J., Leutwyler, H., Baggott, C., Kober, K., Aouizerat, B. E., & Miaskowski, C. (2015). Associations between cytokine genes and a symptom cluster of pain, fatigue, sleep disturbance, and depression in patients prior to breast cancer surgery. *Biological Research in Nursing*, *17*(3), 237-247. https://doi.org/10.1177/1099800414550394

Fletcher, B. S., Paul, S. M., Dodd, M. J., Schumacher, K., West, C., Cooper, B., Lee, K., Aouizerat, B., Swift, P., Wara, W., & Miaskowski, C. A. (2008). Prevalence, severity, and impact of symptoms on female family caregivers of patients at the initiation of radiation therapy for prostate cancer. *Journal of Clinical Oncology*, *26*(4), 599-605. https://doi.org/10.1200/JCO.2007.12.2838

Franjic, D., Babic, D., Marijanovic, I., & Martinac, M. (2021). Association between resilience and quality of life in patients with colon cancer. *Psychiatria Danubina*, *33*(Suppl 13), 297-303. https://www.ncbi.nlm.nih.gov/pubmed/35150498

Gallagher, S., Bennett, K. M., & Roper, L. (2021). Loneliness and depression in patients with cancer during COVID-19. *Journal of Psychosocial Oncology*, *39*(3), 445-451. https://doi.org/10.1080/07347332.2020.1853653

George, M., Smith, A., Sabesan, S., & Ranmuthugala, G. (2021). Physical comorbidities and their relationship with cancer treatment and its outcomes in older adult populations: Systematic review. *JMIR Cancer*, *7*(4), e26425. https://doi.org/10.2196/26425

Giacco, D. (2023). Loneliness and mood disorders: consequence, cause and/or unholy alliance? *Current Opinions in Psychiatry*, *36*(1), 47-53. https://doi.org/10.1097/YCO.0000000000000832

Hallal, P. C., & Victora, C. G. (2004). Reliability and validity of the International Physical Activity Questionnaire (IPAQ). *Medicine & Science in Sports & Exercise*, *36*(3), 556. https://doi.org/10.1249/01.mss.0000117161.66394.07

Hammer, M. J., Cooper, B., Paul, S. M., Kober, K. M., Cartwright, F., Conley, Y. P., Wright, F., Levine, J. D., & Miaskowski, C. (2022). Identification of distinct symptom profiles in cancer patients using a pre-specified symptom cluster. *Journal of Pain and Symptom Management*, *64*(1), 17-27. https://doi.org/10.1016/j.jpainsymman.2022.03.007

Harden, K., Price, D. M., Mason, H., & Bigelow, A. (2020). COVID-19 shines a spotlight on the age-old problem of social isolation. *Journal of Hospice and Palliative Care Nursing*, *22*(6), 435-441. https://doi.org/10.1097/NJH.0000000000000693

Harris, P. A., Taylor, R., Minor, B. L., Elliott, V., Fernandez, M., O'Neal, L., McLeod, L., Delacqua, G., Delacqua, F., Kirby, J., Duda, S. N., & Consortium, R. E. (2019). The REDCap consortium: Building an international community of software platform partners. *Journal of Biomedical Informatics*, *95*, 103208. https://doi.org/10.1016/j.jbi.2019.103208

Hawkins, R. B., Charles, E. J., & Mehaffey, J. H. (2020). Socio-economic status and COVID-19-related cases and fatalities. *Public Health*, *189*, 129-134. https://doi.org/10.1016/j.puhe.2020.09.016

Hilbold, E., Bar, C., & Thum, T. (2023). COVID-19: Insights into long-term manifestations and lockdown impacts. *Journal of Sport and Health Science*. https://doi.org/10.1016/j.jshs.2023.02.006

Huang, V., Mackin, L., Kober, K. M., Paul, S. M., Cooper, B. A., Conley, Y. P., Hammer, M. J., Levine, J. D., & Miaskowski, C. (2022). Distinct sleep disturbance and cognitive dysfunction profiles in oncology outpatients receiving chemotherapy. *Supportive Care in Cancer*, *30*(11), 9243-9254. https://doi.org/10.1007/s00520-022-07350-6

Jamil, A., Syed, J., Kanwal, S., Ain, Q. U., Namroz, N., Gul, A., & Jamil, A. (2023). Loneliness and mental health related impacts of COVID-19: a narrative review. *International Journal of Adolescent Medicine and Health*, *35*(1), 21-30. https://doi.org/10.1515/ijamh-2022-0032

Jammu, A. S., Chasen, M. R., Lofters, A. K., & Bhargava, R. (2021). Systematic rapid living review of the impact of the COVID-19 pandemic on cancer survivors: update to August 27, 2020. *Supportive Care in Cancer*, *29*(6), 2841-2850. https://doi.org/10.1007/s00520-020-05908-w

Janelsins, M. C., Kesler, S. R., Ahles, T. A., & Morrow, G. R. (2014). Prevalence, mechanisms, and management of cancer-related cognitive impairment. *International Reviews in Psychiatry*, *26*(1), 102-113. https://doi.org/10.3109/09540261.2013.864260

Joyce, S., Shand, F., Tighe, J., Laurent, S. J., Bryant, R. A., & Harvey, S. B. (2018). Road to resilience: a systematic review and meta-analysis of resilience training programmes and interventions. *BMJ Open*, *8*(6), e017858. https://doi.org/10.1136/bmjopen-2017-017858

Karnofsky, D. (1977). *Performance scale*. Plenum Press.

