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Adverse Childhood Experiences Are Associated With Severe Pain and Decrements in Cognitive Function in Patients Receiving Chemotherapy

by
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Adverse Childhood Experiences Are Associated With Severe Pain and Decrements in Cognitive Function in Patients Receiving Chemotherapy

Jacqueline Chen

ABSTRACT

Unrelieved pain and cognitive impairment are common symptoms in oncology patients that exhibit a large amount of inter-individual variability. However, limited information is available on the co-occurrence of these two symptoms and their relationship with stress. Purposes were to identify subgroups of patients (n=1342) with distinct joint profiles of worst pain AND cognitive function (CF) and evaluate for differences in demographic and clinical characteristics, as well as the severity of three distinct types of stress, resilience, and coping. Measures of pain and CF were evaluated six times over two cycles of chemotherapy. The other measures were completed at enrollment (i.e., prior to the second or third cycle of chemotherapy). Using latent profile analysis, four distinct profiles were identified (i.e., No Pain+Moderate CF (27.6%), Moderate Pain+High CF (22.4%) Moderate Pain and Moderate CF (32.4%, Both Moderate), Severe Pain and Low CF (17.5%, Both Severe)). Both Moderate and Both Severe classes reported higher global, cancer-specific, and cumulative life stress, lower levels of resilience, and greater use of disengagement coping strategies. These two class had higher occurrence rates and effect scores for a number of adverse childhood experiences. Risk factors associated with membership in these two profiles included: being female, having a lower annual income, having a higher comorbidity burden, and a poorer functional status. Findings suggest that 72.4% of the patients reported pain scores in the moderate to severe range and 77.6% reported low to moderate levels of CF. Clinicians need to assess for both symptoms and ACEs on a routine basis.

Perspective: Over 50% of oncology patients have moderate to severe pain and impairments in cognitive function. These patients have higher levels of global, cancer-specific, and cumulative life stress, including higher occurrence rates for adverse childhood experiences.

Key words: adverse childhood experiences; cancer; chemotherapy; cognition; cognitive impairment; coping; pain; post-traumatic stress disorder; stress; resilience

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INTRODUCTION

Unrelieved pain[74] and cognitive impairment[48] are common symptoms reported by oncology patients. Between 32.4%[74] and 82.5%[69] of patients report moderate to severe pain. Unrelieved pain can result in interruptions in cancer treatment[17] and significant decrements in quality of life (QOL).[20] Equally disabling, decrements in cognitive function (CF) in over 50% of patients.[26, 40] Most of these patients report decrements in attention, working memory, and multi-tasking.[6] These impairments have a negative impact on patients' ability to work and engage in meaningful social functioning.[7, 48]

Both symptoms exhibit a large amount of inter-individual variability. Recent efforts from our group and others sought to identify risk factors associated with higher levels of pain[25, 68, 69] and cognitive impairment[1, 4] as single symptoms. For example, in our study, that used latent profile analysis (LPA) to identify subgroups of oncology patients with distinct pain profiles,[68] characteristics associated with membership in the severe pain class included fewer years of education, lower annual income, increased likelihood of being single and unemployed, having a worse comorbidity profile, and higher rates of osteoporosis and back pain. In a study that evaluated for risk factors for cognitive impairment,[4] three subgroups with low, moderate, and high levels of CF were identified. Characteristics associated with low levels of CF included younger age, being female, having fewer years of education, and being unemployed.

While no studies have evaluated for inter-individual variability in the co-occurrence of these two symptoms in oncology patients, one plausible underlying mechanism for the co-occurrence and increased severity of BOTH symptoms is unrelieved stress. As noted in a review on the inter-relationships between pain, stress, and executive functions,[29] the functional connectivity between the prefrontal cortex and the limbic system is essential for the "adaptive regulation of primitive, emotional, and stress responses and for emotions that influence

cognitive mechanisms" (p.189). This functional connectivity suggests that reciprocal relationships can occur between/among pain, CF, and stress.

A growing body of evidence suggests that higher levels of perceived stress and cumulative life stress and/or the occurrence of post-traumatic stress disorder (PTSD), are associated with a variety of chronic pain conditions.[8, 39, 45, 51, 70] In our recent study,[68] compared to oncology patients without pain, patients with severe pain reported higher levels of global, cancer-specific, and cumulative life stress, as well as lower levels of resilience.

Similar to pain, in a recent review on associations between psychological variables and cognitive impairment in patients with breast cancer,[78] higher levels of cognitive impairment or poorer performance on neurocognitive tests were associated with higher levels of cancer-specific stress and/or the occurrence of PTSD. In our study of oncology patients,[4] individuals with low levels of CF had higher levels of global stress, Impact of Event Scale-Revised scores suggestive of posttraumatic stress disorder (PTSD), and had lower levels of resilience.

Patients receiving chemotherapy experience various types of unrelieved stress.[3] In the current study, to obtain a more comprehensive evaluation of patients' experiences, three types of stress (i.e., global, cancer-specific, and cumulative life stress) were evaluated. As noted above, unrelieved pain[74] and decrements in CF[48] are common symptoms in patients undergoing chemotherapy. However, no studies have evaluated for inter-individual variability in the co-occurrence of pain and decrements in CF and its association with stress in the same sample of patients. Therefore, study purposes were to identify subgroups of patients with distinct joint profiles of worst pain AND CF and evaluate for differences among these subgroups in demographic and clinical characteristics, as well as the severity of three distinct types of stress, resilience, and coping. In addition, differences the occurrence and effect of specific stressful life events (SLEs) were evaluated.

METHODS

Patients and Settings

This longitudinal study evaluated the symptom experience of oncology outpatients receiving chemotherapy 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. For this analysis, data were available from 1342 patients who completed the measures of pain and CF.

Instruments

Demographic and clinical characteristics

A demographic questionnaire obtained information on age, gender, ethnicity, marital status, living arrangements, education, employment status, and income. In addition, patients completed the Karnofsky Performance Status (KPS) scale,[43] the Alcohol Use Disorders Identification Test,[5] and the Self-administered Comorbidity Questionnaire (SCQ).[65] MAX 2 score was used to evaluate the toxicity of the chemotherapy regimen.[28]

Pain and CF measures

Worst pain severity was assessed using the Brief Pain Inventory (BPI).[24] Patients were asked to indicate whether they were generally bothered by pain (yes/no). If they were generally bothered by pain, they rated their worst pain in the past 24 hours using a 0 (no pain) to 10 (worst pain imaginable) numeric rating scale (NRS).

Self-reported CF was assessed using the Attentional Function Index (i.e., AFI),[16] a 16-item instrument designed to assesses an individual's perceived effectiveness in performing daily

activities that are supported by attention, working memory, and executive functions (e.g., setting goals, planning and carrying out tasks). A higher total mean score on a 0 to 10 NRS indicates greater capacity to direct attention.[16] Clinically meaningful cutpoints for attentional function are as follows: <5.0 low function, 5.0 to 7.5 moderate function, >7.5 high function.[15] Cronbach's alpha for the AFI was 0.93.

