

UCSF

UC San Francisco Electronic Theses and Dissertations

Title

Worse Morning Energy Profiles Are Associated with Significant Levels of Stress and Decrements in Resilience in Patients Receiving Chemotherapy

Permalink

<https://escholarship.org/uc/item/7220d42r>

Author

Shelley, Alexandra Elane

Publication Date

2024

Supplemental Material

<https://escholarship.org/uc/item/7220d42r#supplemental>

Peer reviewed|Thesis/dissertation

Worse Morning Energy Profiles Are Associated with Significant Levels of Stress and
Decrements in Resilience in Patients Receiving Chemotherapy

by
Alexandra Shelley

THESIS

Submitted in partial satisfaction of the requirements for degree of
MASTER OF SCIENCE

in

Nursing

in the

GRADUATE DIVISION

of the

UNIVERSITY OF CALIFORNIA, SAN FRANCISCO

Approved:

DocuSigned by:

Christine Miaskowski

Christine Miaskowski

4058DA2CA6554BB...

Chair

DocuSigned by:

Astrid Block

Astrid Block

DocuSigned by:

Sueann Mark

Sueann Mark

7BEF7AA80D17483...

Committee Members

Copyright 2024

by

Alexandra Shelley

Acknowledgments

I express my deepest gratitude to my thesis advisor, Dr. Christine Miaskowski, for her unconditional support, guidance, and encouragement throughout this journey. Her expertise and insightful feedback have been invaluable, and her belief in my potential has inspired me to strive for excellence. Without her dedicated mentorship, this thesis would not have been possible.

I also want to thank Astrid Block and Sueann Mark for serving on my thesis committee. Their time, effort, and thoughtful critiques have significantly enriched this research. Their diverse perspectives and constructive suggestions have been instrumental in shaping my graduate school experience and master's thesis outcome, and I sincerely appreciate their commitment and support.

I am profoundly grateful to my family and friends for their unwavering support throughout my graduate school experience. Their love and encouragement have been a constant source of strength and motivation. I also would like to thank my partner, Joseph Hefta, for his unconditional love and support. Finally, I thank my Adult-Gerontology Clinical Nurse Specialist cohort for their camaraderie and support through every class. Our cohort's friendships and collaborative spirit have significantly contributed to my academic journey, making it exciting and enjoyable. Thank you all for being part of this significant milestone in my educational career.

Worse Morning Energy Profiles Are Associated with Significant Levels of Stress and
Decrements in Resilience in Patients Receiving Chemotherapy

Alexandra Shelley

Abstract

Background: Evidence suggests that lower levels of morning energy are associated with higher levels of stress and lower levels of resilience in patients receiving chemotherapy. **Purpose:** Study purposes were to identify subgroups of patients with distinct morning energy profiles; evaluate for differences among the profiles in demographic and clinical characteristics, as well as measures of stress, resilience, and coping. **Methods:** A total of 1,343 outpatients receiving chemotherapy completed a demographic questionnaire and measures of global, cancer-related, and cumulative life stress, and resilience at study enrollment. Morning energy was assessed using the Lee Fatigue Scale at six time points over two cycles of chemotherapy. **Results:** Latent profile analysis was used to identify subgroups of patients with distinct morning energy profiles. Three morning energy profiles were identified (i.e., High (17.3%), Low (60.3%), Very Low (22.4%)). Compared to High class, the other two morning energy classes were less likely to be employed; had a lower functional status and a higher comorbidity burden; and were more likely to self-report depression and back pain. For all three types of stress, significant differences were found among the three classes with scores that demonstrated a dose response effect (i.e., High < Low < Very Low; as decrements in morning energy increased, stress scores increased). Compared to High class, Very Low class reported higher rates of physical and sexual abuse. The resilience scores exhibited a dose response effect as well (i.e., High > Low > Very Low). Patients with the two worst energy profiles reported a higher use of disengagement coping strategies. **Conclusions/Implications for Practice:** Findings highlight the complex relationships among decrements in morning energy, various types of stress, resilience, and coping in patients undergoing chemotherapy. Clinicians need to assess for stress and adverse

childhood experiences to develop individualized management plans to increase patients' energy levels.

Table of Contents

INTRODUCTION.....	1
Demographic and clinical risk factors	1
Stress, resilience, and coping	2
METHODS	3
Patients and Settings.....	3
Instruments.....	3
Study Procedures.....	6
Data Analysis	6
RESULTS.....	7
Latent Class Solution.....	7
Demographic and Clinical Characteristics	7
Stress and Resilience.....	8
Occurrence of Life Stressors.....	8
Effects of Various Stressors.....	8
Coping Strategies.....	9
DISCUSSION.....	9
Demographic and Clinical Risk Factors.....	10
Stress	13
Resilience	14

Coping.....	14
Limitations	15
Implications for Clinical Practice and Research	15
REFERENCES.....	31

Table of Figures

Figure 1 – Trajectories of morning energy for the three latent classes.....	17
--	----

List of Tables

Table 1 – Latent Profile Solutions and Fit Indices for One through Four Classes for Morning Energy	18
Table 2 – Differences in Demographic and Clinical Characteristics Among the Morning Energy Classes at Enrollment.....	19
Table 3 – Differences in Stress and Resilience Measures Among the Morning Energy Classes at Enrollment	24
Table 4 – Differences Among the Morning Energy Classes in the Percentage of Patients Exposed to Specific Stressors at Enrollment	24
Table 5 – Differences Among the Morning Energy Classes in the Effect of Stressor on Life In The Past Year	26
Table 6 – Differences Among the Morning Energy Classes in the Brief COPE Subscale Scores at Enrollment.....	28
Table 7 – Characteristics Associated with Membership in the Low and Very Low Morning Energy Latent Classes	29

List of Abbreviations

ACE – Adverse Childhood Events

AIC – Akaike’s Information Criterion

AUDIT – Alcohol Use Disorder Identification Test

BMI – Body Mass Index

BIC – Bayesian Information Criterion

CDRS – Connor-Davidson Resilience Scale

HIV – Human Immunodeficiency Virus

HPA – Hypothalamic-Pituitary-Adrenal

IES-R – Impact of Event Scale-Revised

KPS – Karnofsky Performance Status

LFS – Lee Fatigue Scale

LPA – Latent Profile Analysis

LSC-R – Life Stressor Checklist-Revised

NRS – Numeric Rating Scale

NY – New York

PMS – Profile of Mood States

PTSD – Post-Traumatic Stress Disorder

PSS – Perceived Stress Scale

QOL – Quality of Life

US – United States

VLMR – Vuong-Lo-Mendell-Rubin

LL – Log-likelihood

N/a – Not Applicable

Ns – Not Significant

INTRODUCTION

Chemotherapy is a common treatment that mitigates disease progression and improves survival in patients with cancer. However, this treatment is associated with numerous symptoms. While fatigue is one of the most common symptoms associated with chemotherapy,¹ recent evidence demonstrates that energy is a distinct but related symptom.²⁻⁴ Support for research on energy as a distinct symptom came from studies that used measures that assessed both symptoms in patients with cancer,⁵ as well as in the general population.^{6, 7} For example, the Profile of Mood States (POMS) contains subscales that assess fatigue-inertia and vigor-activity (i.e., energy).⁸ Based on qualitative analyses, energy is defined as “an individual’s potential to perform mental and physical activities”.^{2, 3} In patients with cancer, decrements in energy levels have a negative impact their ability to carry out daily activities and adversely effects their overall quality of life (QOL).⁹

Recent evidence from our research team suggests that diurnal variations exist in energy levels with higher and lower levels reported in the morning and evening, respectively.^{10, 11} However, limited information exists on modifiable risk factors for decrements in morning or evening energy in patients receiving chemotherapy. Because of its potential negative impact on patients’ ability to perform daily activities, this study evaluated for inter-individual variability in decrements in morning energy.

Demographic and clinical risk factors

In a study of patients undergoing radiation therapy and their family caregivers, that used latent variable modeling to identify high risk groups,¹⁰ 50.8% of the participants reported low levels of morning energy over a period of six months. Participants in the low morning energy class were younger and more likely to be female, not married or partnered, and self-reported their race/ethnicity as Black. In addition, these individuals had a higher number of comorbidities and a lower functional status. In another study of oncology outpatients receiving chemotherapy,

that used hierarchical linear modeling,¹¹ risk factors for lower levels of morning energy included: living alone, having childcare responsibilities, not exercising on a regular basis, having a higher body mass index (BMI), having a lower functional status, and having lower hemoglobin levels. However, no studies have evaluated for decrements in morning energy in a sample of oncology patients receiving chemotherapy using latent variable modeling. This analytic approach allows for the identification of subgroups of patients with distinct morning energy profiles, as well as the determination of modifiable and non-modifiable risk factors.

Stress, resilience, and coping

One potential modifiable risk factor for decrements in energy in patients with cancer is unrelieved stress. In addition to everyday stress (i.e., global stress), cancer-related stress is experienced by most patients following a cancer diagnosis and subsequent treatments.¹²⁻¹⁴ Equally important, evidence suggests that higher levels of cumulative life stress, including adverse childhood experiences (ACEs) are associated with increases in fatigue,¹⁵ pain,¹⁶ depression,^{17, 18} and anxiety.¹⁹ However, no studies have evaluated for associations between stress and decrements in morning energy in patients receiving chemotherapy. Of note, in a study of post-menopausal women, that assessed levels of energy using the vitality scale of the Medical Outcomes Study-Short Form 36 and the vigor scale of the POMS,²⁰ higher scores on the Perceived Stress Scale (PSS; i.e., a measure of global stress) were associated with lower levels of vitality but not vigor.