Killgore, W. D. S., Cloonan, S. A., Taylor, E. C., Lucas, D. A., & Dailey, N. S. (2020). Loneliness during the first half-year of COVID-19 Lockdowns. *Psychiatry Research*, *294*, 113551. https://doi.org/10.1016/j.psychres.2020.113551

Knight, R. G., Chisholm, B. J., Marsh, N. V., & Godfrey, H. P. (1988). Some normative, reliability, and factor analytic data for the revised UCLA Loneliness Scale. *Journal of Clinical Psychology*, *44*(2), 203-206. https://doi.org/10.1002/1097-4679(198803)44:2<203::aid-jclp2270440218>3.0.co;2-5

Kotwal, A. A., Cenzer, I. S., Waite, L. J., Covinsky, K. E., Perissinotto, C. M., Boscardin, W. J., Hawkley, L. C., Dale, W., & Smith, A. K. (2021). The epidemiology of social isolation and loneliness among older adults during the last years of life. *Journal of the American Geriatrics Society*, *69*(11), 3081-3091. https://doi.org/10.1111/jgs.17366

Langford, D. J., Eaton, L., Kober, K. M., Paul, S. M., Cooper, B. A., Hammer, M. J., Conley, Y. P., Wright, F., Dunn, L. B., Levine, J. D., & Miaskowski, C. (2022). A high stress profile is associated with severe pain in oncology patients receiving chemotherapy. *European Journal of Oncology Nursing*, *58*, 102135. https://doi.org/10.1016/j.ejon.2022.102135

Lanza, S., Flaherty, BP, Collins, LM, editors. (2003). *Latent class and latent transition analysis* (Vol. 2). Hoboken, NJ: John Wiley & Sons, Inc.

Larson, E. A., Dalamaga, M., & Magkos, F. (2023). The role of exercise in obesity-related cancers: Current evidence and biological mechanisms. *Seminars in Cancer Biology*, *91*, 16-26. https://doi.org/10.1016/j.semcancer.2023.02.008

Lee, K. A., Hicks, G., & Nino-Murcia, G. (1991). Validity and reliability of a scale to assess fatigue. *Psychiatry Research*, *36*(3), 291-298. https://doi.org/10.1016/0165-1781(91)90027-m

Lin, Y., Bailey, D. E., Xiao, C., Hammer, M., Paul, S. M., Cooper, B. A., Conley, Y. P., Levine, J. D., Kober, K. M., & Miaskowski, C. (2022). Distinct co-occurring morning and evening fatigue profiles in patients with gastrointestinal cancers receiving chemotherapy. *Cancer Nursing*. https://doi.org/10.1097/NCC.0000000000001148

Llanos, A. A. M., Ashrafi, A., Ghosh, N., Tsui, J., Lin, Y., Fong, A. J., Ganesan, S., & Heckman, C. J. (2023). Evaluation of inequities in cancer treatment delay or discontinuation rollowing SARS-CoV-2 infection. *JAMA Network Open*, *6*(1), e2251165. https://doi.org/10.1001/jamanetworkopen.2022.51165

Ludolph, P., Kunzler, A. M., Stoffers-Winterling, J., Helmreich, I., & Lieb, K. (2019). Interventions to promote resilience in cancer patients. *Deutsches Arzteblatt International*, *51-52*(51-52), 865-872. https://doi.org/10.3238/arztebl.2019.0865

Macia, P., Barranco, M., Gorbena, S., & Iraurgi, I. (2020). Expression of resilience, coping and quality of life in people with cancer. *PLoS One*, *15*(7), e0236572. https://doi.org/10.1371/journal.pone.0236572

Mafi, A. R., Ghanbari Motlagh, A., & Azadeh, P. (2022). The impact of COVID-19 on cancer recurrence: A narrative review. *Archives of Iranian Medicine*, *25*(7), 450-455. https://doi.org/10.34172/aim.2022.74

Matthews, E. E., Janssen, D. W., Djalilova, D. M., & Berger, A. M. (2018). Effects of exercise on sleep in women with breast cancer: A systematic review. *Sleep Medicine Clinics*, *13*(3), 395-417. https://doi.org/10.1016/j.jsmc.2018.04.007

Mauri, D., Kamposioras, K., Tolia, M., Alongi, F., Tzachanis, D., International Oncology, P., & European Cancer Patient Coalition, c. (2020). Summary of international recommendations in 23 languages for patients with cancer during the COVID-19 pandemic. *Lancet Oncology*, *21*(6), 759-760. https://doi.org/10.1016/S1470-2045(20)30278-3