Stress and Resilience Measures

The 14-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 week.[18] In a probability sample drawn from the United States population,[19] scores of 18.8 and 20.2 were reported by male and female participants, respectively. Its Cronbach's alpha was 0.85.

The 22-item IES-R was used to measure cancer-specific stress.[36] 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". Three subscales evaluate levels of intrusion, avoidance, and hyperarousal perceived by the patient. Sum scores of $\geq$24 indicate clinically meaningful post traumatic symptomatology and scores of $\geq$33 indicate probable PTSD.[22] 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., death of a loved one, sexual assault).[77] The total LSC–R score is obtained by summing the total number of events endorsed. If patients endorsed an event, they were asked to indicate how much that stressor effected their life in the past year. These responses were summed to yield a total "Affected" sum 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"; "I tend to bounce

back after illness, injury, or other hardships").[10] 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 (±5.4). [9] Its Cronbach's alpha was 0.90.

Coping measure

The 28-item Brief Cope scale was designed to assess a broad range of coping responses among adults.[12] Each item was rated on a Likert scale that ranged from 1 (I haven't been doing this at all) to 4 (I have been doing this a lot). Higher scores indicate greater use of the various coping strategies by the patient. In total, 14 dimensions are evaluated using this instrument (with their respective Cronbach's alphas), namely: self-distraction (0.46), active coping (0.75), denial (0.72), substance use (0.87), use of emotional support (0.77), use of instrumental support (0.77), behavioral disengagement (0.57), venting (0.65), positive reframing (0.79), planning (0.74), humor (0.83), acceptance (0.68), religion (0.92), and self-blame (0.73). Each dimension is evaluated using two items.

Study Procedures

The 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. Eligible patients were approached by a research staff member in the infusion unit during their first or second cycle of chemotherapy to discuss participation in the study. Written informed consent was obtained from all patients. Patients completed the pain and CF measures, 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). Medical records were reviewed for disease and treatment information.

Data Analysis

Latent profile analysis (LPA) was used to identify subgroups of patients with distinct joint worst pain **AND** CF profiles. Before performing the LPA, patients who reported the occurrence of pain for ≤1 of the six assessments were identified and labeled as the "None" class (n=371, 27.6%) and their mean AFI scores were calculated for the six assessments. Then, the LPA was performed on the remaining 971 patients. This LPA was done with the combined set of variables over time (i.e., using the worst pain intensity and AFI scores obtained during the six assessments in a single LPA). This approach provides a profile description of these **two symptoms** with parallel profiles over time. The LPA was done using Mplus version 8.4.[56]

In order to incorporate expected correlations among the repeated measures of the same variable and cross-correlations of the series of the two variables (i.e., worst pain and AFI scores), we included covariance parameters among measures at the same occasion and those that were one or two occasions apart. Covariances of each variable with the other at the same assessments were included in the model, and autoregressive covariances were estimated with a lag of two with the same measures and with a lag of one for each variable's series with the other variable. We limited the covariance structure to a lag of two to accommodate the expected reduction in the correlations that would be introduced by two chemotherapy cycles within each set of three measurement occasions and to reduce model complexity.[42] Model fit was evaluated to identify the solution that best characterized the observed latent class structure with the Bayesian Information Criterion, Vuong-Lo-Mendell-Rubin likelihood ratio test (VLMR), entropy, and latent class percentages that were large enough to be reliable.[55] Missing data were accommodated for with the use of the Expectation-Maximization (EM) algorithm.[54]

Data were analyzed using SPSS version 28 (IBM Corporation, Armonk, NY). Descriptive statistics and frequency distributions were calculated for demographic and clinical characteristics. Differences among the worst pain AND CF classes in the enrollment measures were evaluated using parametric and nonparametric tests. A p-value of <0.05 was considered

statistically significant. Post hoc contrasts were done using a Bonferroni corrected p-value of <.008 (.05/6 possible pairwise comparisons).

RESULTS

Latent Profile Analysis

The 371 patients (27.6%) who had ≤1 occurrence of pain over the six assessments were classified as the No Pain and Moderate CF class (No Pain + Moderate CF). For the remaining 971 patients whose data were entered into the LPA, a 3-class solution was selected based on the criteria listed in Table 1. Figure 1 displays the trajectories of worst pain and CF for the four classes. The latent classes were named based on clinically meaningful cutpoints for worst pain and AFI scores. Of the total 1342 patients, 27.6% were in the No Pain + Moderate CF, 22.4% in the Moderate Pain and High CF (Moderate Pain + High CF), 32.4% in the Moderate Pain and Moderate CF (Both Moderate), and 17.5% in the Severe Pain and Low CF (Both Severe) classes. For all of the study measures, detailed differences among the four classes are found in Tables 2 through 6. Comparisons between the No Pain + Moderate CF class and the other three classes are summarized in Table 7.

Differences in Demographic and Clinical Characteristics

As shown in Table 2, compared to the No Pain + Moderate CF class, the Both Severe class was younger, less likely to be married or partnered, more likely to live alone, and more likely to have a past or current history of smoking. Compared to the No Pain + Moderate CF class, the Both Moderate and Both Severe classes were more likely to be female, have fewer years of education, were less likely to be employed, more likely to have a lower annual household income, and less likely to exercise on a regular basis.

Compared to the No Pain + Moderate CF class, the Both Severe class had a higher body mass index (BMI) and was more likely to self-report heart disease and diabetes, and was more likely to have had surgery, chemotherapy, and radiation therapy. Compared to the No Pain + Moderate CF class, the Both Moderate and Both Severe classes were more likely to

have a lower functional status, a higher comorbidity burden, were more likely to self-report anemia or blood disease, depression, osteoarthritis, and back pain, and were less likely to have gastrointestinal cancer (Table 2).

Differences in Stress and Resilience Measures

As shown in Table 3, compared to the No Pain + Moderate CF class, the Both Severe class had higher IES-R avoidance, LSC-R total, and LSC-R PTSD sum scores. Compared to the No Pain + Moderate CF class, the Both Moderate and Both Severe classes had higher PSS, IES-R total, IES-R intrusion, IES-R hyperarousal, and LSC-R affected scores and lower CDRS scores.

Differences in the Occurrence and Effect of Life Stressors

As shown in Table 4, compared to the No Pain + Moderate CF class, the Both Severe class reported higher occurrence rates for the following stressors: family violence in childhood, emotional abuse, physical neglect, physical abuse at $\leq$16 and $\geq$16 years of age, forced sex at $\leq$16 and $\geq$16 years of age, had a serious accident of injury, had a family member in jail, had parents who were separated or divorced, and had been separated from a child. Compared to the No Pain + Moderate CF class, the Both Moderate and Both Severe classes reported higher occurrence rates for the following stressors: sexual harassment, forced to touch at $\leq$16 and $\geq$16 years of age, serious money problems, and had a serious physical or mental illness that was not related to cancer.