Similar to stress, lower levels of resilience and the use of less than optimal coping strategies are potential risk factors that can be changed to improve patients' level of energy. Enhancing patients' level of resilience (defined as one's ability to respond to and/or adapt to stress²¹), as well as the use of more engagement type coping strategies, may decrease patients' level of stress with associated increases in energy. However, this hypothesis warrants investigation.

Given the paucity of research on the relationships between decrements in morning energy and stress, resilience, and coping, the purposes of this study, in a sample of patients receiving chemotherapy (n=1343), were to identify subgroups of patients with distinct morning energy profiles and evaluate for differences in demographic and clinical characteristics, as well as in levels of stress (i.e., global stress, cancer-related stress, and cumulative life stress), resilience, and coping. We hypothesized that patients with lower levels of morning energy would report higher levels of all three types of stress, lower levels of resilience, and use more disengagement type coping strategies.

METHODS

Patients and Settings

This longitudinal study is described in detail elsewhere.²² Eligible patients were ≥18 years of age; had a diagnosis of breast, gastrointestinal, gynecological, or lung cancer; had received chemotherapy within the preceding four weeks; were scheduled to receive at least two additional cycles of chemotherapy; were able to read, write, and understand English; and gave written informed consent. Patients were recruited from two Comprehensive Cancer Centers, one Veteran's Affairs hospital, and four community-based oncology programs. A total of 2234 patients were approached and 1343 consented to participate (60.1% response rate). The major reason for refusal was being overwhelmed with their cancer treatment.

Instruments

Demographic and clinical characteristics

Patients completed a demographic questionnaire, Karnofsky Performance Status (KPS) scale,²³ Alcohol Use Disorders Identification Test (AUDIT),²⁴ and Self-Administered Comorbidity Questionnaire (SCQ).²⁵ The MAX-2 score was used to evaluate the toxicity of the chemotherapy regimen.²⁶ Medical records were reviewed for disease and treatment information.

Morning Energy Measure

The 18-item Lee Fatigue Scale (LFS) was designed to assess physical fatigue and energy.²⁷ Each item was rated on a 0 to 10 numeric rating scale (NRS). Total fatigue and energy scores were calculated as the mean of the 13 fatigue and the 5 energy items, respectively. Higher scores indicate greater fatigue severity and higher levels of energy. Using separate LFS questionnaires, 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) and energy (i.e., ≤ 6.2 for morning energy, ≤ 3.5 for evening energy).²⁸ Cronbach's alphas were 0.96 for morning and 0.93 for evening fatigue and 0.95 for morning and 0.93 for evening energy. Patients' ratings of morning energy were used in this analysis to evaluate their associations with demographic and clinical characteristics, as well as with the stress, resilience, and coping measures.

Stress, Resilience, and Coping Measures

The 14-item 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 week.²⁹ Each item was rated on a 0 to 4 Likert scale (i.e., 0 = never, 1 = almost never, 2 = sometimes, 3 = fairly often, 4 = very often). Total PSS scores can range from 0 to 56. Its Cronbach's alpha was 0.89.

The 22-item Impact of Event Scale-Revised (IES-R) was used to measure cancer-related distress.³⁰ Patients rated each item based on how distressing each potential difficulty was for them during the past week "with respect to their cancer and its treatment". Each item was rated on a 0 (not at all) to 4 (extremely) Likert scale. Three subscales evaluate levels of intrusion, avoidance, and hyperarousal perceived by the patient. The total score can range from 0 to 88. Sum scores of ≥ 24 indicate clinically meaningful post-traumatic symptomatology and

scores of ≥ 33 indicate probable post-traumatic stress disorder (PTSD).³¹ Cronbach's alpha for the IES-R total score was 0.92.

The 30-item Life Stressor Checklist-Revised (LSC-R) is an index of lifetime trauma exposure (e.g., being mugged, sexual assault).³² The LSC-R assesses whether each stressful event occurred, at what ages the events occurred, how many times each event occurred, how dangerous the event was, and whether the individual had an intense emotional reaction to the event(s). The total LSC-R score is obtained by summing the total number of events endorsed (range of 0 to 30). If the patient endorsed an event, the patient was asked to indicate how much that stressor affected their life in the past year, from 1 (not at all) to 5 (extremely). These responses were summed to yield a total "affected" score. In addition, a PTSD sum score was created based on the number of positively endorsed items (out of 21) that reflect the DSM-IV PTSD Criteria A for having experienced a traumatic event.

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").^{33, 34} Items are scored on a 5-point Likert scale ("not true at all" to "true nearly all of the time"). 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 (standard deviation of 5.4),³⁴ with an estimated minimal clinically important difference of 2.7.³⁵ Its Cronbach's alpha was 0.90.

The 28-item Brief COPE was used to assess patients' use of 14 coping strategies.³⁶ Patients rated their use of each coping strategy "since beginning chemotherapy." Use of each coping strategy was evaluated using 2 items. Each item was rated on a 4-point Likert scale that ranged from 1 ("I haven't been doing this at all") to 4 ("I have been doing this a lot"). Scores for each coping strategy can range from 2 to 8, with higher scores indicating greater use of each strategy. Engagement coping strategies and their associated Cronbach's alphas include active coping (0.75), planning (0.74), positive reframing (0.79), acceptance (0.68), humor (0.83), religion (0.92), emotional support (0.77), and instrumental support (0.77). Disengagement

coping strategies and their associated Cronbach's alphas include self-distraction (0.46), denial (0.72), venting (0.65), substance use (0.87), behavioral disengagement (0.57), and self-blame (0.73).

Study Procedures

Study was approved by the Committee on Human Research at the University of California, San Francisco and by the Institutional Review Board at each of the study sites. Patients were approached in the infusion unit by a research nurse during their first or second cycle of chemotherapy to determine interest and obtain written informed consent. Patients completed the LFS, in their homes using paper questionnaires, a total of six times over two cycles of chemotherapy (i.e., prior to chemotherapy administration (Assessments 1 and 4), approximately 1 week after chemotherapy administration (Assessments 2 and 5), approximately 2 weeks after chemotherapy administration (Assessments 3 and 6). All of the other measures were completed at enrollment (i.e., prior to the second or third cycle of chemotherapy).

Data Analysis

Latent profile analysis (LPA) was used to identify subgroups of patients (i.e., latent classes) with distinct morning energy profiles over the six assessments, using Mplus version 8.4.³⁷ Given the complexity of the pattern of change in morning energy over the two cycles of chemotherapy, means were estimated for the morning and evening energy scores at each of the six assessments with covariances included to incorporate the expected correlations among the repeated measures to reduce model complexity. Estimation was carried out with full information maximum likelihood with standard errors and a Chi-square test that are robust to non-normality and non-independence of observations. Model fit was evaluated using the Bayesian Information Criterion, entropy, Vuong-Lo-Mendell-Rubin likelihood ratio test, and latent class percentages that were large enough to be reliable (likely to replicate in new samples).³⁸ Missing data were accommodated with the use of the Expectation-Maximization algorithm.³⁹

Additional analyses were done using IBM SPSS Statistics version 29 (IBM Corporation, Armonk, NY). Differences among the morning energy classes in demographic and clinical characteristics, as well as in stress, resilience, and coping scores were evaluated using parametric and nonparametric tests. A Bonferroni corrected p-value of <0.017 was considered statistically significant for the pairwise contrasts (i.e., $.05/3$ possible pairwise contrasts).

RESULTS

Latent Class Solution

The rationale for the selection of the three-class solution is provided in Table 1. The three latent classes were named based on the clinically meaningful cutoff score for decrements in morning energy (i.e., ≤ 6.2)²⁸ and our previously published categorizations.¹⁰ As shown in Figure 1, patients in the High class (17.3%) had morning energy scores that increased over time. For the Low class (60.3%), energy scores decreased at assessments 2 and 5 (i.e., week following the administration of chemotherapy). For the Very Low class (22.4%), morning energy scores remained low across all six assessments.

Demographic and Clinical Characteristics

Compared to the High class, patients in the other two classes were more likely to report a current or past history of smoking, were less likely to have gastrointestinal and more likely to have gynecologic cancer, and had a higher MAX2 score (Table 2). Compared to the other two classes, the Very Low class was more likely to self-report their race/ethnicity as Hispanic, mixed, or other; were less likely to be married or partnered, were more likely to live alone, and had a lower annual household income. Differences in employment status, exercising on a regular basis, and KPS scores (High > Low > Very Low), as well as number of comorbidities, SCQ scores, and self-reported diagnoses of depression and back pain (High < Low < Very Low) followed similar patterns.

Stress and Resilience

The PSS scores, IES-R intrusion, hyperarousal, and total scores, and the LSCR affected sum and total scores followed the same pattern (High < Low < Very Low; Table 3). Compared to the High class, patients in the other two classes had higher IES-R avoidance scores. Compared to the other two classes, patients in the Very Low class had higher LSC-R PTSD scores. The CDRS scores showed the following pattern: High > Low > Very Low.

Occurrence of Life Stressors

Compared to the High class, patients in the Very Low class reported higher occurrence rates for: sexual harassment, physical abuse at ≥ 16 years of age, being forced to touch at ≤ 16 years of age, being forced have sex at ≤ 16 years of age, and caring for someone with a severe physical or mental handicap (Table 4). Compared to the other two classes, patients in the Very Low class reported higher occurrence rates for: physical neglect, being separated or divorced, and serious money problems. Compared to the High class, patients in the other two classes reported higher occurrence rates for having a serious physical or mental illness not related to cancer. Differences among the three classes in the occurrence of emotional abuse showed the following pattern: High < Low < Very Low.