Mazor, M., Paul, S. M., Chesney, M. A., Chen, L. M., Smoot, B., Topp, K., Conley, Y. P., Levine, J. D., & Miaskowski, C. (2019). Perceived stress is associated with a higher symptom burden in cancer survivors. *Cancer*, *125*(24), 4509-4515. https://doi.org/10.1002/cncr.32477

Miaskowski, C., Cooper, B. A., Melisko, M., Chen, L. M., Mastick, J., West, C., Paul, S. M., Dunn, L. B., Schmidt, B. L., Hammer, M., Cartwright, F., Wright, F., Langford, D. J., Lee, K., & Aouizerat, B. E. (2014). Disease and treatment characteristics do not predict symptom occurrence profiles in oncology outpatients receiving chemotherapy. *Cancer*, *120*(15), 2371-2378. https://doi.org/10.1002/cncr.28699

Miaskowski, C., Cooper, B. A., Paul, S. M., Dodd, M., Lee, K., Aouizerat, B. E., West, C., Cho, M., & Bank, A. (2006). Subgroups of patients with cancer with different symptom experiences and quality-of-life outcomes: a cluster analysis. *Oncology Nursing Forum*, *33*(5), E79-89. https://doi.org/10.1188/06.ONF.E79-E89

Miaskowski, C., Paul, S. M., Mastick, J., Abrams, G., Topp, K., Smoot, B., Kober, K. M., Chesney, M., Mazor, M., Mausisa, G., Schumacher, M., Conley, Y. P., Sabes, J. H., Cheung, S., Wallhagen, M., & Levine, J. D. (2018). Associations between perceived stress and chemotherapy-induced peripheral neuropathy and otoxicity in adult cancer survivors. *Journal of Pain and Symptom Management*, *56*(1), 88-97. https://doi.org/10.1016/j.jpainsymman.2018.02.021

Miaskowski, C., Paul, S. M., Snowberg, K., Abbott, M., Borno, H., Chang, S., Chen, L. M., Cohen, B., Hammer, M. J., Kenfield, S. A., Kober, K. M., Levine, J. D., Pozzar, R., Rhoads, K. F., Van Blarigan, E. L., & Van Loon, K. (2020). Stress and symptom burden in oncology patients during the COVID-19 pandemic. *Journal of Pain and Symptom Management*, *60*(5), e25-e34. https://doi.org/10.1016/j.jpainsymman.2020.08.037

Montani, D., Savale, L., Noel, N., Meyrignac, O., Colle, R., Gasnier, M., Corruble, E., Beurnier, A., Jutant, E. M., Pham, T., Lecoq, A. L., Papon, J. F., Figueiredo, S., Harrois, A., Humbert, M., Monnet, X., & Group, C. S. (2022). Post-acute COVID-19 syndrome. *European Respiratory Revies*, *31*(163). https://doi.org/10.1183/16000617.0185-2021

Moraliyage, H., De Silva, D., Ranasinghe, W., Adikari, A., Alahakoon, D., Prasad, R., Lawrentschuk, N., & Bolton, D. (2021). Cancer in lockdown: Impact of the COVID-19 pandemic on patients with cancer. *Oncologist*, *26*(2), e342-e344. https://doi.org/10.1002/onco.13604

Morina, N., Ehring, T., & Priebe, S. (2013). Diagnostic utility of the impact of event scale-revised in two samples of survivors of war. *PLoS One*, *8*(12), e83916. https://doi.org/10.1371/journal.pone.0083916

Muthen, B., & Shedden, K. (1999). Finite mixture modeling with mixture outcomes using the EM algorithm. *Biometrics*, *55*(2), 463-469. https://doi.org/10.1111/j.0006-341x.1999.00463.x

Muthen, B. O. (2002). Beyond SEM: General latent variable modeling. *Behaviormetrika*, *29*(1), 81-117.

Muthen, L., Muthen, BO. (1989-2010b). *Mplus user's guide.* Los Angeles, CA: Author.

Nicholson, N. R., Feinn, R., Casey, E. A., & Dixon, J. (2020). Psychometric evaluation of the Social Isolation Scale in older adults. *Gerontologist*, *60*(7), e491-e501. https://doi.org/10.1093/geront/gnz083

Nylund, K. L., Asparouhov, T., & Muthén, B. O. (2007). Deciding on the number of classes in latent class analysis and growth mixture modeling: A Monte Carlo simulation study. *Structural Equation Modeling: A Multidisciplinary Journal*, *14*(4), 535-569. https://doi.org/10.1080/10705510701575396

Oppegaard, K., Harris, C. S., Shin, J., Paul, S. M., Cooper, B. A., Levine, J. D., Conley, Y. P., Hammer, M., Cartwright, F., Wright, F., Dunn, L., Kober, K. M., & Miaskowski, C. (2021). Anxiety profiles are associated with stress, resilience and symptom severity in outpatients receiving chemotherapy. *Supportive Care in Cancer*, *29*(12), 7825-7836. https://doi.org/10.1007/s00520-021-06372-w

