

# Stress and Coping in Patients With Cancer With Depression and Sleep Disturbance

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**OBJECTIVES:** To evaluate for differences in global, cancer-specific, and cumulative life stress, as well as resilience and use of various coping strategies among five groups (no depression or sleep disturbance, no depression and moderate sleep disturbance, subsyndromal depression and very high sleep disturbance, moderate depression and moderate sleep disturbance [Both Moderate]; and high depression and very high sleep disturbance [Both High]).

**SAMPLE & SETTING:** Patients (N = 1,331) receiving chemotherapy were recruited from outpatient oncology clinics.

**METHODS & VARIABLES:** Measures of global, cancer-specific, and cumulative life stress, resilience, and coping were obtained. Differences were evaluated using parametric and nonparametric tests.

**RESULTS:** Global and cancer-specific stress scores increased as joint profiles worsened. Both Moderate and Both High classes had cancer-specific stress scores suggestive of post-traumatic stress. Both Moderate and Both High classes reported higher occurrence rates for several stressful life events and higher use of disengagement coping. Both Moderate and Both High classes had resilience scores below the normative score for the United States.

**IMPLICATIONS FOR NURSING:** Clinicians need to screen vulnerable patients for post-traumatic stress disorder and implement interventions to reduce stress.

**KEYWORDS** adverse childhood experiences; cancer; chemotherapy; depression; sleep disturbance; stress  
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Although depression and sleep disturbance are often evaluated independently, limited evidence suggests that these two symptoms co-occur in patients receiving chemotherapy (Brant et al., 2011; Whisenant et al., 2019). For example, in a longitudinal study of patients with breast cancer that explored whether membership in the sleep disturbance and depressed mood classes was associated with other symptoms (Whisenant et al., 2019), women in the higher sleep disturbance class reported more days with moderate to severe depressed mood. In another study of patients with cancer (Brant et al., 2011), depression and sleep disturbance co-occurred with pain, distress, and fatigue during the first six cycles of chemotherapy. The current authors used latent profile analysis (LPA) to evaluate for subgroups of patients with distinct joint depression and sleep disturbance profiles during chemotherapy (Calvo-Schimmel et al., 2022). More than 45% of these patients had subsyndromal to high levels of depression and moderate or very high levels of sleep disturbance. Risk factors associated with the worse joint depression and sleep disturbance profiles included being female and unemployed; having a lower functional status and a higher comorbidity burden; and reporting higher severity scores for anxiety, fatigue, and pain.

Although these three studies evaluated for the co-occurrence of depression and sleep disturbance in patients with cancer undergoing chemotherapy (Brant et al., 2011; Calvo-Schimmel et al., 2022; Whisenant et al., 2019), limited information is available on modifiable and nonmodifiable risk factors. Emerging evidence suggests that higher levels of stress (a modifiable risk factor) are associated with an increased risk of depression and sleep disturbance in patients with cancer. For example, in a study of patients with relapsed/refractory chronic

lymphocytic leukemia (Goyal et al., 2018), higher levels of cancer-specific stress were associated with higher levels of depression and sleep disturbance at the initiation of chemotherapy. In addition, higher levels of cancer-specific stress were associated with worse depressive symptoms at five months post-treatment. In another study of patients with ovarian cancer (Garvin et al., 2021), a higher number and severity of chronic, but not acute, stressful life events (SLEs) were associated with higher levels of depression and sleep disturbance from prior to surgery or neoadjuvant chemotherapy through one year following the cancer diagnosis. In a study of women with metastatic breast cancer (Palesh et al., 2007), higher levels of life stress and depression at enrollment were associated with more problems with sleep initiation and maintenance, as well as higher levels of daytime sleepiness. In addition, increases in depressive symptoms during the course of 12 months were associated with fewer hours of sleep, more problems with sleep maintenance, and more daytime sleepiness. Although this limited evidence provides some insights into the associations between stress and depression and sleep disturbance as single symptoms, none of these studies evaluated for the co-occurrence of these two symptoms in patients with cancer and its relationship with three distinct types of stress (i.e., global, cancer-specific, and cumulative life stress), as well as resilience and coping.

Although the characterization of resilience is complex, it represents an adaptive response to stress (Osório et al., 2017). Specifically in patients with cancer, higher levels of resilience allow for a better adjustment to SLEs and better symptom management (Osório et al., 2017; Tamura, 2021). For example, in a study of patients with heterogeneous types of cancer (Mungase et al., 2021), higher levels of depression were associated with lower levels of resilience. In another study of patients with breast cancer (Lai et al., 2020), worse sleep quality was associated with lower levels of resilience.