Effects of Various Stressors

For most of the stressors, no differences in effect scores were found among the morning energy classes (Table 5). Compared to the High class, patients in the Low class reported higher effect scores for being forced to touch at ≥ 16 years. Compared to the other two classes, patients in the Very Low class reported higher effect scores for the not sudden death of someone close.

Coping Strategies

Compared to the High class, patients in the other two classes reported lower scores for the use of active coping and acceptance and higher scores for the use of venting (Table 6). Compared to the High class, the Low class reported higher use of denial. Compared to the High class, the Very Low class reported lower use of positive reframing. Compared to the other two classes, the Very Low class reported higher use of behavioral disengagement. Differences among the three classes in the use of self-blame showed the following pattern: High < Low < Very Low.

DISCUSSION

This study is the first to use LPA to identify three distinct morning energy profiles in patients receiving chemotherapy and evaluate for modifiable and nonmodifiable risk factors associated with significant decrements in morning energy (i.e., demographic and clinical characteristics, three types of stress, levels of resilience, and use of engagement and disengagement coping strategies). As noted in Figure 1, for all three profiles, decrements in morning energy remained relatively stable across the two cycles of chemotherapy. In our previous study of patients undergoing radiation therapy and their family caregivers,¹⁰ Low (50.8%) and Moderate (49.2%) morning energy profiles were identified. For both the previous study¹⁰ and the current sample (60.3%), the prevalence rates for the Low morning energy profile were comparable and the severity scores were equivalent (i.e., ~5). However, in the current sample of patients receiving chemotherapy, a Very Low class was identified and clinically meaningful decrements in morning energy were reported by 82.7% of the current sample (i.e., Low (60.3%) and Very Low (22.4%)). These between study differences in occurrence rates may be related to differences in cancer treatments; the inclusion of family caregivers;¹⁰ and/or the duration of the assessments (i.e., approximately two months versus 6 months¹⁰).

One of the stated purposes of this study was to identify modifiable risk factors associated with the worst morning energy profiles. Table 7 summarizes the risk factors associated with membership in the Low and Very Low Morning Energy classes compared to the High Morning Energy class. Given the paucity of research on decrements in morning energy, studies that evaluated decrements in average energy and/or diurnal variations in energy in oncology patients, the general population, and patients with other chronic conditions will be cited in the Discussion.⁴⁰

Demographic and Clinical Risk Factors

Most of the findings on associations between various demographic characteristics and decrements in energy are inconsistent. In terms of gender, while in one study of oncology patients, no gender differences were identified,¹¹ in another study of patients receiving radiation therapy and their family caregivers,¹⁰ women reported more severe decrements in morning energy. Similarly, in older adults who participated in the Health, Aging, and Body Composition Study, either no differences⁴¹ or being female⁴² was associated with lower levels of energy. Similar to gender, findings regarding differences in morning energy levels among various racial/ethnic groups are inconsistent. For example, in one study,¹⁰ oncology patients and their family caregivers with lower levels of morning energy were more likely to self-identify as Black. In contrast, in studies of women with breast cancer⁴³ and HIV,⁴⁴ no associations were found between self-reported race/ethnicity and decrements in energy levels. Additional research is warranted on associations between age, gender, race/ethnicity, and other social determinants of health and decrements in morning energy levels.

In the current study, patients in the Very Low Morning Energy class were more likely to not be married or partnered and live alone. While no studies were identified that evaluated for associations with marital status, in three studies of oncology patients^{10, 43, 45} and in a study of patients with HIV,⁴⁴ no associations were found between living alone and decrements in morning

energy levels. However, in another study of oncology patients,¹¹ living alone was associated with more severe decrements in morning energy. While an explanation for these inconsistent findings is not readily apparent, it is reasonable to hypothesize that patients who live alone may not have adequate assistance to perform routine activities (e.g., housekeeping, grocery shopping) that leads to decrements in morning energy.

While previous studies found no associations,^{10, 11, 43} in the current study being unemployed and/or having a lower annual income was associated with membership in the lower morning energy classes. In addition, 29.7% of the patients in the Very Low Morning Energy class reported serious money problems on the LSC-R. These results warrant additional investigation given that the findings from systematic reviews suggest that financial toxicity, associated with the high costs of cancer and its treatment, is associated with higher levels of stress⁴⁶ and overall symptom burden⁴⁷ in patients with cancer.

As shown in Table 7, the majority of the clinical characteristics that were evaluated in the current study were risk factors for membership in both the Low and Very Low Morning Energy classes. While in one study,⁴⁵ older oncology patients who reported a past or current history of smoking had lower levels of morning energy, in other studies of patients with cancer¹¹ and older adults⁴⁸ no relationship with smoking status was found. Given that smoking is associated with changes in inflammatory responses⁴⁹ and previous research found relationships between decrements in morning energy and inflammatory mechanisms,^{10, 43} additional research is warranted on the impact of smoking and smoking cessation on patients' morning energy levels.

In terms of comorbidity, while in two studies,^{11, 45} no association was found, in the current study and in two previous studies of patients with cancer,^{10, 43} a higher number of comorbid conditions and a higher comorbidity burden were associated with significant decrements in morning energy. It should be noted that in the current study, across the three morning energy profiles, the comorbidity burden increased in a dose-response fashion (i.e., as the comorbidity burden increased, decrements in energy increased). The differences in SCQ scores between

the High and the Low ($d = 0.41$) and the High and Very Low ($d = 0.72$) Morning Energy classes represent clinically meaningful increases in comorbidity burden.⁵⁰ In terms of specific comorbidities, higher occurrence rates for self-reported diagnoses of depression and back pain were associated with membership in the two lower morning energy classes (N.B. occurrence rates for both conditions increased in a dose response fashion across the three morning energy classes). While no associations were seen in a study of oncology patients,⁴⁵ in an analysis from the Health, Age, and Body Composition Study,⁴² the specific comorbid conditions associated with lower average energy levels included heart disease, high blood pressure, lung disease, diabetes, anemia, and osteoarthritis. Common underlying mechanisms (e.g., inflammation⁵¹) and treatments for these chronic conditions may explain the associated decrements in morning energy. Given that between 40% and 69% of oncology patients experience multimorbidity,^{52, 53} clinicians need to assess the impact of these conditions and associated treatments on morning energy levels.

Findings regarding associations between functional status and decrements in energy are consistent with previous reports in oncology patients^{10, 11, 43, 45} and older adults.^{42, 48} Similar to comorbidity burden, differences in KPS scores exhibited a dose-response effect across the three morning energy classes. In addition, compared to the High class, differences in KPS scores in the Low ($d = 0.64$) and Very Low ($d = 0.97$) Morning Energy classes represent clinically meaningful decrements in functional status.⁵⁰ Given that functional status is one of the most important outcomes for oncology patients,⁵⁴ studies are needed to determine if interventions that increase morning energy levels will improve patients' functional status.

Across studies of oncology patients^{11, 55} and older adults,^{41, 42} the lack of regular exercise was associated with decrements in energy levels. Again, in the current study, across the three energy classes, the proportion of patients who did not exercise on a regular basis increased in a dose response fashion. Given that regular exercise decreases inflammatory responses,⁵⁶⁻⁵⁹ as well as improves patients' overall health status and level of function, additional research is

warranted on which types and duration of exercise will increase the morning energy levels of patients receiving chemotherapy.

Stress

This study is the first to report on associations between decrements in morning energy and three distinct types of stress. Of note, as the morning energy profiles worsened, PSS (global stress), IES-R (cancer-specific stress) and LSC-R (cumulative life stress) total scores increased in a dose response pattern. While a clinically meaningful cutoff score for the PSS is not available, the mean scores for the Low (18.6) and Very Low (22.3) Morning Energy classes are comparable to the mean scores of 18.8 and 20.2 reported by male and female participants, respectively, in a probability sample that was drawn from the population of the United States.⁶⁰ In terms of the IES-R, 40.1% and 22.2% of the patients in the Very Low Morning Energy class had total scores suggestive of PTSD symptomatology and probable PTSD, respectively. These percentages are higher than the prevalence rates of 7.3% to 13.8% reported in a review of PTSD in patients with cancer.⁶¹

While the total number of stressors on the LSC-R increased across the morning energy profiles, the occurrence rates for eight of the ten stressors listed on Table 7 were higher in the Very Low Morning Energy class. Many of these stressors are considered ACEs (e.g., physical neglect, forced to touch at <16 years, forced sex at <16 years). Equally important these stressors had a significant effect on these patients in the past year. While these findings warrant confirmation in future studies, given that significant decrements in morning energy can impede patients' abilities to perform routine activities, work, and engage in a variety of social activities, clinicians need to determine if the use of stress reduction techniques (e.g., relaxation exercises, mindfulness based activities⁶²) will increase patients' morning energy levels. In addition, patients with high levels of cumulative life stress, particularly ACEs, and/or symptoms of PTSD warrant referrals to psychological services.