Oppegaard, K., Shin, J., Harris, C. S., Schimmel, A., Paul, S. M., Cooper, B. A., Levine, J. D., Conley, Y. P., Hammer, M., Dunn, L., Kober, K. M., & Miaskowski, C. (2022). Higher stress and symptom severity are associated with worse depressive symptom profiles in patients receiving chemotherapy. *European Journal of Oncology Nursing*, *58*, 102031. https://doi.org/10.1016/j.ejon.2021.102031

Paice, J. A. (2022). Cancer pain during an epidemic and a pandemic. *Current Opinion in Supportive and Palliative Care*, *16*(2), 55-59. https://doi.org/10.1097/SPC.0000000000000594

Pietrabissa, G., & Simpson, S. G. (2020). Psychological consequences of ocial isolation during COVID-19 outbreak. *Frontiers in Psychology*, *11*, 2201. https://doi.org/10.3389/fpsyg.2020.02201

Pud, D., Ben Ami, S., Cooper, B. A., Aouizerat, B. E., Cohen, D., Radiano, R., Naveh, P., Nikkhou-Abeles, R., Hagbi, V., Kachta, O., Yaffe, A., & Miaskowski, C. (2008). The symptom experience of oncology outpatients has a different impact on quality-of-life outcomes. *Journal of Pain and Symptom Management*, *35*(2), 162-170. https://doi.org/10.1016/j.jpainsymman.2007.03.010

Quinn-Scoggins, H. D., Cannings-John, R., Moriarty, Y., Whitelock, V., Whitaker, K. L., Grozeva, D., Hughes, J., Townson, J., Osborne, K., Goddard, M., McCutchan, G. M., Waller, J., Robling, M., Hepburn, J., Moore, G., Gjini, A., & Brain, K. (2021). Cancer symptom experience and help-seeking behaviour during the COVID-19 pandemic in the UK: a cross-sectional population survey. *BMJ Open*, *11*(9), e053095. https://doi.org/10.1136/bmjopen-2021-053095

Radloff, L. S. (1977). The CES-D Scale: A self-report depression scale for research in the general population. *Applied Psychological Measurement*, *1*(3), 385-401.

Rentscher, K. E., Zhou, X., Small, B. J., Cohen, H. J., Dilawari, A. A., Patel, S. K., Bethea, T. N., Van Dyk, K. M., Nakamura, Z. M., Ahn, J., Zhai, W., Ahles, T. A., Jim, H. S. L., McDonald, B. C., Saykin, A. J., Root, J. C., Graham, D. M. A., Carroll, J. E., & Mandelblatt, J. S. (2021). Loneliness and mental health during the COVID-19 pandemic in older breast cancer survivors and noncancer controls. *Cancer*, *127*(19), 3671-3679. https://doi.org/10.1002/cncr.33687

Russell, D., Peplau, L. A., & Cutrona, C. E. (1980). The revised UCLA Loneliness Scale: concurrent and discriminant validity evidence. *Journal of Personality and Social Psychology*, *39*(3), 472-480. https://doi.org/10.1037//0022-3514.39.3.472

Russell, D., Peplau, L. A., & Ferguson, M. L. (1978). Developing a measure of loneliness. *Journal of Personality Assessment*, *42*(3), 290-294. https://doi.org/10.1207/s15327752jpa4203_11

Russell, D. W. (1996). UCLA Loneliness Scale (Version 3): reliability, validity, and factor structure. *Journal of Personality Assessment*, *66*(1), 20-40. https://doi.org/10.1207/s15327752jpa6601_2

Saini, K. S., Tagliamento, M., Lambertini, M., McNally, R., Romano, M., Leone, M., Curigliano, G., & de Azambuja, E. (2020). Mortality in patients with cancer and coronavirus disease 2019: A systematic review and pooled analysis of 52 studies. *European Journal of Cancer*, *139*, 43-50. https://doi.org/10.1016/j.ejca.2020.08.011

Salari, N., Hosseinian-Far, A., Jalali, R., Vaisi-Raygani, A., Rasoulpoor, S., Mohammadi, M., Rasoulpoor, S., & Khaledi-Paveh, B. (2020). Prevalence of stress, anxiety, depression among the general population during the COVID-19 pandemic: a systematic review and meta-analysis. *Global Health*, *16*(1), 57. https://doi.org/10.1186/s12992-020-00589-w

Sangha, O., Stucki, G., Liang, M. H., Fossel, A. H., & Katz, J. N. (2003). The Self-Administered Comorbidity Questionnaire: a new method to assess comorbidity for clinical and health services research. *Arthritis and Rheumatism*, *49*(2), 156-163. https://doi.org/10.1002/art.10993

Shin, J., Harris, C., Oppegaard, K., Kober, K. M., Paul, S. M., Cooper, B. A., Hammer, M., Conley, Y., Levine, J. D., & Miaskowski, C. (2022). Worst pain severity profiles of oncology patients are associated with significant stress and multiple co-occurring symptoms. *Journal of Pain*, *23*(1), 74-88. https://doi.org/10.1016/j.jpain.2021.07.001

Singh, S., Fletcher, G. G., Yao, X., & Sussman, J. (2021). Virtual care in patients with cancer: A systematic review. *Current Oncology*, *28*(5), 3488-3506. https://doi.org/10.3390/curroncol28050301

Spielberger, C. G., Gorsuch, R. L., Suchene, R., Vagg, P. R., & Jacobs, G. A. (1983). *Manual for the State-Anxiety (Form Y): Self Evaluation Questionnaire*. Consulting Psychologists Press.