As shown in Table 5, compared to the No Pain + Moderate CF class, the Both Severe class reported higher effect of life stressor scores for the following stressors: family violence in childhood, been in a serious disaster, being separated or divorced, having a serious physical or mental illness that was not related to cancer, and having an abortion or miscarriage. Compared to the No Pain + Moderate CF class, the Both Moderate and Both Severe classes reported higher effect of life stressor scores for had a serious accident or injury and had some close die that was not sudden.

Differences in Coping Strategies

As shown in Table 6, compared to the No Pain + Moderate CF class, the Both Severe class reported less use of active coping and acceptance and higher use of denial and behavioral disengagement. Compared to the No Pain + Moderate CF class, the Both Moderate and Both Severe classes reported higher use of religion, venting, substance use, and self-blame.

DISCUSSION

This study is the first to identify subgroups of patients with distinct joint worst pain and CF profiles. Examination of the four distinct profiles warrant consideration. Of note, 72.4% of the patients reported pain scores in the moderate to severe range and 77.6% reported low to moderate levels of CF. However, for 50% of the sample only one symptom was in the moderate range. In addition, for the brief period of approximately two months, within each class, severity of the two symptoms remained relatively stable. These data are consistent with studies of older adults that suggested that reciprocal relationships exist between pain and CF.[41, 76]

Stress

Compared to No Pain+Moderate CF class, Both Moderate and Both Severe classes had higher PSS scores. These patients' scores were slightly lower than PSS score of 29.6 reported by stroke patients.[61] However, they are higher than scores reported by oncology patients during the COVID-19 pandemic.[52] In terms of cancer-specific stress, a similar pattern was observed. While the IES-R total score for Both Severe class suggests clinically meaningful PTSD symptomatology, 15.2% and 35.4% of patients in Both Moderate and Both Severe classes, respectively had scores that indicated probable PTSD. Of note, compared to No Pain+Moderate CF class, Both Severe class had higher LSC-R scores, higher occurrence rates for over 50% of the stressors listed on the LSC-R, and higher effect scores for seven of the endorsed stressors. Majority of these stressors are categorized as adverse childhood

experiences (ACEs; i.e., family violence in childhood, emotional abuse, physical neglect, physical abuse at <16 years of age and being forced to touch and have sex at <16 years of age).

In terms of ACEs, early life stress increases the risk of developing disorders related to stress,[30, 53] pain,[44, 49, 73] and cognitive impairments.[21, 33] For example, children exposed to ACEs have reduced prefrontal cortex volumes and demonstrate dysregulation of the hypothalamic-pituitary-adrenal axis (HPA).[23, 58] In addition, early life stress is associated with altered receptor sensitivity within HPA axis and blunted reactivity,[11] as well as with decreases in hippocampal-prefrontal connections that may impair learning.[72]

Given that 25% of women and 8% of men in the United States have experienced sexual abuse during childhood,[59] oncology clinicians need to assess for both symptoms and ACEs. Integration of this type of evaluation into routine care is important given the findings from a study of cancer survivors who experienced ACEs.[66] For these survivors, cancer and its treatments triggered thoughts and emotions associated with the original abuse and negative evaluations of themselves and their future. While clinicians may argue that an assessment of ACEs is time consuming, in a study that used a single item as a proxy for ACEs,[47] lower relationship scores were associated with an increased risk for 21 suboptimal health outcomes.

Interactions among pain, CF, and stress are complex. As noted in one review,[29] "executive functions" is a collective term that encompasses working attention, memory, and multi-tasking ability. These aspects of CF occur in the prefrontal cortex, a region of the brain that has functional connections with the limbic system (e.g., hippocampus) that is involved in the processing of emotion-related information. In addition, these brain regions are connected to the brainstem which plays a role in arousal and autonomic control. Pathways between the hippocampus and the prefrontal cortex are essential for executive functioning and emotional regulation. Of note, this pathway is vulnerable to dysregulation by chronic stress and chronic

pain. Therefore, because pain, CF, and stress share common neural circuits, any acute and/or chronic alterations among them can manifest as increases in pain and/or decrements in CF.

Patient Characteristics

Common demographic characteristics associated with membership in Both Moderate and Both Severe classes included: being female, having fewer years of education, being unemployed, and having a lower annual household income. Our results are consistent with previous reports that found that women report higher occurrence rates for a variety of chronic pain conditions.[13, 31, 34, 62] In terms of CF,[46] gender differences in this symptom vary by neurological disorder and are influenced by age. For example, males typically do better on spatial tasks while women do better on verbal tasks. In addition, sex differences exist in brain networks that are activated during cognitive and learning tasks. Given the high percentage of females in our study, future studies need to recruit patients with cancers that have an equal gender distribution to be able to draw definitive conclusions on gender differences.

In the general population[64, 71] and oncology patients,[14, 35, 37] moderate to severe pain and decrements in CF are associated with changes in employment status, loss of income, and financial stress. These associations are supported by the fact that 22.9% and 34.1% of the patients in the Both Moderate and Both Severe classes, respectively reported stress associated with serious money problems. As noted in one study,[75] given the strong associations between pain and financial worries and low income, interventions to decrease pain need to address economic instability and financial stressors.

It is not surprising that compared to No Pain+Moderate CF class, the other three classes with moderate to severe pain reported higher occurrence rates for osteoarthritis and back pain, as well as a higher comorbidity burden. In addition, Both Moderate and Both Severe classes reported higher rates of depression and a poorer functional status. While not evaluated in this study, it is reasonable to hypothesize that unrelieved pain and associated worry, anxiety, and

depression are mentally exhausting. The depletion of cognitive reserves can lead to decrements in CF.[29] Equally plausible, patients who are taking analgesics may experience adverse effects including impairments in cognition.

Resilience

Resilience is described as the ability to adapt to and overcome difficult situations in the face of adversity.[67] In the current study, three profiles with low to moderate levels of CF had CDRS scores below the normative score for the United States population. As noted in one review, cognitive dysfunction, avoidance behaviors, and impaired resilience may be a byproduct of ACEs. While the mechanisms of resilience are unknown, evidence suggests that the brain's reward system plays a critical role in modulating stress responses in ways that confer resilience.[27]

Coping

Compared to No Pain+Moderate CF class, Both Moderate and Both Severe classes reported higher use of one engagement coping strategy, namely religion. While evidence from one review suggests that religious and spiritual interventions had only small effects on improving health behaviors and QOL,[32] clinicians need to assess the spiritual beliefs and practices of oncology patients. The use of this coping strategy may enhance personal growth, psychological resilience, and improve cognitive health.[60]

In terms of disengagement coping, while not evaluated in this study, pain catastrophizing may be related to venting. Pain catastrophizing is a maladaptive cognitive strategy that is associated with magnification of threats from painful sensations and/or the anticipation of pain.[63] Our results are consistent with a study that found that higher catastrophizing scores were associated with poorer CF.[50] In addition, given that our patients had higher scores for substance use and that positive associations were found between pain catastrophizing scores and pain medication use,[38] the Both Moderate and Both High classes need to be assessed regarding the

efficacy of their pain management plan and the concurrent use of alcohol and other licit and illicit substances.