Equally important, the mechanisms that underlie the associations between decrements in morning energy and stress warrant evaluation. As noted in a paper that proposed a Multidimensional Model of Energy in Patients with Cancer,⁴⁰ multiple mechanisms may influence energy levels (e.g., inflammation, neurotransmitter dysregulation, disruptions in circadian rhythms, mitochondrial dysfunction). It is interesting to note that similar mechanisms are involved in mediating physiologic responses to stress. For example, the hypothalamic-pituitary-adrenal (HPA) axis is one of several endogenous stress-reactive systems that impacts energy levels and circadian rhythms.⁶³ Stress-induced activation of the HPA axis results in dysregulation of diurnal variations in the secretion of cortisol.⁶⁴⁻⁶⁶ These changes in cortisol secretion can result in alterations in energy levels, as well as in inflammatory responses and neuronal function.^{67, 68}

Resilience

As noted in the Introduction, resilience refers to the ability of an individual to maintain or restore stability when confronted with stressful life events or adversity.⁶⁹ In the current study, over 80% of the patients had CDRS scores that were below the normative score for the population of the United States. Of note, while no comparative data are available, several lines of evidence suggest that resilience is modifiable and dynamic.⁷⁰ Given that increases in resilience can foster adaptation to cancer-related stress,⁶⁹ clinicians need to educate patients about strategies to enhance resilience (e.g., attention and interpretation therapy, promotion of cognitive flexibility, self-efficacy, and self-esteem).^{71, 72}

Coping

This study is the first to evaluate for associations between decrements in morning energy levels and the use of a variety of engagement and disengagement coping strategies. Similar to our previous LPA study of morning fatigue,⁷³ patients in the two worst morning energy profiles reported higher use of disengagement coping strategies (e.g., venting, self-blame).

Additional research is warranted to understand the associations between decrements in morning energy, increases in stress, and the use of disengagement coping strategies.

Limitations

Several limitations warrant consideration. Given that the current sample was primarily white, well-educated, and female, these findings may not generalize to more diverse samples. Given that the primary reason for refusal to participate was that patients were overwhelmed with their current treatment, our findings may underestimate actual decrements in morning energy, as well as the levels of stress experienced by patients receiving chemotherapy.

Implications for Clinical Practice and Research

Findings from this study suggest that clinicians need to perform comprehensive assessments of energy and stress levels in patients receiving chemotherapy. Given the negative impact that all three types of stress had on patients' levels of morning energy, an evaluation of specific stressors, as well as symptoms of PTSD are warranted in order to initiate referrals for counseling or other supportive care services. Patients would benefit from education on the use of a variety of stress reduction techniques and ongoing support in using these techniques. While not empirically tested, patients may benefit from education on energy conservation strategies that are outlined in the Fatigue Guideline published by the National Comprehensive Cancer Network.⁷⁴

In terms of directions for future research, given that this study is the first to evaluate for inter-individual variability in morning energy in patients receiving chemotherapy, the profiles and risk factors warrant confirmation. In addition, future studies need to evaluate for differences in morning energy profiles in patients with different types of cancer; among different types of cancer treatment; and across the continuum of cancer care (e.g., active treatment, survivorship, palliative care). Equally important, studies are needed that determine the underlying

mechanisms for decrements in energy, as well as common and distinct mechanisms associated with decrements in energy and increases in stress.

Appendix

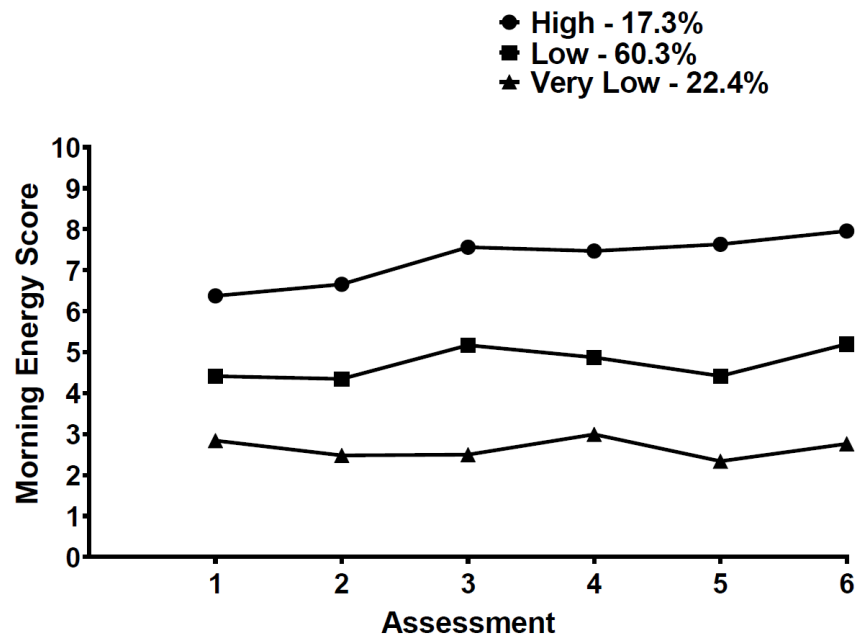


Figure 1– Trajectories of morning energy for the three latent classes.

Table 1 – Latent Profile Solutions and Fit Indices for One through Four Classes for Morning Energy

Model	LL	AIC	BIC	Entropy	VLMR
1 Class	-14538.90	29119.79	29228.89	n/a	n/a
2 Class	-14311.45	28678.89	28824.36	0.65	454.90 ⁺
3 Class ^a	-14177.10	28424.19	28606.02	0.71	268.70 ⁺
4 Class	-14096.83	28277.67	28495.87	0.71	ns

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

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

⁺p < .00005

^aThe 3-class solution was selected because the BIC for that solution was lower than the BIC for the 2-class solution. In addition, the VLMR was significant for the 3-class solution, indicating that three classes fit the data better than two classes. Although the BIC was smaller for the 4-class than for the 3-class solution, the VLMR for 4-classes was not significant, indicating that too many classes had been extracted.

Table 2 – Differences in Demographic and Clinical Characteristics Among the Morning Energy Classes at Enrollment

Characteristic	High Morning Energy (0) 17.3% (n=231)	Low Morning Energy (1) 60.3% (n=804)	Very Low Morning Energy (2) 22.4% (n=298)	Statistics
	Mean (SD)	Mean (SD)	Mean (SD)	
Age (years)	57.2 (10.6)	56.7 (12.5)	58.2 (13.1)	F = 1.51, p = .222
Education (years)	16.6 (3.0)	16.2 (3.0)	16.0 (3.1)	F = 2.52, p = .081
Body mass index (kg/m ²)	25.5 (4.9)	26.1 (5.5)	27.0 (6.5)	F = 4.64, p = .010 0 < 2
Alcohol Use Disorders Identification Test score	2.9 (2.0)	3.1 (2.6)	2.7 (2.3)	F = 1.75, p = .175
Karnofsky Performance Status score	87.6 (10.0)	79.6 (12.2)	75.3 (12.3)	F = 67.72, p < .001 0 > 1 > 2
Number of comorbid conditions	2.0 (1.2)	2.4 (1.4)	2.8 (1.5)	F = 19.72, p < .001 0 < 1 < 2
Self-administered Comorbidity Questionnaire score	4.2 (2.3)	5.5 (3.1)	6.5 (3.7)	F = 33.25, p < .001 0 < 1 < 2
Time since diagnosis (years)	2.0 (3.7)	2.0 (3.8)	2.1 (4.1)	KW = 1.00, p = .606
Time since diagnosis (years, median)	0.41	0.42	0.45	
Number of prior cancer treatments	1.5 (1.5)	1.6 (1.5)	1.7 (1.5)	F = 0.81, p = .447
Number of metastatic sites including lymph node involvement ^a	1.3 (1.1)	1.2 (1.3)	1.3 (1.2)	F = 0.21, p = .808
Number of metastatic sites excluding lymph node involvement	0.8 (1.0)	0.8 (1.1)	0.8 (1.1)	F = 0.16, p = .853
MAX2 score	0.16 (0.08)	0.18 (0.08)	0.18 (0.08)	F = 7.86, p < .001 0 < 1 and 2

Characteristic	High Morning Energy (0) 17.3% (n=231)	Low Morning Energy (1) 60.3% (n=804)	Very Low Morning Energy (2) 22.4% (n=298)	Statistics
	% (n)	% (n)	% (n)	
Gender (% female)	71.0 (164)	78.5 (630)	81.9 (244)	$X^2 = 9.29$, $p = .010$ $0 < 1$
Self-reported ethnicity				$X^2 = 20.46$, $p = .002$
White	68.1 (154)	69.7 (554)	70.2 (207)	NS
Asian or Pacific Islander	16.4 (37)	12.7 (101)	9.2 (27)	$0 > 1$
Black	8.8 (20)	7.7 (61)	4.7 (14)	NS
Hispanic, Mixed, or Other	6.6 (15)	9.9 (79)	15.9 (47)	$0 \text{ and } 1 < 2$
Married or partnered (% yes)	70.6 (161)	66.2 (524)	54.8 (161)	$X^2 = 16.82$, $p < .001$ $0 \text{ and } 1 < 2$
Characteristic	High Morning Energy (0) 17.3% (n=231)	Low Morning Energy (1) 60.3% (n=804)	Very Low Morning Energy (2) 22.4% (n=298)	Statistics
	n%	n%	n%	
Lives alone (% yes)	16.2 (37)	19.9 (158)	30.0 (88)	$X^2 = 17.67$, $p < .001$ $0 \text{ and } 1 < 2$
Currently employed (% yes)	46.2 (104)	35.1 (280)	26.7 (79)	$X^2 = 21.41$, $p < .001$ $0 > 1 > 2$
Annual household income				$KW = 29.25$, $p < .001$ $0 \text{ and } 1 > 2$
Less than \$30,000	10.9 (21)	17.4 (127)	26.1 (71)	
\$30,000 to \$70,000	18.7 (36)	20.7 (151)	23.9 (65)	
\$70,000 to \$100,000	17.1 (33)	16.5 (120)	18.0 (49)	
Greater than \$100,000	53.4 (103)	45.3 (330)	32.0 (87)	