Sprangers, M. A., & Schwartz, C. E. (1999). The challenge of response shift for quality-of-life-based clinical oncology research. *Annals of Oncology*, *10*(7), 747-749. https://doi.org/10.1023/a:1008305523548

Stacker, T., Kober, K. M., Dunn, L., Viele, C., Paul, S. M., Hammer, M., Conley, Y. P., Levine, J. D., & Miaskowski, C. (2023). Associations between demographic, clinical, and symptom characteristics and stress in oncology patients receiving chemotherapy. *Cancer Nursing*, *46*(1), E62-E69. https://doi.org/10.1097/NCC.0000000000001069

Su, Y., Rao, W., Li, M., Caron, G., D'Arcy, C., & Meng, X. (2022). Prevalence of loneliness and social isolation among older adults during the COVID-19 pandemic: A systematic review and meta-analysis. *International Psychogeriatrics*, 1-13. https://doi.org/10.1017/S1041610222000199

Tamura, S. (2021). Factors related to resilience, anxiety/depression, and quality of life in patients with colorectal cancer undergoing chemotherapy in Japan. *Asian Pacific Journal of Oncology Nursing*, *8*(4), 393-402. https://doi.org/10.4103/apjon.apjon-2099

Tamura, S., Suzuki, K., Ito, Y., & Fukawa, A. (2021). Factors related to the resilience and mental health of adult cancer patients: a systematic review. *Supportive Care in Cancer*, *29*(7), 3471-3486. https://doi.org/10.1007/s00520-020-05943-7

van den Beuken-van Everdingen, M. H., Hochstenbach, L. M., Joosten, E. A., Tjan-Heijnen, V. C., & Janssen, D. J. (2016). Update on prevalence of pain in patients with cancer: Systematic review and meta-analysis. *Journal of Pain and Symptom Management*, *51*(6), 1070-1090 e1079. https://doi.org/10.1016/j.jpainsymman.2015.12.340

Venkatesulu, B. P., Chandrasekar, V. T., Girdhar, P., Advani, P., Sharma, A., Elumalai, T., Hsieh, C. E., Elghazawy, H. I., Verma, V., & Krishnan, S. (2021). A systematic review and meta-analysis of cancer patients affected by a novel coronavirus. *JNCI Cancer Spectrum*, *5*(2), pkaa102. https://doi.org/10.1093/jncics/pkaa102

Vermunt, J., & Magidson, J. (2002). Latent Class Cluster Analyses. In. New York, NY: Cambridge University Press.

Weiss, D. S., & Marmar, C. R. (1997). *The Impact of Event Scale - Revised*. Guilford Press.

Wright, F., Hammer, M., Paul, S. M., Aouizerat, B. E., Kober, K. M., Conley, Y. P., Cooper, B. A., Dunn, L. B., Levine, J. D., G, D. E. M., & Miaskowski, C. (2017). Inflammatory pathway genes associated with inter-individual variability in the trajectories of morning and evening fatigue in patients receiving chemotherapy. *Cytokine*, *91*, 187-210. https://doi.org/10.1016/j.cyto.2016.12.023

Zhang, H., Zhao, Q., Cao, P., & Ren, G. (2017). Resilience and quality of life: Exploring the mediator role of social support in patients with breast cancer. *Medical Science Monitor*, *23*, 5969-5979. https://doi.org/10.12659/msm.907730

Zhang, Y. B., Zhong, X. M., Han, N., Tang, H., Wang, S. Y., & Lin, W. X. (2023). Effectiveness of exercise interventions in the management of cancer-related fatigue: a systematic review of systematic reviews. *Supportive Care in Cancer*, *31*(3), 153. https://doi.org/10.1007/s00520-023-07619-4

Zhu, C., Ma, H., He, A., Li, Y., He, C., & Xia, Y. (2022). Exercise in cancer prevention and anticancer therapy: Efficacy, molecular mechanisms and clinical information. *Cancer Letter*, *544*, 215814. https://doi.org/10.1016/j.canlet.2022.215814

Table 1 – Latent Profile Solutions and Fit Indices for One through Five Classes for Nine Co-Occurring Symptoms During COVID-19

Model	LL	AIC	BIC	Entropy	VLMR
1 Class	-28928.98	57895.96	57991.78	n/a	n/a
2 Class	-27267.95	54595.90	54747.20	0.88	3322.05‡
3 Class	-26670.04	53422.08	53628.85	0.87	1195.82‡
4 Class[a]	-26428.65	52961.29	53223.54	0.86	482.79*
5 Class	-26312.04	52750.08	53067.80	0.84	NS

Baseline entropy and VLMR are not applicable for the one-class solution

*p < .005; ‡p < .00005

[a]The 4-class solution was selected because the BIC for that solution was lower than the BIC for the 3-class solution. In addition, the VLMR was significant for the 4-class solution, indicating that four classes fit the data better than three classes. Although the BIC was smaller for the 5-class than for the 4-class solution, the VLMR for 5-classes was not significant, indicating that too many classes had been extracted.