Limitations

Given that the majority of the sample was female, White, well-educated, and had a relatively high annual income, additional research is warranted on the influences of gender, level of education, and financial instability on the severity of pain and cognitive impairments. Because detailed information was not obtained on analgesic prescriptions, how the effects of analgesics influence the joint pain and CF profiles warrant additional investigation. Future studies need to evaluate patients' pain and CF using subjective and objective measures and changes in stress over time.

Implications for Practice and Research

A variety of interventions may be used to decrease pain and improve CF in the context of the high levels of stress, particularly ACEs, identified in patients in the Both Moderate and Both High classes. Clinicians need to perform detailed assessments of pain, CF, stress, resilience, and coping. Particular attention needs to be paid to the causes of cancer and non-cancer pain and the efficacy of the patients' pain management interventions. Given that 63% of this sample reported non-cancer pain, oncology clinicians will need to coordinate with primary care providers to optimize the management of these conditions. Patients will benefit from referrals to mental health professionals who can provide guidance on stress reduction techniques and cognitive behavioral interventions.

Given the paucity of research on the co-occurrence of pain and decrements in CF in oncology patients, future studies using a similar design and analytic methods should be done across various types of cancer treatments. To increase our knowledge of the pain experience of oncology patients, future studies should include measures or pain catastrophizing[57] and pain self-efficacy.[2] Associations between these joint pain and CF profiles and other common symptoms and QOL outcomes warrant evaluation.

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Trajectories of Joint pain and Cognitive Function Profiles