Characteristic	High Morning Energy (0) 17.3% (n=231)	Low Morning Energy (1) 60.3% (n=804)	Very Low Morning Energy (2) 22.4% (n=298)	Statistics
	% (n)	% (n)	% (n)	
Childcare responsibilities (% yes)	24.0 (54)	23.2 (183)	18.0 (52)	$X^2 = 3.81, p = .149$
Elder care responsibilities (% yes)	5.7 (12)	8.6 (63)	7.5 (20)	$X^2 = 2.09, p = .352$
Past or current history of smoking (% yes)	26.2 (60)	36.0 (285)	40.5 (118)	$X^2 = 12.00, p = .002$ $0 < 1 \text{ and } 2$
Exercise on a regular basis (% yes)	82.8 (227)	72.6 (571)	56.7 (164)	$X^2 = 44.67, p < .001$ $0 > 1 > 2$
Specific comorbid conditions				
Heart disease	4.8 (11)	5.3 (41)	7.0 (21)	$X^2 = 1.58, p = .455$
High blood pressure	28.1 (65)	29.4 (236)	33.9 (101)	$X^2 = 2.67, p = .263$
Lung disease	7.8 (18)	11.9 (96)	12.4 (37)	$X^2 = 3.53, p = 1.71$
Diabetes	6.5 (15)	9.1 (73)	10.7 (32)	$X^2 = 2.88, p = .237$
Ulcer or stomach disease	2.2 (5)	5.1 (41)	6.4 (19)	$X^2 = 5.19, p = .075$
Kidney disease	0.4 (1)	1.2 (10)	2.7 (8)	$X^2 = 5.17, p = .075$
Liver disease	7.8 (18)	7.0 (56)	4.0 (12)	$X^2 = 3.94, p = .139$
Anemia or blood disease	9.5 (22)	12.2 (98)	14.4 (43)	$X^2 = 2.92, p = .232$
Depression	4.8 (11)	18.8 (151)	31.9 (95)	$X^2 = 61.81, p < .001$ $0 < 1 < 2$
Osteoarthritis	10.0 (23)	11.3 (91)	15.4 (46)	$X^2 = 4.60, p = .100$
Back pain	14.3 (33)	25.6 (206)	34.9 (104)	$X^2 = 28.95, p < .001$ $0 < 1 < 2$
Rheumatoid arthritis	5.2 (12)	2.0 (16)	4.4 (13)	$X^2 = 8.31, p = .016$ $0 > 1$

Characteristic	High Morning Energy (0) 17.3% (n=231)	Low Morning Energy (1) 60.3% (n=804)	Very Low Morning Energy (2) 22.4% (n=298)	Statistics
	% (n)	% (n)	% (n)	
Cancer diagnosis				$\chi^2 = 29.34$, $p < .001$ NS 0 > 1 and 2 0 < 1 and 2 0 < 1
Breast cancer	38.5 (89)	41.0 (330)	40.3 (120)	
Gastrointestinal cancer	43.3 (100)	27.5 (221)	27.9 (83)	
Gynecological cancer	10.8 (25)	18.2 (146)	20.8 (62)	
Lung cancer	7.4 (17)	13.3 (107)	11.1 (33)	
Prior cancer treatment				$\chi^2 = 4.45$, $p = .616$
No prior treatment				
Only surgery, CTX, or RT	29.6 (66)	23.7 (185)	24.6 (72)	
Surgery and CTX, or surgery and RT, or CTX and RT	38.1 (85)	43.5 (340)	41.3 (121)	
Surgery and CTX and RT	19.7 (44)	19.3 (151)	21.5 (63)	
	12.6 (28)	13.6 (106)	12.6 (37)	
Metastatic sites				$\chi^2 = 9.57$, $p = .144$
No metastasis	28.5 (65)	34.2 (271)	30.5 (90)	
Only lymph node metastasis	22.4 (51)	20.6 (163)	25.8 (76)	
Only metastatic disease in other sites	26.3 (60)	19.7 (156)	21.0 (62)	
Metastatic disease in lymph nodes and other sites	22.8 (52)	25.6 (203)	22.7 (67)	
Cycle length				KW = 6.54, $p = .038$ No significant pairwise contrasts
14-day cycle	49.6 (114)	40.7 (324)	39.5 (116)	
21-day cycle	44.3 (102)	52.1 (415)	52.4 (154)	
28-day cycle	6.1 (14)	7.3 (58)	8.2 (24)	
Emetogenicity of the CTX regimen				KW = 0.86, $p = .650$
Minimal/low	20.0 (46)	18.8 (150)	21.0 (62)	
Moderate	62.6 (144)	61.1 (487)	59.3 (175)	
High	17.4 (40)	20.1 (160)	19.7 (58)	
Antiemetic regimen				$\chi^2 = 12.19$, $p = .058$
None				
Steroid alone or serotonin receptor antagonist alone	10.9 (24)	6.4 (50)	6.3 (18)	
Serotonin receptor antagonist and steroid	16.7 (37)	21.1 (165)	21.9 (63)	
NK-1 receptor antagonist and two other antiemetics	52.5 (116)	47.4 (371)	44.1 (127)	
	19.9 (44)	25.1 (196)	27.8 (80)	

Abbreviations: CTX = chemotherapy, kg = kilograms, KW = Kruskal Wallis, m² = meters squared, n/a = not applicable, NK-1 = neurokinin-1, NS = not significant, RT = radiation therapy, SD = standard deviation

^aTotal number of metastatic sites evaluated was 9.

Table 3 – Differences in Stress and Resilience Measures Among the Morning Energy Classes at Enrollment

Measures ^a	High Morning Energy (0) 17.3% (n=231)	Low Morning Energy (1) 60.3% (n=804)	Very Low Morning Energy (2) 22.4% (n=298)	Statistics
	Mean (SD)	Mean (SD)	Mean (SD)	
PSS total score (range 0 to 56)	13.6 (6.6)	18.6 (7.6)	22.3 (8.8)	F = 79.65, p <.001 0 < 1 < 2
IES-R total sum score (≥24 – clinically meaningful PTSD symptomatology) (≥33 – probable PTSD)	13.1 (9.1)	19.0 (12.9)	22.6 (14.9)	F = 34.29, p <.001 0 < 1 < 2
IES-R intrusion	0.6 (0.5)	0.9 (0.7)	1.1 (0.8)	F = 33.61, p <.001 0 < 1 < 2
IES-R avoidance	0.8 (0.6)	0.9 (0.7)	1.1 (0.7)	F = 8.46, p <.001 0 < 1 and 2
IES-R hyperarousal	0.3 (0.4)	0.7 (0.6)	0.9 (0.8)	F = 52.38, p <.001 0 < 1 < 2
LSC-R total score (range 0–30)	5.2 (3.5)	6.0 (3.8)	7.1 (4.3)	F = 13.49, p <.001 0 < 1 < 2
LSC-R affected sum (range 0-150)	9.4 (9.3)	11.6 (10.5)	14.7 (12.4)	F = 14.01, p <.001 0 < 1 < 2
LSC-R PTSD sum (range 0-21)	2.5 (2.6)	3.0 (3.0)	3.8 (3.3)	F = 9.69, p <.001 0 and 1 < 2
CDRS total score (31.8 (±5.4) – normative range for the United States population)	32.9 (5.9)	29.9 (6.1)	28.3 (6.8)	F = 34.02, p <.001 0 > 1 > 2

Abbreviations: CDRS = Connor Davidson Resilience Scale, IES-R = Impact of Event Scale-Revised, LSC-R = Life Stressor Checklist-Revised, PSS = Perceived Stress Scale, PTSD = post-traumatic stress disorder, SD = standard deviation

^aClinically meaningful cutoff scores or range of scores are in parentheses.

Table 4 – Differences Among the Morning Energy Classes in the Percentage of Patients Exposed to Specific Stressors at Enrollment

Stressful Life Event	High Morning Energy (0) 17.3% (n=231)	Low Morning Energy (1) 60.3% (n=804)	Very Low Morning Energy (2) 22.4% (n=298)	Statistics
	% (n)	% (n)	% (n)	
Interpersonal Violence, Abuse, and Neglect Stressors				
Family violence in childhood	17.3 (34)	24.6 (146)	26.8 (63)	X ² = 5.90, p = .052
Emotional abuse	9.6 (19)	21.6 (129)	31.9 (76)	X ² = 31.54, p <.001 0 < 1 < 2
Physical neglect	2.0 (4)	4.2 (25)	8.9 (21)	X ² = 12.28, p = .002 0 and 1 < 2
Sexual harassment	13.3 (26)	17.6 (105)	23.6 (55)	X ² = 7.80, p = .020 0 < 2
Physical abuse - <16 years	11.7 (23)	13.8 (82)	17.9 (42)	X ² = 3.68, p = .159
Physical abuse - ≥16 years	7.7 (15)	13.6 (81)	17.9 (42)	X ² = 9.73, p = .008 0 < 2
Forced to touch - <16 years	5.6 (11)	11.5 (68)	16.8 (40)	X ² = 13.00, p = .002 0 < 2
Forced to touch - ≥16 years	3.6 (7)	6.8 (40)	6.4 (15)	X ² = 2.63, p = .268
Forced sex - <16 years	1.5 (3)	4.0 (24)	7.7 (18)	X ² = 9.91, p = .007 0 < 2
Forced sex - ≥16 years	3.6 (7)	6.9 (41)	7.6 (18)	X ² = 3.39, p = .183
Other Stressors				
Been in a serious disaster	47.4 (93)	38.3 (228)	41.8 (100)	X ² = 5.21, p = .074
Seen serious accident	34.5 (68)	32.4 (193)	32.1 (77)	X ² = 0.36, p = .834
Had serious accident or injury	21.1 (41)	24.0 (142)	27.3 (65)	X ² = 2.26, p = .324
Jail (family member)	16.2 (32)	20.3 (121)	25.0 (59)	X ² = 5.21, p = .074
Jail (self)	4.5 (9)	7.5 (45)	6.7 (16)	X ² = 2.09, p = .351
Foster care or put up for adoption	3.0 (6)	2.0 (12)	2.9 (7)	X ² = 1.01, p = .605