Abbreviations: AIC = Akaike's Information Criterion; BIC = Bayesian Information Criterion; LL = log-likelihood; n/a = not applicable; NS = not significant, VLMR = Vuong-Lo-Mendell-Rubin likelihood ratio test for the K vs. K-1 model

Table 2 – Estimated Means for Each of the Symptom Severity Scores for the Four Latent Classes

Symptoms[a]	None (0) 28.5% (n=327)	Low (1) 37.7% (n=432)	High (2) 25.9% (n=296)	Very High (3) 7.9% (n=90)
	Estimated Means	Estimated Means	Estimated Means	Estimated Means
Depression (≥16.0)	5.115	12.577	23.322	37.628
State anxiety (≥32.2)	24.393	31.995	45.998	61.293
Cognitive function (<5 = low, 5 to 7.5 = moderate, >7.5 = high)	8.480	6.924	5.414	3.538
Morning fatigue (≥3.2)	0.994	3.417	5.408	7.205
Evening fatigue (≥5.6)	3.746	5.455	6.295	7.186
Morning energy (≤6.2)	7.495	4.459	3.475	1.949
Evening energy (≤3.5)	4.028	2.692	2.581	1.645
Sleep disturbance (≥43.0)	30.837	49.765	65.941	79.480
Any pain	0.385	0.652	0.768	0.857
For patients with pain – worst pain intensity Mild – 1 to 3 Moderate – 4 to 6 Severe - ≥7	5.732	6.093	6.958	7.969

[a]Clinically meaningful cutpoints are listed in parentheses for each of the measures when available.

Table 3 – Differences in Demographic and Clinical Characteristics Among the Symptom Latent Classes

Demographic Characteristic	None (0) 28.5% (n=327)	Low (1) 37.7% (n=432)	High (2) 25.9% (n=296)	Very High (3) 7.9% (n=90)	Statistics
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	
Age (years)	66.6 (9.9)	62.2 (11.2)	59.3 (11.5)	57.2 (11.3)	F = 30.19, p<0.001 0 > 1 > 2 and 3
Number of people in your household including yourself	2.0 (0.9)	2.1 (1.0)	2.3 (1.2)	2.1 (1.2)	F = 3.10, p=0.026 0 < 2
Total metabolic equivalents	3845.1 (3614.1)	2909.6 (2976.2)	2630.5 (2835.7)	2356.7 (3288.4)	KW = 39.15, p<0.001 0 > 1, 2, and 3; 1 > 3
	% (n)	% (n)	% (n)	% (n)	
Female (% yes)	74.7 (239)	85.7 (365)	89.0 (259)	92.1 (82)	X^2 = 31.22, p<0.001 0 < 1, 2, and 3
Living arrangements					
Private home or apartment	99.1 (323)	98.8 (426)	100.0 (295)	98.9 (89)	X^2 = 4.50, p=0.609
Assisted living facility	0.0 (0)	0.2 (1)	0.0 (0)	0.0 (0)	
Other	0.9 (3)	0.9 (4)	0.0 (0)	1.1 (1)	
Lives alone (% yes)	23.9 (78)	23.7 (101)	22.3 (66)	33.7 (30)	X^2 = 5.06, p=0.167
Married/partnered (% yes)	70.9 (231)	67.4 (291)	67.8 (200)	55.6 (50)	X^2 = 7.55, p=0.056
Race/ethnicity					
White	85.0 (278)	87.2 (376)	84.5 (250)	74.4 (67)	X^2 = 9.55, p=0.023 1 > 3
Non-White	15.0 (49)	12.8 (55)	15.5 (46)	25.6 (23)	
Highest level of education					
Grade school	0.6 (2)	0.2 (1)	0.7 (2)	0.0 (0)	KW = 14.25, p=0.003 0, 1, and 2 > 3
High school	3.1 (10)	2.3 (10)	3.1 (9)	6.7 (6)	
Some college	15.3 (50)	15.2 (65)	14.2 (42)	29.2 (26)	
College graduate	22.9 (75)	23.8 (102)	27.8 (82)	22.5 (20)	
Some graduate school	10.4 (34)	9.1 (39)	10.2 (30)	9.0 (8)	
Advanced degree	47.7 (156)	49.4 (212)	44.1 (130)	32.6 (29)	
Currently employed (% yes)	35.9 (117)	49.0 (210)	45.8 (135)	40.0 (36)	X^2 = 13.90 p=0.003 0 < 1
Annual household income					
<$20,000	2.3 (6)	2.0 (7)	5.3 (13)	11.7 (9)	KW = 27.19, p<0.001 0, 1, and 2 > 3
$20,000 to $59,000	14.7 (38)	17.9 (63)	18.9 (46)	32.5 (25)	
$60,000 to $100,000	24.0 (62)	23.0 (81)	22.1 (54)	23.4 (18)	
>$100,000	58.9 (152)	57.1 (201)	53.7 (131)	32.5 (25)	
Level of exercise					
Low	15.9 (52)	22.5 (97)	30.4 (90)	45.6 (41)	KW = 34.96, p<0.001 0 > 1, 2, and 3; 1 > 3
Moderate	36.7 (120)	41.4 (179)	36.5 (108)	25.6 (23)	
High	47.4 (155)	36.1 (156)	33.1 (99)	28.9 (26)	