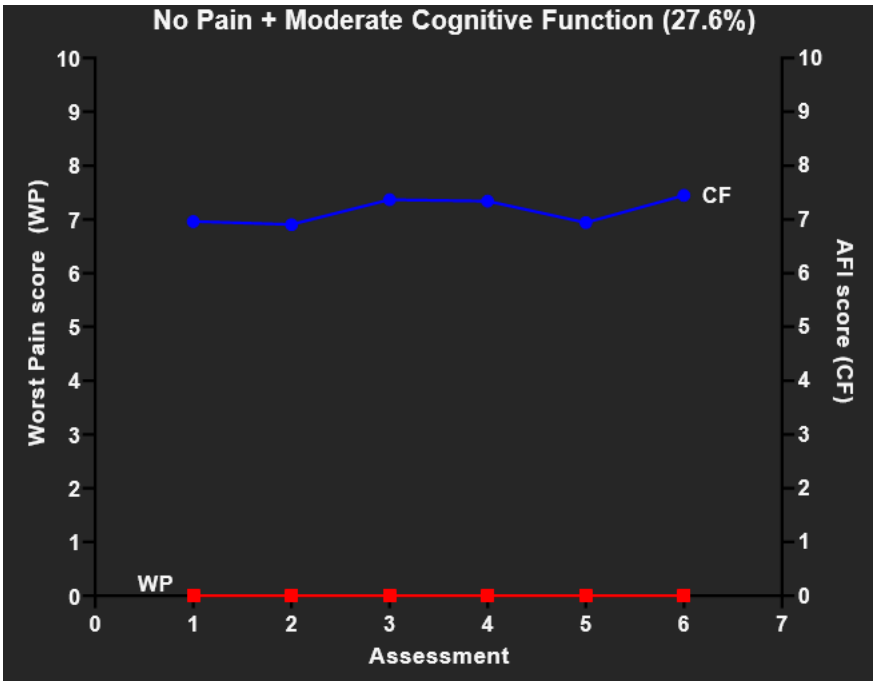

Figure 1.1

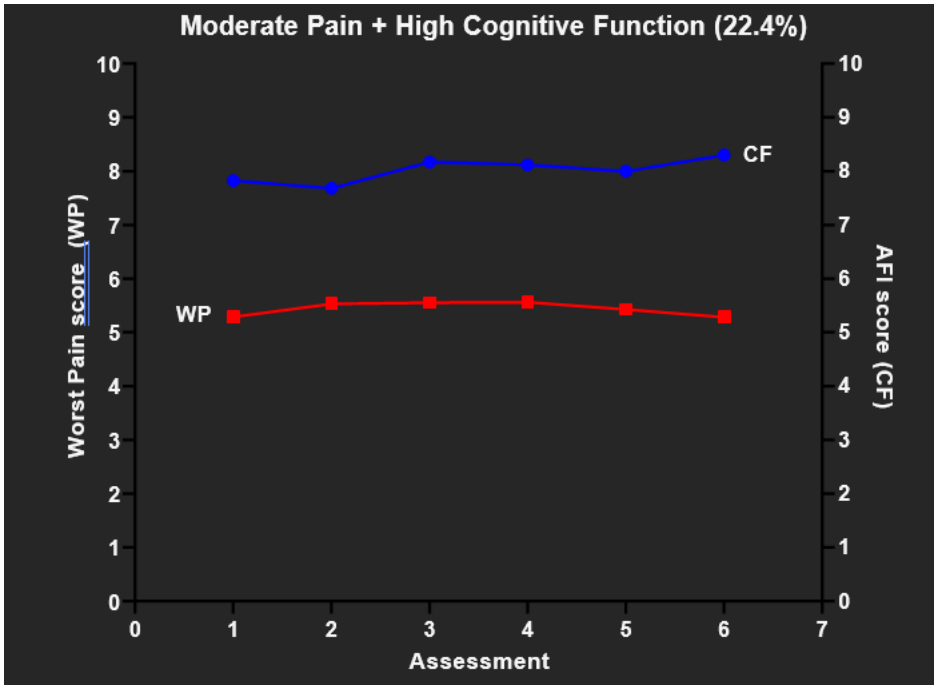

Figure 1.2

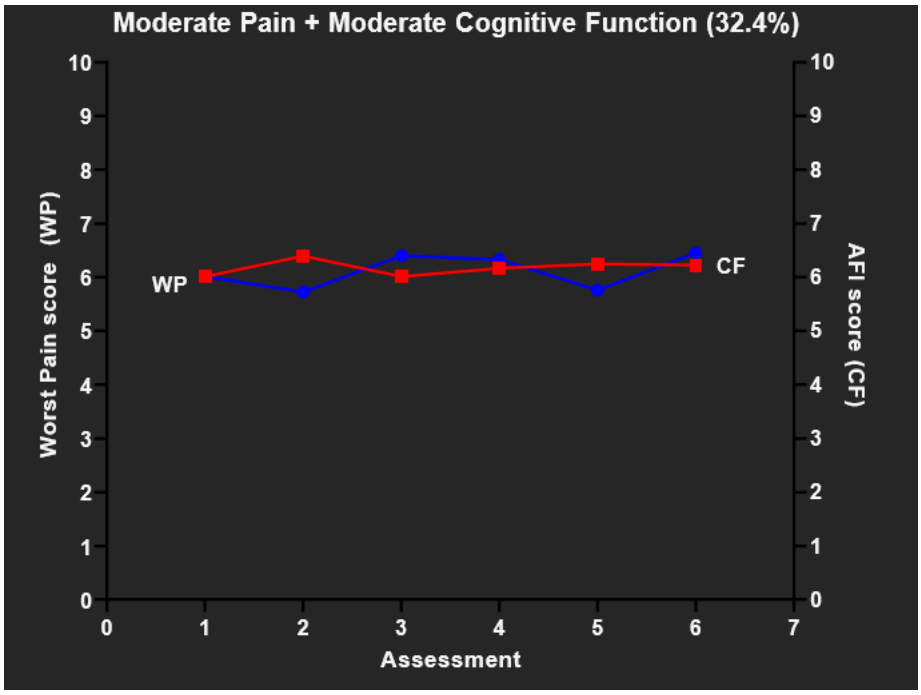

Figure 1.3

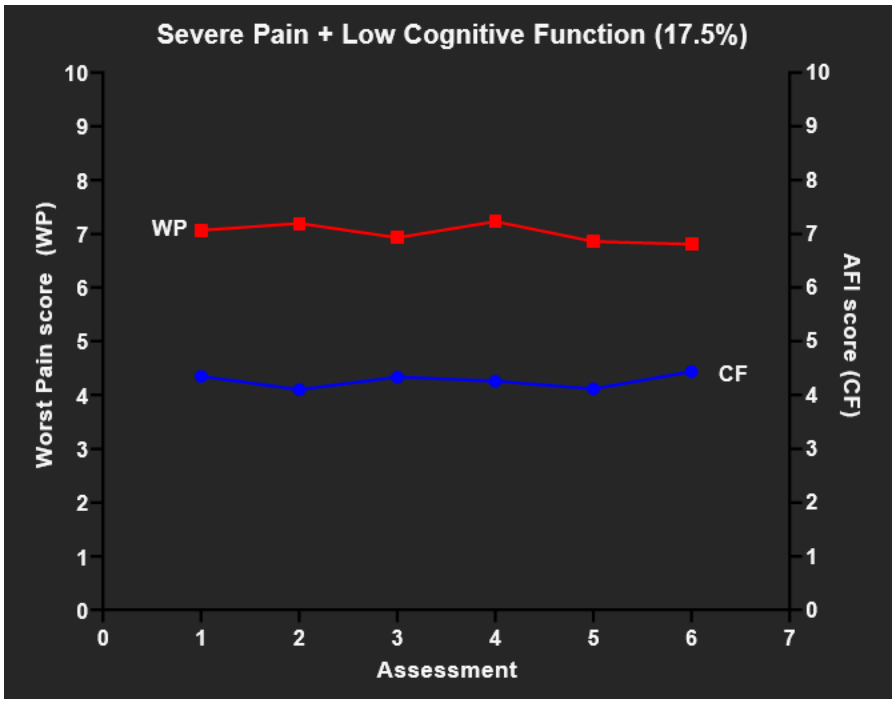

Figure 1.4

Table 1 – Worst Pain and Attentional Function Index Scores over Six Assessments: Latent Profile Solutions and Fit Indices for One through Four Classes

Model	LL	AIC	BIC	Entropy	VLMR
1 Class	-16546.57	33225.15	33547.12	n/a	n/a
2 Class	-16198.24	32554.48	32939.87	0.77	696.67‡
3 Class[a]	-16069.68	32323.35	32772.16	0.75	257.13*
4 Class	-15950.92	32111.85	32624.07	0.76	ns

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

*p <.05; ‡p <.00005

[a]The 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 was not significant for the 4-class solution, indicating that too many classes were 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 – Differences in Demographic and Clinical Characteristics Among the Pain and Cognitive Function Latent Classes at Enrollment

Characteristic	No Pain and Moderate Cognitive Function (0) 27.6% (n=371)	Moderate Pain and High Cognitive Function (1) 22.4% (n=301)	Moderate Pain and Moderate Cognitive Function (2) 32.4% (n=435)	Severe Pain and Low Cognitive Function (3) 17.5% (n=235)	Statistics
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	
Age (years)	58.2 (11.9)	58.5 (11.0)	56.4 (13.3)	55.1 (12.5)	F = 4.78, p = .003 0 and 1 > 3
Education (years)	16.7 (3.2)	16.4 (3.0)	15.9 (2.9)	15.8 (3.0)	F = 5.84, p = .001 0 > 2 and 3
Body mass index (kg/m^2)	25.5 (5.5)	26.2 (5.1)	26.3 (5.6)	27.0 (6.5)	F = 3.34, p = .019 0 < 3
Alcohol Use Disorders Identification Test score	3.0 (2.0)	2.7 (2.0)	3.0 (2.8)	3.2 (3.1)	F = 1.47, p = .220
Karnofsky Performance Status score	84.8 (11.5)	83.6 (11.5)	77.7 (11.2)	71.6 (12.4)	F = 74.58, p <.001 0 and 1 > 2 and 3; 2 > 3
Number of comorbid conditions	1.9 (1.1)	2.4 (1.4)	2.5 (1.5)	3.0 (1.6)	F = 31.56, p <.001 0, 1, and 2 < 3; 0 < 1 and 2
Self-administered Comorbidity Questionnaire score	4.3 (2.4)	5.2 (2.7)	5.8 (3.2)	7.2 (3.9)	F = 46.01, p <.001 0 < 1 < 2 < 3
Time since diagnosis (years)	1.7 (3.2)	2.4 (4.2)	1.9 (4.0)	2.1 (4.1)	KW = 15.28, p = .002 0 and 2 < 1
Time since diagnosis (years, median)	0.40	0.49	0.40	0.45	
Number of prior cancer treatments	1.3 (1.3)	1.8 (1.6)	1.6 (1.5)	1.9 (1.6)	F = 8.46, p <.001 0 < 1 and 3; 2 < 3
Number of metastatic sites including lymph node involvement[a]	1.1 (1.2)	1.4 (1.2)	1.3 (1.3)	1.2 (1.3)	F = 2.78, p = .040 0 < 1
Number of metastatic sites excluding lymph node involvement	0.7 (0.9)	0.9 (1.1)	0.8 (1.1)	0.8 (1.1)	F = 3.03, p = .029 0 < 1
MAX2 score	0.17 (0.08)	0.16 (0.08)	0.18 (0.08)	0.19 (0.08)	F = 6.09, p <.001 1 < 2 and 3
	% (n)	% (n)	% (n)	% (n)	
Gender (% female)	71.9 (266)	70.4 (212)	84.4 (367)	84.3 (198)	X^2 = 33.45, p <.001 0 and 1 < 2 and 3
Self-reported ethnicity					X^2 = 19.28, p = .023
White	70.5 (260)	69.2 (204)	72.1 (308)	63.2 (148)	NS
Asian or Pacific Islander	12.5 (46)	12.5 (37)	13.3 (57)	12.0 (28)	NS
Black	6.8 (25)	10.2 (30)	4.9 (21)	8.1 (19)	1 > 2
Hispanic, Mixed, or Other	10.3 (38)	8.1 (24)	9.6 (41)	16.7 (39)	1 and 2 < 3