Stressful Life Event	High Morning Energy (0) 17.3% (n=231)	Low Morning Energy (1) 60.3% (n=804)	Very Low Morning Energy (2) 22.4% (n=208)	Statistics
	% (n)	% (n)	% (n)	
Other Stressors				
Separated/divorced (parents)	16.2 (32)	22.7 (136)	23.8 (57)	X ² = 4.60, p = .100
Separated/divorced (self)	31.2 (62)	33.8 (203)	46.2 (109)	X ² = 13.92, p < .001 0 and 1 < 2
Serious money problems	11.6 (23)	18.8 (113)	29.7 (70)	X ² = 23.04, p <.001 0 and 1 < 2
Had serious physical or mental illness (not cancer)	10.1 (20)	19.4 (117)	25.2 (60)	X ² = 16.42, p <.001 0 < 1 and 2
Abortion or miscarriage	43.4 (62)	44.9 (213)	43.1 (85)	X ² = 0.23, p = .890
Separated from child	1.0 (2)	1.9 (11)	3.5 (8)	X ² = 3.38, p = .185
Care for child with handicap	4.2 (8)	3.1 (18)	5.7 (13)	X ² = 2.97, p = .277
Care for someone with severe physical or mental handicap	19.0 (37)	23.6 (139)	30.9 (72)	X ² = 8.63, p = .013 0 < 2
Death of someone close (sudden)	53.1 (104)	48.6 (286)	48.3 (113)	X ² = 1.33, p = .513
Death of someone close (not sudden)	78.6 (151)	77.5 (455)	83.2 (193)	X ² = 3.26, p = .196
Seen robbery/mugging	19.2 (38)	22.1 (132)	24.1 (57)	X ² = 1.50, p = .473
Been robbed/mugged	24.2 (48)	27.3 (162)	26.9 (63)	X ² = 0.73, p = .694

Table 5 – Differences Among the Morning Energy Classes in the Effect of Stressor on Life In The Past Year

Stressful Life Event*	High Morning Energy (0) 17.3% (n=231)	Low Morning Energy (1) 60.3% (n=804)	Very Low Morning Energy (2) 22.4% (n=298)	Statistics
	Mean (SD)	Mean (SD)	Mean (SD)	
Interpersonal violence, abuse, and neglect stressors				
Family violence in childhood	1.8 (1.2)	1.8 (1.1)	2.1 (1.2)	KW = 3.51, p = .173
Emotional abuse	3.0 (1.5)	2.4 (1.3)	2.8 (1.3)	KW = 4.99, p = .082
Physical neglect	3.0 (1.8)	2.7 (1.4)	2.9 (1.2)	KW = 0.46 p = .795
Sexual harassment	1.5 (1.1)	1.5 (1.0)	1.4 (0.8)	KW = 0.84, p = .657
Physical abuse - <16 years	1.9 (1.3)	1.9 (1.3)	2.1 (1.2)	KW = 1.59, p = .452
Physical abuse - ≥16 years	1.9 (1.3)	2.0 (1.3)	1.7 (0.9)	KW = 0.73 p = .694
Forced to touch - <16 years	1.9 (1.5)	1.9 (1.3)	2.3 (1.3)	KW = 3.51, p = .173
Forced to touch - ≥16 years	1.0 (0.0)	2.1 (1.2)	1.9 (1.4)	KW = 7.02, p = .030 0 < 1
Forced sex - <16 years	2.0 (1.7)	1.9 (1.4)	2.2 (1.2)	KW = 1.27, p = .529
Forced sex - ≥16 years	1.9 (1.6)	1.8 (1.3)	1.6 (0.9)	KW = 0.29, p = .866
Been in a serious disaster	1.3 (0.9)	1.3 (0.8)	1.4 (0.8)	KW = 0.05, p = .974
Seen serious accident	1.5 (1.0)	1.5 (0.9)	1.4 (.8)	KW = 1.57, p = .456
Had serious accident or injury	1.5 (1.0)	1.6 (1.1)	1.7 (1.0)	KW = 2.47, p = .291
Jail (family member)	1.8 (1.3)	1.8 (1.3)	2.1 (1.5)	KW = 0.81, p = .666
Jail (self)	2.1 (1.2)	1.7 (1.2)	1.8 (1.3)	KW = 1.97, p = .373
Foster care or put up for adoption	3.0 (1.9)	2.2 (1.4)	1.8 (1.0)	KW = 1.35, p = .508
Separated/divorced (parents)	1.4 (0.9)	1.8 (1.1)	1.9 (1.3)	KW = 5.38, p = .068
Separated/divorced (self)	1.8 (1.3)	2.1 (1.3)	2.2 (1.5)	KW = 5.41, p = .067
Serious money problems	2.2 (1.8)	2.7 (1.6)	2.9 (1.7)	KW = 3.16, p = .206

Stressful Life Event*	High Morning Energy (0) 17.3% (n=231)	Low Morning Energy (1) 60.3% (n=804)	Very Low Morning Energy (2) 22.4% (n=298)	Statistics
	Mean (SD)	Mean (SD)	Mean (SD)	
Interpersonal violence, abuse, and neglect stressors				
Had serious physical or mental illness (not cancer)	2.5 (1.6)	2.4 (1.3)	2.5 (1.4)	KW = 0.39, p = .821
Abortion or miscarriage	1.4 (0.9)	1.5 (1.0)	1.6 (1.1)	KW = 2.56, p = .278
Separated from child	2.0 (1.4)	2.6 (1.6)	3.4 (1.7)	KW = 1.65, p = .439
Care for child with handicap	3.0 (1.6)	3.7 (1.2)	2.8 (1.3)	KW = 4.02, p = .134
Care for someone with severe physical or mental handicap	2.4 (1.5)	2.5 (1.4)	2.7 (1.5)	KW = 1.07, p = .587
Death of someone close (sudden)	2.1 (1.4)	2.1 (1.3)	2.4 (1.4)	KW = 4.93, p = .085
Death of someone close (not sudden)	2.0 (1.2)	2.1 (1.3)	2.5 (1.4)	KW = 11.65, p = .003 0 and 1 < 2
Seen robbery/mugging	1.5 (1.1)	1.6 (1.0)	1.4 (0.9)	KW = 1.77, p = .412
Been robbed/mugged	1.5 (1.1)	1.7 (1.1)	1.5 (1.0)	KW = 1.98, p = .372

Abbreviations: KW = Kruskal Wallis, SD = standard deviation

*Range = 1 “not at all” to 5 “extremely”

^aThese data are reported for those patients who reported the occurrence of the stressor (see Table 4).

Table 6 – Differences Among the Morning Energy Classes in the Brief COPE Subscale Scores at Enrollment

Subscale*	High Morning Energy (0) 17.3% (n=231)	Low Morning Energy (1) 60.3% (n=804)	Very Low Morning Energy (2) 22.4% (n=298)	Statistics
	Mean (SD)	Mean (SD)	Mean (SD)	
Engagement coping strategies				
Active coping	6.4 (1.7)	6.0 (1.6)	5.7 (1.7)	F = 11.12, p <.001 0 > 1 and 2
Planning	5.5 (2.0)	5.3 (1.7)	5.2 (1.8)	F = 1.88, p = .153
Positive reframing	5.6 (2.0)	5.4 (1.9)	5.2 (1.9)	F = 3.47, p = .031 0 > 2
Acceptance	7.0 (1.2)	6.7 (1.3)	6.6 (1.4)	F = 7.46, p <.001 0 > 1 and 2
Humor	4.4 (2.1)	4.3 (1.9)	4.2 (2.0)	F = .99, p = .370
Religion	5.1 (2.3)	5.1 (2.3)	4.8 (2.3)	F = 1.22, p = .297
Using emotional support	6.3 (1.7)	6.4 (1.6)	6.2 (1.7)	F = 1.82, p = .162
Using instrumental support	5.3 (1.9)	5.4 (1.7)	5.2 (1.8)	F = 1.95, p = .143
Disengagement coping strategies				
Self-distraction	5.4 (1.9)	5.5 (1.6)	5.5 (1.6)	F = .43, p = .650
Denial	2.3 (.8)	2.6 (1.2)	2.5 (1.1)	F = 6.35, p = .002 0 < 1
Venting	3.7 (1.7)	4.0 (1.6)	4.1 (1.7)	F = 5.60, p = .004 0 < 1 and 2
Substance use	2.1 (0.6)	2.2 (0.8)	2.3 (0.8)	F = 2.25, p = .106
Behavioral disengagement	2.1 (0.5)	2.2 (0.7)	2.4 (0.9)	F = 9.52, p <.001 0 and 1 < 2
Self-blame	2.4 (1.0)	2.9 (1.2)	3.1 (1.5)	F = 19.89, p <.001 0 < 1 < 2

Abbreviation: SD = standard deviation

*Each item was rate on a 4-point Likert scale that ranged from 1 ("I haven't been doing this at all") to 4 ("I have been doing this a lot"). Each coping strategy is evaluated using 2 items. Scores can range from 2 to 8 with higher scores indicating greater use of each of the coping strategies.