Abbreviations: kg = kilograms, KW = Kruskal Wallis, m^2 = meters squared, NS = not significant, SD = standard deviation

Clinical Characteristic	None (0) 28.5% (n=327)	Low (1) 37.7% (n=432)	High (2) 25.9% (n=296)	Very High (3) 7.9% (n=90)	Statistics
	% (n)	% (n)	% (n)	% (n)	
Chronic conditions (% yes)					
Heart disease	9.0 (29)	11.8 (50)	13.1 (38)	11.1 (10)	$X^2 = 2.73$, p=0.435
High blood pressure	33.6 (109)	32.5 (140)	32.2 (94)	33.3 (30)	$X^2 = 0.18$, p=0.980
Lung disease	4.7 (15)	6.1 (26)	5.5 (16)	9.1 (8)	$X^2 = 2.67$, p=0.446
Diabetes	5.6 (18)	6.1 (26)	7.5 (22)	8.0 (7)	$X^2 = 1.37$, p=0.713
Ulcer or stomach disease	1.9 (6)	4.5 (19)	6.2 (18)	6.8 (6)	$X^2 = 8.55$, p=0.036 0 < 2
Kidney disease	3.1 (10)	3.1 (13)	2.1 (6)	4.5 (4)	$X^2 = 1.64$, p=0.650
Liver disease	2.8 (9)	2.2 (9)	3.8 (11)	2.3 (2)	$X^2 = 1.80$, p=0.616
Anemia or blood disease	5.6 (18)	9.4 (39)	9.3 (27)	12.2 (11)	$X^2 = 5.75$, p=0.124
Depression	6.3 (20)	20.0 (84)	43.6 (126)	77.5 (69)	$X^2 = 237.42$, p<0.001 0 <1 < 2 < 3
Osteoarthritis	26.0 (84)	27.8 (118)	32.5 (95)	33.3 (30)	$X^2 = 4.28$, p=0.233
Back pain	19.8 (63)	32.4 (137)	39.9 (117)	57.8 (52)	$X^2 = 56.58$, p<0.001 0 < 1 and 2 < 3
Rheumatoid arthritis	1.9 (6)	2.9 (12)	4.3 (12)	8.4 (7)	$X^2 = 9.61$, p=0.022 0 < 3
Cancer diagnosis (% yes)					$X^2 = 64.35$, p<0.001
Breast	58.9 (186)	68.0 (291)	79.2 (232)	72.7 (64)	0 and 1 < 2
Gastrointestinal	5.1 (16)	4.9 (21)	2.0 (6)	1.1 (1)	NS
Head and neck	0.9 (3)	0.9 (4)	1.4 (4)	1.1 (1)	NS
Multiple myeloma	2.5 (8)	2.1 (9)	2.0 (6)	0.0 (0)	NS
Leukemia	1.3 (4)	1.2 (5)	1.4 (4)	3.4 (3)	NS
Lung	0.9 (3)	0.7 (3)	0.3 (1)	0.0 (0)	NS
Malignant melanoma	0.6 (2)	0.2 (1)	0.0 (0)	2.3 (2)	NS
Lymphoma	1.3 (4)	2.6 (11)	0.3 (1)	0.0 (0)	NS
Gynecological	1.9 (6)	2.1 (9)	1.0 (3)	4.5 (4)	NS
Prostate	9.8 (31)	6.1 (26)	4.4 (13)	2.3 (2)	NS
Brain	0.6 (2)	0.2 (1)	0.3 (1)	0.0 (0)	NS
Multiple or other	16.1 (51)	11.0 (47)	7.5 (22)	12.5 (11)	0 > 2
Presence of metastatic disease (% yes)	23.6 (74)	26.8 (110)	28.4 (80)	40.5 (34)	$X^2 = 9.65$, p=0.022 0 < 3
Currently receiving cancer treatment (% yes)	36.1 (118)	44.2 (191)	50.0 (148)	50.0 (45)	$X^2 = 13.96$, p=0.003 0 < 2
Tested for COVID-19 No Yes and tested negative Yes and tested positive Yes and prefer not to report my results	 60.6 (197) 37.5 (122) 1.5 (5) 0.3 (1)	 58.0 (250) 40.4 (174) 1.4 (6) 0.2 (1)	 62.9 (183) 36.1 (105) 1.0 (3) 0.0 (0)	 48.9 (44) 47.6 (42) 3.3 (3) 1.1 (1)	$X^2 = 10.62$, p=0.303