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Table 2 – Differences in Demographic and Clinical Characteristics Among the Pain and Cognitive Function Latent Classes at Enrollment

Hispanic, Mixed, or Other	10.3 (38)	8.1 (24)	9.6 (41)	16.7 (39)	1 and 2 < 3
Married or partnered (% yes)	69.6 (256)	68.9 (204)	63.5 (273)	52.8 (121)	X^2 = 20.45, p <.001 0, 1, and 2 > 3
Lives alone (% yes)	18.8 (69)	17.6 (52)	22.6 (97)	28.1 (65)	X^2 = 10.65, p = .014 0 and 1 < 3
Currently employed (% yes)	42.2 (154)	39.9 (119)	32.5 (140)	22.6 (53)	X^2 = 28.34, p <.001 0 > 2 > 3; 1 > 3
Annual household income Less than $30,000 $30,000 to $70,000 $70,000 to $100,000 Greater than $100,000	 9.7 (32) 17.0 (56) 19.7 (65) 53.6 (177)	 14.2 (37) 19.9 (52) 18.8 (49) 47.1 (123)	 20.1 (79) 24.9 (98) 16.0 (63) 38.9 (153)	 33.3 (72) 22.2 (48) 12.0 (26) 32.4 (70)	KW = 55.47, p <.001 0, 1, and 2 > 3; 0 > 2
Child care responsibilities (% yes)	22.0 (80)	19.5 (57)	22.2 (95)	25.1 (58)	X^2 = 2.35, p = 0.503
Elder care responsibilities (% yes)	6.2 (21)	7.6 (21)	9.3 (36)	8.9 (19)	X^2 = 2.59, p = 0.460
Past or current history of smoking (% yes)	30.2 (110)	35.5 (106)	35.8 (152)	42.2 (98)	X^2 = 9.05, p = .029 0 < 3
Exercise on a regular basis (% yes)	77.7 (283)	73.9 (221)	68.1 (288)	60.6 (137)	X^2 = 22.74, p <.001 0 > 2 and 3; 1 > 3
Specific comorbid conditions (% yes)					
Heart disease	3.2 (12)	7.3 (22)	5.1 (22)	8.5 (20)	X^2 = 9.49, p = .023 0 < 3
High blood pressure	29.1 (108)	33.2 (100)	29.2 (127)	29.8 (70)	X^2 = 1.74, p = .628
Lung disease	9.4 (35)	11.0 (33)	11.7 (51)	14.5 (34)	X^2 = 3.71, p = .294
Diabetes	7.0 (26)	11.6 (35)	6.7 (29)	13.5 (32)	X^2 = 13.21, p = .004 0 and 2 < 3
Ulcer or stomach disease	3.0 (11)	4.7 (14)	5.1 (22)	7.7 (18)	X^2 = 6.95, p = .073
Kidney disease	0.8 (3)	0.3 (1)	2.1 (9)	2.6 (6)	X^2 = 7.02, p = .071
Liver disease	5.4 (20)	7.6 (23)	7.4 (32)	5.1 (12)	X^2 = 2.68, p = .444
Anemia or blood disease	8.4 (31)	10.0 (30)	14.7 (64)	16.6 (39)	X^2 = 13.30, p = .004 0 < 2 and 3
Depression	10.5 (39)	9.0 (27)	21.1 (92)	42.1 (99)	X^2 = 119.28, p <.001 0 and 1 < 2 and 3; 2 < 3
Osteoarthritis	5.9 (22)	14.3 (43)	14.7 (64)	14.5 (34)	X^2 = 18.60, p <.001 0 < 1, 2, and 3
Back pain	7.3 (27)	25.5 (76)	33.3 (145)	41.3 (97)	X^2 = 109.08, p <.001 0 < 1, 2, and 3; 1 < 3
Rheumatoid arthritis	0.8 (3)	4.7 (14)	3.4 (15)	4.3 (10)	X^2 = 10.02, p = .018 0 < 1 and 3

Table 2 – Differences in Demographic and Clinical Characteristics Among the Pain and Cognitive Function Latent Classes at Enrollment

Cancer diagnosis					$X^2 = 26.94$, p = .001
Breast cancer	38.5 (143)	36.9 (111)	42.5 (185)	43.0 (101)	NS
Gastrointestinal cancer	35.6 (132)	37.2 (112)	25.3 (110)	24.3 (57)	0 and 1 > 2 and 3
Gynecological cancer	13.2 (49)	14.6 (44)	21.1 (92)	20.4 (48)	0 < 2
Lung cancer	12.7 (47)	11.3 (34)	11.0 (48)	12.3 (29)	NS
Prior cancer treatment					$X^2 = 28.24$, p = .001
No prior treatment	29.2 (105)	22.9 (67)	24.9 (105)	20.3 (47)	NS
Only surgery, CTX, or RT	44.0 (158)	37.3 (109)	45.1 (190)	39.7 (92)	NS
Surgery and CTX, or surgery and RT, or CTX and RT	15.3 (55)	25.3 (74)	19.7 (83)	20.3 (47)	0 < 1
Surgery and CTX and RT	11.4 (41)	14.4 (42)	10.2 (43)	19.8 (46)	0 < 3
Metastatic sites					
No metastasis	34.8 (126)	26.4 (79)	33.0 (142)	34.5 (80)	
Only lymph node metastasis	22.4 (81)	22.1 (66)	21.4 (92)	22.8 (53)	$X^2 = 8.22$, p = .513
Only metastatic disease in other sites	19.1 (69)	24.4 (73)	21.6 (93)	19.4 (45)	
Metastatic disease in lymph nodes and other sites	23.8 (86)	27.1 (81)	24.0 (103)	23.3 (54)	
Receipt of targeted therapy					
No	73.5 (263)	63.2 (187)	71.3 (306)	71.4 (165)	$X^2 = 9.21$, p = .027
Yes	26.5 (95)	36.8 (109)	28.7 (123)	28.6 (66)	Targeted - yes – 0 < 1
Cycle length					
14 day cycle	45.4 (166)	45.2 (135)	40.5 (174)	35.5 (82)	KW = 5.62, p = .132
21 day cycle	48.2 (176)	46.2 (138)	51.9 (223)	58.0 (134)	
28 day cycle	6.3 (23)	8.7 (26)	7.7 (33)	6.5 (15)	
Emetogenicity of the CTX regimen					
Minimal/low	14.8 (54)	22.7 (68)	19.7 (85)	22.5 (52)	KW = 14.88, p = .002
Moderate	60.8 (222)	62.9 (188)	61.0 (263)	58.9 (136)	0 > 1
High	24.4 (89)	14.4 (43)	19.3 (83)	18.6 (43)	
Antiemetic regimen					
None	6.7 (24)	10.0 (29)	5.0 (21)	8.0 (18)	
Steroid alone or serotonin receptor antagonist alone	18.5 (66)	19.2 (56)	23.7 (100)	19.0 (43)	
Serotonin receptor antagonist and steroid	48.3 (172)	48.8 (142)	47.2 (199)	46.0 (104)	$X^2 = 11.65$, p = .234
NK-1 receptor antagonist and two other antiemetics	26.4 (94)	22.0 (64)	24.2 (102)	27.0 (61)	