Table 7 – Characteristics Associated with Membership in the Low and Very Low Morning Energy Latent Classes

Characteristic ^a	Low Morning Energy	Very Low Morning Energy
Demographic Characteristics		
More likely to be female	■	
Less likely to be Asian or Pacific Islander	■	
More likely to be Hispanic, Mixed, or other ethnicity		■
Less likely to be married or partnered		■
More likely to live alone		■
Less likely to be employed	■	■
More likely to have a lower annual household income		■
More likely to have a current or past history of smoking	■	■
Less likely to exercise on a regular basis	■	■
Clinical Characteristics		
Higher body mass index		■
Lower functional status	■	■
Higher number of comorbidities	■	■
Higher comorbidity burden	■	■
Higher MAX2 score	■	■
Less likely to have gastrointestinal cancer	■	■
More likely to have gynecologic cancer	■	■
More likely to have lung cancer	■	
More likely to self-report depression	■	■
More likely to self-report back pain	■	■
Less likely to report rheumatoid arthritis	■	
Stress Characteristics		
Higher Perceived Stress Scale score	■	■
Higher Impact of Event Scale-Revised total score	■	■
Higher Impact of Event Scale-Revised intrusion score	■	■
Higher Impact of Event Scale-Revised avoidance score	■	■
Higher Impact of Event Scale-Revised hyperarousal score	■	■
Higher Life Stressor Checklist-Revised total score	■	■
Higher Life Stressor Checklist-Revised affected sum score	■	■
Higher Life Stressor Checklist-Revised PTSD sum score		■
Lower Connor Davidson Resilience Scale total score	■	■
Higher Occurrence of Life Stressors		
Emotional abuse	■	■
Physical neglect		■
Sexual harassment		■
Physical abuse - ≥16 years		■
Forced touch – <16 years		■
Forced sex – <16 years		■
Separated/divorced - self		■
Serious money problems		■
Had serious physical or mental illness (not cancer)	■	■

Characteristic ^a	Low Morning Energy	Very Low Morning Energy
Higher Occurrence of Life Stressors		
Caring for someone with a severe physical or mental handicap		■
Higher Effect of Life Stressors		
Forced to touch - >16 years	■	
Death of someone close (not sudden)		■
Use of Coping Strategies		
Lower use of active coping	■	■
Lower use of positive reframing		■
Lower use of acceptance	■	■
Higher use of denial	■	
Higher use of venting	■	■
Higher use of behavioral disengagement		■
Higher use of self-blame	■	■

Abbreviation: PTSD = post-traumatic stress disorder

^aComparisons done with the High Morning Energy class.

■ – Indicates the presence of the risk factor compared to the High Morning Energy class

REFERENCES

1. Wang Y, Tian L, Liu X, et al. Multidimensional predictors of cancer-related fatigue based on the predisposing, precipitating, and perpetuating (3P) model: A systematic review. *Cancers*. 2023;15(24).
2. Lerdal A. A concept analysis of energy. Its meaning in the lives of three individuals with chronic illness. *Scand J Caring Sci*. 1998;12(1): 3-10.
3. Lerdal A. A theoretical extension of the concept of energy through an empirical study. *Scand J Caring Sci*. 2002;16(2): 197-206.
4. Eshragh J, Dhruva A, Paul SM, et al. Associations between neurotransmitter genes and fatigue and energy levels in women after breast cancer surgery. *J Pain Symptom Manage*. 2017;53(1): 67-84 e67.
5. Glover J, Dibble SL, Dodd MJ, Miaskowski C. Mood states of oncology outpatients: does pain make a difference? *J Pain Symptom Manage*. 1995;10(2): 120-128.
6. Fagan TJ, Lira FT. Profile of Mood States: racial differences in a delinquent population. *Psychol Rep*. 1978;43(2): 348-350.
7. Pollock V, Cho DW, Reker D, Volavka J. Profile of Mood States: the factors and their physiological correlates. *J Nerv Ment Dis*. 1979;167(10): 612-614.
8. McNair DM, Lorr M, Droppleman LF. EDITS Manual for the Profile of Mood States. San Diego, CA: Educational and Industrial Testing Service; 1971.
9. Davis JK, Mark S, Mackin L, et al. Sleep disturbance and decrements in morning energy contribute to a higher symptom burden in oncology patients. *Sleep Med*. 2023;108: 124-136.
10. Aouizerat BE, Dhruva A, Paul SM, Cooper BA, Kober KM, Miaskowski C. Phenotypic and molecular evidence suggests that decrements in morning and evening energy are distinct but related symptoms. *J Pain Symptom Manage*. 2015;50(5): 599-614 e593.

11. Abid H, Kober KM, Smoot B, et al. Common and distinct characteristics associated with trajectories of morning and evening energy in oncology patients receiving chemotherapy. *J Pain Symptom Manage*. 2017;53(5): 887-900 e882.
12. Cordova MJ, Riba MB, Spiegel D. Post-traumatic stress disorder and cancer. *Lancet Psychiatry*. 2017;4(4): 330-338.
13. Abbey G, Thompson SB, Hickish T, Heathcote D. A meta-analysis of prevalence rates and moderating factors for cancer-related post-traumatic stress disorder. *Psychooncology*. 2015;24(4): 371-381.
14. Weber D, O'Brien K. Cancer and cancer-related fatigue and the interrelationships with depression, stress, and inflammation. *J Evid Based Complementary Altern Med*. 2017;22(3): 502-512.
15. Morse L, Paul SM, Cooper BA, et al. Higher stress in oncology patients is associated with cognitive and evening physical fatigue severity. *J Pain Symptom Manage*. 2022.
16. Shin J, Harris C, Oppegaard K, et al. Worst pain severity profiles of oncology patients are associated with significant stress and multiple co-occurring symptoms. *J Pain*. 2022;23(1): 74-88.
17. Stacker T, Kober KM, Dunn L, et al. Associations between demographic, clinical, and symptom characteristics and stress in oncology patients receiving chemotherapy. *Cancer Nurs*. 2023;46(1): E62-E69.
18. Oppegaard K, Shin J, Harris CS, et al. Higher stress and symptom severity are associated with worse depressive symptom profiles in patients receiving chemotherapy. *Eur J Oncol Nurs*. 2022;58: 102031.
19. Oppegaard K, Harris CS, Shin J, et al. Anxiety profiles are associated with stress, resilience and symptom severity in outpatients receiving chemotherapy. *Support Care Cancer*. 2021;29(12): 7825-7836.

20. Ward-Ritacco CL, Adrian AL, O'Connor PJ, et al. Feelings of energy are associated with physical activity and sleep quality, but not adiposity, in middle-aged postmenopausal women. *Menopause*. 2015;22(3): 304-311.
21. Marcolongo-Pereira C, Castro F, Barcelos RM, et al. Neurobiological mechanisms of mood disorders: Stress vulnerability and resilience. *Front Behav Neurosci*. 2022;16: 1006836.
22. Miaskowski C, Cooper BA, Aouizerat B, et al. The symptom phenotype of oncology outpatients remains relatively stable from prior to through 1 week following chemotherapy. *Eur J Cancer Care (Engl)*. 2017;26(3).
23. Karnofsky D. Performance scale. New York: Plenum Press; 1977.
24. Babor TF, Higgins-Biddle JC, Saunders JB, Monteiro MG. AUDIT: The Alcohol Use Disorders Identification Test: Guidelines for Use in Primary Care. Geneva, Switzerland: World Health Organization; 2001.
25. Sangha O, Stucki G, Liang MH, Fossel AH, Katz JN. The Self-Administered Comorbidity Questionnaire: a new method to assess comorbidity for clinical and health services research. *Arthritis Rheum*. 2003;49(2): 156-163.
26. Extermann M, Bonetti M, Sledge GW, O'Dwyer PJ, Bonomi P, Benson AB, 3rd. MAX2--a convenient index to estimate the average per patient risk for chemotherapy toxicity; validation in ECOG trials. *Eur J Cancer*. 2004;40(8): 1193-1198.
27. Lee KA, Hicks G, Nino-Murcia G. Validity and reliability of a scale to assess fatigue. *Psychiatry Res*. 1991;36(3): 291-298.
28. Fletcher BS, Paul SM, Dodd MJ, et al. Prevalence, severity, and impact of symptoms on female family caregivers of patients at the initiation of radiation therapy for prostate cancer. *J Clin Oncol*. 2008;26(4): 599-605.
29. Cohen S, Kamarck T, Mermelstein R. A global measure of perceived stress. *J Health Soc Behav*. 1983;24(4): 385-396.