Clinical Characteristic	None (0) 28.5% (n=327)	Low (1) 37.7% (n=432)	High (2) 25.9% (n=296)	Very High (3) 7.9% (n=90)	Statistics
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	
Body mass index (kg/m^2)	26.0 (5.2)	26.8 (5.7)	27.4 (6.1)	29.9 (8.2)	F = 10.54, p<0.001 0, 1, and 2 < 3; 0 < 2
Karnofsky Performance Status score	96.3 (7.0)	91.5 (8.4)	87.8 (11.4)	78.8 (13.7)	F = 95.90, p<0.001 0 > 1 > 2 > 3
Number of comorbidities	1.5 (1.3)	2.0 (1.5)	2.4 (1.7)	3.1 (1.8)	F = 33.86, p<0.001 0 < 1 < 2 < 3
Self-administered Comorbidity Questionnaire score	2.8 (2.7)	3.9 (3.3)	5.0 (3.9)	7.5 (4.4)	F = 55.05, p<0.001 0 < 1 < 2 < 3
Time since cancer diagnosis (years)	9.9 (8.9)	8.4 (7.5)	7.5 (6.9)	8.3 (8.4)	KW = 11.68, p=.009 0 > 2
Time since diagnosis (median)	7.66	6.11	5.26	5.26	
Number of previous cancer treatments	2.5 (1.2)	2.7 (1.2)	2.9 (1.2)	2.6 (1.3)	F = 5.35, p=0.001 0 and 1 < 2
Number of current cancer treatments	0.4 (0.6)	0.5 (0.7)	0.6 (0.7)	0.6 (0.7)	F = 4.91, p=0.002 0 < 2
Number of metastatic sites[a]	0.3 (0.6)	0.3 (0.6)	0.4 (0.7)	0.6 (1.0)	F = 4.09, p=0.007 0, 1, and 2 < 3

[a]Total number of metastatic sites evaluated was 9.

Table 4 – Differences in Stress and Resilience Scores Among the Symptom Latent Classes

Measures[a]	None (0) 28.5% (n=327)	Low (1) 37.7% (n=432)	High (2) 25.9% (n=296)	Very High (3) 7.9% (n=90)	Statistics
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	
Impact of Event Scale-Revised ≥24 partial PTSD symptoms ≥33 probable PTSD	8.6 (8.3)	16.6 (10.6)	28.7 (14.0)	44.0 (18.4)	F = 288.20, p<0.001 0 < 1 < 2 < 3
Perceived Stress Scale (0 to 40)	7.7 (4.7)	13.5 (5.1)	20.4 (5.0)	27.3 (5.4)	F = 543.24, p<0.001 0 < 1 < 2 < 3
Social Isolation Scale 10 to 15 – Risk for social isolation ≤9 – Social isolation	24.4 (3.6)	23.1 (3.8)	20.8 (4.0)	17.1 (4.1)	F = 110.14, p<0.001 0 > 1 > 2 > 3
UCLA Loneliness Scale (≥36) 36-49 - Moderate 50 to 64 - Moderately high ≥65 - High	31.1 (8.4)	37.0 (9.6)	45.8 (10.6)	57.5 (11.3)	F = 237.07, p<0.001 0 < 1 < 2 <3
Connor Davidson Resilience Scale (31.8 (±5.4) – Normative score for the United States population)	34.3 (4.8)	30.4 (5.1)	26.4 (5.7)	21.5 (7.1)	F = 189.93, p<0.001 0 > 1 > 2 > 3

Abbreviation: PTSD = Post-traumatic Stress Disorder, SD = standard deviation, UCLA – University of California, Los Angeles

[a]Clinically meaningful cutpoints are provided for each scale when available

Table 5 – Characteristics Associated with Membership in the Other Three Symptom Latent Classes Compared to the None Class

Characteristic	Low	High	Very High
Demographic Characteristics			
More likely to be younger	■	■	■
More likely to be female	■	■	■
Lower level of education			■
More likely to be employed	■		
Higher number of people in household		■	
Lower annual household income			■
Lower level of total metabolic equivalents	■	■	■
Lower level of exercise	■	■	■
Clinical Characteristics			
Higher body mass index		■	■
Lower functional status	■	■	■
Higher number of comorbidities	■	■	■
Higher level of comorbidity	■	■	■
Fewer years since diagnosis		■	
Higher number of previous cancer treatments		■	
Higher number of current cancer treatments		■	
Higher number of metastatic sites			■
More likely to self-report ulcer or stomach disease		■	
More likely to self-report depression	■	■	■
More likely to self-report back pain	■	■	■
More likely to report rheumatoid arthritis			■
More likely to report breast cancer		■	
Less likely to report multiple or other cancer diagnoses		■	
More likely to report metastatic disease			■
More likely to report receiving current cancer treatment		■	
Stress Characteristics			
Higher Impact of Event Scale-Revised total score	■	■	■
Higher Perceived Stress Scale score	■	■	■
Lower Social Isolation Scale score[b]	■	■	■
Higher UCLA Loneliness Scale score	■	■	■
Lower Connor Davidson Resilience Scale score	■	■	■

Abbreviations: UCLA – University of California, Los Angeles

[a]Comparisons done with the None Class

[b]Lower Social Isolation Scale score indicates a higher level of social isolation.

■ – Indicates the presence of the risk factor compared to the None Class

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