[a]Total number of metastatic sites evaluated was 9 Abbreviations: CTX = chemotherapy, kg = kilograms, KW = Kruskal Wallis, m^2 = meters squared, NK-1 = neurokinin-1, NS = not significant, RT = radiation therapy, SD = standard deviation

Table 3 – Differences in Stress and Resilience Measures Among the Pain and Cognitive Function Latent Classes at Enrollment

Measures[a]	No Pain and Moderate Cognitive Function (0) 27.6% (n=371)	Moderate Pain and High Cognitive Function (1) 22.4% (n=301)	Moderate Pain and Moderate Cognitive Function (2) 32.4% (n=435)	Severe Pain and Low Cognitive Function (3) 17.5% (n=235)	Statistics
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	
PSS total score (0 to 56)	16.0 (7.9)	14.1 (6.1)	19.8 (7.1)	25.7 (7.4)	F = 131.64, p <.001 1 < 0 < 2 < 3
IES-R total score (≥24 – clinically meaningful symptomatology) (≥33 – probable PTSD) for PTSD	15.5 (10.6)	13.8 (9.0)	20.0 (12.8)	28.3 (16.2)	F = 71.60, p <.001 0 and 1 < 2 and 3; 2 < 3
IES-R intrusion	0.7 (0.6)	0.7 (0.5)	1.0 (0.7)	1.4 (0.8)	F = 63.74, p <.001 0 and 1 < 2 and 3; 2 < 3
IES-R avoidance	0.9 (0.6)	0.8 (0.6)	1.0 (0.7)	1.2 (0.8)	F = 15.16, p <.001 0, 1, and 2 < 3; 1 < 2
IES-R hyperarousal	0.5 (0.5)	0.3 (0.4)	0.7 (0.6)	1.3 (0.8)	F= 124.99, p <.001 1 < 0 < 2 < 3
LSC-R total score (range 0–30)	4.8 (3.2)	5.6 (3.6)	6.3 (3.8)	7.9 (4.8)	F= 25.11, p <.001 0, 1 and 2 < 3; 1 < 3
LSC-R affected sum (range 0-150)	8.3 (7.2)	9.9 (8.9)	12.8 (10.9)	17.9 (14.3)	F= 34.97, p <.001 0 and 1 < 2 and 3; 2 < 3
LSC-R PTSD sum (range 0-21)	2.1 (2.4)	2.8 (2.7)	3.4 (3.0)	4.5 (3.8)	F=27.26, p <.001 0, 1 and 2 < 3; 0 < 2
CDRS total score (31.8 (±5.4) – normative range for the United States population)	31.1 (6.3)	32.3 (5.2)	29.7 (6.0)	26.2 (6.8)	F= 47.91, p <.001 0 and 1 > 2 and 3; 2 > 3

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

[a]Clinically meaningful cutoff scores or range of scores

Table 4 – Differences in the Percentage of Patients Exposed to Various Stressors on the Life-Stressor Checklist-Revised Among the Pain and Cognitive Function Classes

Stressful Life Event	No Pain and Moderate Cognitive Function (0) 27.6% (n=371)	Moderate Pain and High Cognitive Function (1) 22.4% (n=301)	Moderate Pain and Moderate Cognitive Function (2) 32.4% (n=435)	Severe Pain and Low Cognitive Function (3) 17.5% (n=235)	Statistics
	% (n)	% (n)	% (n)	% (n)	
Interpersonal Violence, Abuse, and Neglect Stressors					
Family violence in childhood	19.0 (49)	21.4 (54)	22.7 (76)	35.8 (64)	$X^2 = 18.44$, $p < .001$ 0, 1, and 2 < 3
Emotional abuse	17.1 (44)	14.1 (36)	22.6 (76)	37.2 (68)	$X^2 = 37.99$, $p < .001$ 0, 1, and 2 < 3
Physical neglect	1.5 (4)	3.9 (10)	5.7 (19)	9.3 (17)	$X^2 = 15.09$, $p = .002$ 0 < 3
Sexual harassment	8.5 (22)	15.2 (38)	20.4 (68)	32.2 (58)	$X^2 = 42.98$, $p < .001$ 0 < 2 < 3
Physical abuse - <16 years	10.0 (26)	11.9 (30)	15.3 (51)	22.1 (40)	$X^2 = 14.33$, $p = .002$ 0 and 1 < 3
Physical abuse - ≥16 years	10.0 (26)	9.6 (24)	14.4 (48)	22.3 (40)	$X^2 = 18.30$, $p < .001$ 0 and 1 < 3
Forced to touch - <16 years	6.2 (16)	7.6 (19)	13.9 (46)	20.7 (38)	$X^2 = 27.32$, $p < .001$ 0 < 2 and 3; 1 < 3
Forced to touch - ≥16 years	2.3 (6)	4.8 (12)	7.2 (24)	11.0 (20)	$X^2 = 15.58$, $p = .001$ 0 < 2 and 3
Forced sex - <16 years	1.6 (4)	2.8 (7)	5.7 (19)	8.2 (15)	$X^2 = 14.10$, $p = .003$ 0 < 3
Forced sex - ≥16 years	3.5 (9)	4.0 (10)	7.5 (25)	12.0 (22)	$X^2 = 16.28$, $p = .001$ 0 and 1 < 3

Table 5 – Differences in the Effect of Each of the Stressors on Life Over the Past Year Among the Pain and Cognitive Function Classes

Stressful Life Event[a]	No Pain and Moderate Cognitive Function (0)	Moderate Pain and High Cognitive Function (1)	Moderate Pain and Moderate Cognitive Function (2)	Severe Pain and Low Cognitive Function (3)	Statistics
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	
Interpersonal Violence, Abuse, and Neglect Stressors					
Family violence in childhood	1.6 (1.1)	1.8 (1.1)	1.9 (1.2)	2.3 (1.2)	KW = 12.61, p = .006 0 < 3
Emotional abuse	2.4 (1.4)	2.3 (1.5)	2.5 (1.2)	3.0 (1.2)	KW = 9.72, p =.021 no significant pairwise contrasts
Physical neglect	2.8 (2.1)	3.0 (1.5)	2.7 (1.3)	2.8 (1.2)	KW = 0.50, p = .918
Sexual harassment	1.5 (1.2)	1.2 (0.6)	1.7 (1.1)	1.5 (0.8)	KW = 5.50, p = .139
Physical abuse - <16 years	1.7 (1.1)	1.9 (1.2)	1.8 (1.2)	2.3 (1.4)	KW = 6.39, p = .094
Physical abuse - ≥16 years	1.7 (1.2)	1.8 (1.0)	1.9 (1.3)	2.0 (1.2)	KW = 1.25, p = .742
Forced to touch - <16 years	1.6 (1.3)	1.5 (0.9)	2.0 (1.4)	2.4 (1.4)	KW = 9.13, p = .028 no significant pairwise contrasts
Forced to touch - ≥16 years	1.0 (0.0)	1.9 (1.4)	2.3 (1.4)	1.7 (0.9)	KW = 7.35, p = .061
Forced sex - <16 years	2.0 (1.2)	1.7 (0.8)	2.1 (1.5)	2.1 (1.3)	KW = 0.16, p = .983
Forced sex - ≥16 years	1.6 (1.3)	2.0 (1.5)	1.8 (1.2)	1.6 (1.0)	KW = 1.22, p = .749
Other Stressors					
Been in a serious disaster	1.2 (0.7)	1.3 (0.7)	1.4 (0.9)	1.5 (0.8)	KW = 9.48, p = .024 0 < 3