30. Horowitz M, Wilner N, Alvarez W. Impact of Event Scale: a measure of subjective stress. *Psychosom Med.* 1979;41(3): 209-218.
31. Creamer M, Bell R, Failla S. Psychometric properties of the Impact of Event Scale-Revised. *Behav Res Ther.* 2003;41(12): 1489-1496.
32. Wolfe J, Kimmerling R. Gender issues in the assessment of posttraumatic stress disorder. New York: Guilford; 1997.
33. Connor KM, Davidson JR. Development of a new resilience scale: the Connor-Davidson Resilience Scale (CD-RISC). *Depress Anxiety.* 2003;18(2): 76-82.
34. Campbell-Sills L, Stein MB. Psychometric analysis and refinement of the Connor-Davidson Resilience Scale (CD-RISC): Validation of a 10-item measure of resilience. *J Trauma Stress.* 2007;20(6): 1019-1028.
35. Norman GR, Sloan JA, Wyrwich KW. Interpretation of changes in health-related quality of life: the remarkable universality of half a standard deviation. *Med Care.* 2003;41(5): 582-592.
36. Carver CS. You want to measure coping but your protocol's too long: consider the brief COPE. *Int J Behav Med.* 1997;4(1): 92-100.
37. Muthen LK, Muthen BO. *Mplus User's Guide* (8th ed.). 8th ed. Los Angeles, CA: Muthen & Muthen; 1998-2020.
38. Nylund KL, Asparoutiov T, Muthén BO. Deciding on the number of classes in latent class analysis and growth mixture modeling: A Monte Carlo simulation study. *Struct Equ Modeling.* 2007;14(4): 535-569.
39. Muthen B, Shedden K. Finite mixture modeling with mixture outcomes using the EM algorithm. *Biometrics.* 1999;55(2): 463-469.
40. Asakitogum DA, Nutor JA, Pozzar R, et al. Multidimensional model of energy in patients with cancer. *Semin Oncol Nurs.* in press.

41. Tian Q, Glynn NW, Ehrenkranz RC, Sprague BN, Rosso AL, Rosano C. Perception of energy and objective measures of physical activity in older adults. *J Am Geriatr Soc.* 2020;68(8): 1876-1878.
42. Ehrenkranz R, Rosso AL, Sprague BN, et al. Functional correlates of self-reported energy levels in the Health, Aging and Body Composition Study. *Aging Clin Exp Res.* 2021;33(10): 2787-2795.
43. Kober KM, Smoot B, Paul SM, Cooper BA, Levine JD, Miaskowski C. Polymorphisms in cytokine genes are associated with higher levels of fatigue and lower levels of energy in women after breast cancer surgery. *J Pain Symptom Manage.* 2016;52(5): 695-708.
44. Lerdal A, Kottorp A, Gay CL, Lee KA. Lee Fatigue And Energy Scales: exploring aspects of validity in a sample of women with HIV using an application of a Rasch model. *Psychiatry Res.* 2013;205(3): 241-246.
45. Bischel LE, Ritchie C, Kober KM, et al. Age differences in fatigue, decrements in energy, and sleep disturbance in oncology patients receiving chemotherapy. *Eur J Oncol Nurs.* 2016;23: 115-123.
46. Fitch MI, Longo CJ. Emerging understanding about the impact of financial toxicity related to cancer: Canadian perspectives. *Semin Oncol Nurs.* 2021;37(4): 151174.
47. Chan RJ, Gordon LG, Tan CJ, et al. Relationships between financial toxicity and symptom burden in cancer survivors: A systematic review. *J Pain Symptom Manage.* 2019;57(3): 646-660 e641.
48. Sprague BN, Zhu X, Ehrenkranz RC, et al. Declining energy predicts incident mobility disability and mortality risk in healthy older adults. *J Am Geriatr Soc.* 2021;69(11): 3134-3141.
49. Liu Y, Lu L, Yang H, et al. Dysregulation of immunity by cigarette smoking promotes inflammation and cancer: A review. *Environ Pollut.* 2023;339: 122730.

50. Guyatt GH, Osoba D, Wu AW, Wyrwich KW, Norman GR, Clinical Significance Consensus Meeting G. Methods to explain the clinical significance of health status measures. *Mayo Clin Proc.* 2002;77(4): 371-383.
51. Hosack T, Thomas T, Ravindran R, Uhlig HH, Travis SPL, Buckley CD. Inflammation across tissues: can shared cell biology help design smarter trials? *Nat Rev Rheumatol.* 2023;19(10): 666-674.
52. Sogaard M, Thomsen RW, Bossen KS, Sorensen HT, Norgaard M. The impact of comorbidity on cancer survival: a review. *Clin Epidemiol.* 2013;5(Suppl 1): 3-29.
53. Haase KR, Hall S, Sattar S, Ahmed S. Living with cancer and multimorbidity: A qualitative study of self-management experiences of older adults with cancer. *Eur J Oncol Nurs.* 2021;53: 101982.
54. Fried TR, Bradley EH, Towle VR, Allore H. Understanding the treatment preferences of seriously ill patients. *N Engl J Med.* 2002;346(14): 1061-1066.
55. Moy S, Kober KM, Viele C, et al. Level of exercise influences the severity of fatigue, energy levels, and sleep disturbance in oncology outpatients receiving chemotherapy. *Cancer Nurs.* 2022;45(1): 3-11.
56. Luo B, Xiang D, Ji X, et al. The anti-inflammatory effects of exercise on autoimmune diseases: A 20-year systematic review. *J Sport Health Sci.* 2024.
57. Jin L, Diaz-Canestro C, Wang Y, Tse MA, Xu A. Exerkines and cardiometabolic benefits of exercise: from bench to clinic. *EMBO Mol Med.* 2024.
58. Jia D, Tian Z, Wang R. Exercise mitigates age-related metabolic diseases by improving mitochondrial dysfunction. *Ageing Res Rev.* 2023;91: 102087.
59. Lisi V, Senesi G, Balbi C. Converging protective pathways: Exploring the linkage between physical exercise, extracellular vesicles and oxidative stress. *Free Radic Biol Med.* 2023;208: 718-727.

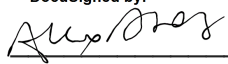
60. Cohen S, Williamson GM. Perceived stress in a probability sample of the United States. In: Spacapan S, Oskamp S, eds. *The Social Psychology of Health*. Newbury Park, CA: Sage; 1988:31-67.
61. Carpenter JS, Andrykowski MA, Sloan P, et al. Postmastectomy/postlumpectomy pain in breast cancer survivors. *J Clin Epidemiol*. 1998;51(12): 1285-1292.
62. Pedro J, Monteiro-Reis S, Carvalho-Maia C, Henrique R, Jerónimo C, Silva ER. Evidence of psychological and biological effects of structured Mindfulness-Based Interventions for cancer patients and survivors: A meta-review. *Psychooncology*. 2021.
63. Welcome MO, Mastorakis NE. Stress-induced blood brain barrier disruption: molecular mechanisms and signaling pathways. *Pharmacol Res*. 2020: 104769.
64. Herman JP, McKlveen JM, Ghosal S, et al. Regulation of the hypothalamic-pituitary-adrenocortical stress response. *Compr Physiol*. 2016;6(2): 603-621.
65. Knezevic E, Nenic K, Milanovic V, Knezevic NN. The role of cortisol in chronic stress, neurodegenerative diseases, and psychological disorders. *Cells*. 2023;12(23).
66. Speer KE, Semple S, Naumovski N, D'Cunha NM, McKune AJ. HPA axis function and diurnal cortisol in post-traumatic stress disorder: A systematic review. *Neurobiol Stress*. 2019;11: 100180.
67. Rao R, Androulakis IP. The physiological significance of the circadian dynamics of the HPA axis: Interplay between circadian rhythms, allostasis and stress resilience. *Horm Behav*. 2019;110: 77-89.
68. De Kloet ER, Vreugdenhil E, Oitzl MS, Joëls M. Brain corticosteroid receptor balance in health and disease. *Endocr Rev*. 1998;19(3): 269-301.
69. Seiler A, Jenewein J. Resilience in Cancer Patients. *Front Psychiatry*. 2019;10: 208.
70. Mancini AD, Bonanno GA. Predictors and parameters of resilience to loss: Toward an individual differences model. *J Personality*. 2009;77(6): 1805-1832.

71. Ang WR, Ang WHD, Cham SQG, de Mel S, Chew HSJ, Devi MK. Effectiveness of resilience interventions among cancer patients - A systematic review, meta-analysis, and meta-regression of randomised controlled trials. *Eur J Oncol Nurs*. 2023;67: 102446.
72. Ding X, Zhao F, Wang Q, et al. Effects of interventions for enhancing resilience in cancer patients: A systematic review and network meta-analysis. *Clin Psychol Rev*. 2024;108: 102381.
73. Wright F, Kober KM, Cooper BA, et al. Higher levels of stress and different coping strategies are associated with greater morning and evening fatigue severity in oncology patients receiving chemotherapy. *Support Care Cancer*. 2020;28(10): 4697-4706.
74. National Comprehensive Cancer Network. NCCN Clinical Practice Guideline In Oncology - Cancer-Related Fatigue; 2022.https://www.nccn.org/professionals/physician_gls/pdf/fatigue.pdf. Accessed January 2 2024.

Publishing Agreement

It is the policy of the University to encourage open access and broad distribution of all theses, dissertations, and manuscripts. The Graduate Division will facilitate the distribution of UCSF theses, dissertations, and manuscripts to the UCSF Library for open access and distribution. UCSF will make such theses, dissertations, and manuscripts accessible to the public and will take reasonable steps to preserve these works in perpetuity.

I hereby grant the non-exclusive, perpetual right to The Regents of the University of California to reproduce, publicly display, distribute, preserve, and publish copies of my thesis, dissertation, or manuscript in any form or media, now existing or later derived, including access online for teaching, research, and public service purposes.

DocuSigned by:

63DF50CFACFB43C... Author Signature

5/13/2024
Date