Table 6 – Differences in Brief COPE Subscale Scores at Enrollment Among the Pain and Cognitive Function Classes

Subscale*	No Pain and Moderate Cognitive Function (0) 27.6% (n=371)	Moderate Pain and High Cognitive Function (1) 22.4% (n=301)	Moderate Pain and Moderate Cognitive Function (2) 32.4% (n=435)	Severe Pain and Low Cognitive Function (3) 17.5% (n=235)	Statistics
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	
Engagement Coping Strategies					
Active coping	6.0 (1.7)	6.3 (1.6)	6.0 (1.6)	5.5 (1.6)	F = 8.93, p <.001 0, 1, and 2 > 3
Planning	5.2 (1.8)	5.3 (1.9)	5.4 (1.8)	5.4 (1.7)	F = 1.30, p = .271
Positive reframing	5.3 (2.0)	5.5 (2.0)	5.5 (1.9)	5.3 (1.8)	F = 1.98, p = .116
Acceptance	6.7 (1.4)	6.9 (1.3)	6.7 (1.3)	6.4 (1.4)	F = 6.96, p <.001 0, 1, and 2 > 3
Humor	4.3 (2.0)	4.2 (2.0)	4.4 (1.9)	4.4 (2.0)	F = 0.69, p = .560
Religion	4.7 (2.3)	5.0 (2.4)	5.1 (2.3)	5.3 (2.2)	F = 3.87, p = .009 0 < 2 and 3
Using emotional support	6.4 (1.7)	6.4 (1.6)	6.4 (1.7)	6.1 (1.6)	F = 2.31, p = .075
Using instrumental support	5.3 (1.8)	5.2 (1.8)	5.4 (1.7)	5.3 (1.7)	F = 1.16, p = .323
Disengagement Coping Strategies					
Self-distraction	5.4 (1.8)	5.5 (1.7)	5.5 (1.6)	5.5 (1.5)	F = 0.36, p = .782
Denial	2.5 (1.0)	2.3 (0.7)	2.6 (1.2)	2.7 (1.3)	F = 8.65, p <.001 0 and 1 < 3; 1 < 2
Venting	3.8 (1.6)	3.6 (1.6)	4.2 (1.6)	4.4 (1.6)	F = 13.49, p <.001 0 and 1 < 2 and 3
Substance use	2.1 (0.5)	2.2 (0.6)	2.3 (0.9)	2.4 (0.9)	F = 7.01, p <.001 0 and 1 < 3; 0 < 2
Behavioral disengagement	2.2 (0.6)	2.1 (0.6)	2.2 (0.7)	2.6 (1.1)	F = 20.51, p <.001 0, 1, and 2 < 3
Self-blame	2.6 (1.0)	2.5 (1.0)	3.0 (1.3)	3.5 (1.5)	F = 37.71, p <.001 0 and 1 < 2 and 3; 2 < 3

Abbreviation: SD = standard deviation *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"). 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 Pain and Cognitive Function Latent Classes

Characteristic[a]	Moderate Pain + High Cognitive Function	Moderate Pain + Moderate Cognitive Function	Severe Pain + Low Cognitive Function
Demographic Characteristics			
More likely to be younger			■
Fewer years of education		■	■
More likely to be female		■	■
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 past or current history of smoking			■
Less likely to exercise on a regular basis		■	■
Clinical Characteristics			
Higher body mass index			■
Lower functional status (KPS score)		■	■
Higher number of comorbidities	■	■	■
Higher comorbidity burden (SCQ score)	■	■	■
Longer time since cancer diagnosis	■		
Higher number of prior cancer treatments	■		■
Higher number of metastatic sites including lymph node involvement	■		
Higher number of metastatic sites excluding lymph node involvement	■		
More likely to self-report heart disease			■
More likely to self-report diabetes			■
More likely to self-report anemia or blood disease		■	■
More likely to self-report depression		■	■
More likely to self-report osteoarthritis	■	■	■
More likely to self-report back pain	■	■	■
More likely to self-report rheumatoid arthritis	■		■
Less likely to have gastrointestinal cancer		■	■
More likely to have gynecological cancer		■	
More likely to have received surgery and CTX, or surgery and RT, or CTX and RT	■		
More likely to have received surgery and CTX and RT			■
More likely to have received targeted therapy	■		
Less likely to have received a highly emetogenic CTX regimen	■		
Stress Characteristics			
Higher Perceived Stress Scale score		■	■

Stress Characteristics			
Lower 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		■	■
Lower 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 PTDS sum score			■
Lower Connor Davidson Resilience Scale total score		■	■
Higher Occurrence of Life Stressors			
Family violence in childhood			■
Emotional abuse			■
Physical neglect			■
Sexual harassment		■	■
Physical abuse - <16 years			■
Physical abuse - ≥16 years			■
Forced to touch – <16 years		■	■
Forced to touch – ≥16 years		■	■
Forced sex – <16 years			■
Forced sex – ≥16 years			■
Been in a serious disaster	■		
Seen serious accident	■	■	
Had serious accident or injury			■
Jail (family member)			■
Separated/divorced (parents)			■
Serious money problems		■	■
Had serious physical or mental illness (not cancer)		■	■
Separated from child			■
Higher Effect of Life Stressors			
Family violence in childhood			■
Been in serious disaster			■
Had serious accident or injury		■	■
Separated/divorced (parents)		■	
Separated/divorced (self)			■
Had serious physical or mental illness (not cancer)			■
Abortion or miscarriage			■

Higher Effect of Life Stressors			
Death of someone close (not sudden)		■	■
Seen robbery or mugging		■	
Use of Coping Strategies			
Less use of active coping			■
Less use of acceptance			■
Higher use of religion		■	■
Higher use of denial			■
Higher use of venting		■	■
Higher use of substances		■	■
Higher use of behavioral disengagement			■
Higher use of self-blame		■	■

[a]Comparisons done with the No Pain and Moderate Cognitive Function class

■ – Indicates the presence of the risk factor compared to the No Pain and Moderate Cognitive Function class

Abbreviation: CTX = chemotherapy, KPS = Karnofsky Performance Statue, PTSD = post-traumatic stress disorder, RT = radiation therapy, SCQ = Self-Administered Comorbidity Questionnaire

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