Coping—which encompasses how patients appraise diverse situations, change their perceptions, and effectively modify their coping strategies based on their resources—is a multidimensional process to deal with various types of stress (Cieślak et al., 2012; Eto et al., 2022). Coping behaviors are often divided into disengagement and engagement strategies. The use of disengagement coping strategies (e.g., avoidance) is more likely to lead to higher distress. In contrast, the use of engagement coping strategies (e.g., humor) is often associated with an increased sense of control

(Dijkstra & Homan, 2016). A limited amount of evidence suggests that coping mediates the relationship between depression and sleep disturbance and stress in patients with cancer (Hyphantis et al., 2016; Seib et al., 2018). For example, in a study of patients with breast cancer (Lee, Youn, et al., 2019), women who slept better and coped with negative SLEs through acceptance experienced fewer depressive symptoms.

Given the paucity of research on the co-occurrence of depression and sleep disturbance in patients undergoing chemotherapy (Brant et al., 2011; Calvo-Schimmel et al., 2022; Whisenant et al., 2019) and its relationship with various types of stress, the purpose of this study, which builds on the current authors' previous LPA analysis (Calvo-Schimmel et al., 2022), was to evaluate for differences in global, cancer-specific, and cumulative life stress, as well as resilience and the use of various coping strategies among five subgroups of patients with distinct joint depression and sleep disturbance profiles. The authors hypothesized that patients in the worse depression and sleep disturbance profiles would report higher levels of all three types of stress, lower levels of resilience, and increased use of disengagement coping strategies.

## Methods

### Patients and Settings

This study is part of a larger, longitudinal study of the symptom experience of outpatients with cancer receiving chemotherapy (Calvo-Schimmel et al., 2022). The theory of symptom management served as the conceptual framework for the larger study (Weiss et al., 2023). Specifically, this study examined the relationship between the symptom experience concept (i.e., depression and sleep disturbance) and the health and illness domain (i.e., cancer, stress).

Briefly, patients were aged 18 years or older; had a diagnosis of breast, gastrointestinal, gynecologic, 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 provided written informed consent. Patients were recruited from two comprehensive cancer centers, one Veterans Affairs hospital, and four community-based oncology programs during their first or second cycle of chemotherapy.

### Study Procedures

The study was approved by the institutional review board at each of the study sites. Of the 2,234 patients approached, 1,343 consented to participate. The major

reason for refusal was being too overwhelmed with their cancer treatment. Patients completed depression and sleep disturbance questionnaires, in their homes, a total of six times during two chemotherapy cycles (i.e., prior to chemotherapy administration, about one week after chemotherapy administration, and about two weeks after chemotherapy administration). All the other measures were completed at enrollment (i.e., prior to the second or third cycle of chemotherapy). A total of 1,331 patients who completed the depression and sleep disturbance measures were included in the LPA.

### Instruments

**Demographic and clinical measures:** Patients completed a demographic questionnaire, the Karnofsky Performance Status Scale (Karnofsky, 1977), the Self-Administered Comorbidity Questionnaire (Sangha et al., 2003), the Alcohol Use Disorders Identification Test (Bohn et al., 1995), and a smoking history questionnaire. The toxicity of each patient's chemotherapy regimen was rated using the MAX2 score (Extermann et al., 2004). Medical records were reviewed for disease and treatment information.

**Depression and sleep disturbance measures:** The 20-item Center for Epidemiological Studies Depression Scale evaluates the major symptoms in the clinical syndrome of depression (Radloff, 1977). A total score can range from 0 to 60, with scores of 16 or greater indicating the need for individuals to seek clinical evaluation for depression (Moon et al., 2017). Its Cronbach's alpha was 0.89.

The 21-item General Sleep Disturbance Scale (GSDS) was designed to assess various aspects of sleep disturbance. Each item was rated on a numeric rating scale ranging from 0 (never) to 7 (every day). The GSDS total score ranges from 0 (no disturbance) to 147 (extreme sleep disturbance) (Lee, 1992). A GSDS total score of 43 or greater indicates a significant level of sleep disturbance that warrants clinical evaluation and management (Fletcher et al., 2008). Cronbach's alpha for the GSDS total score was 0.83.

**Stress, resilience, and coping 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 during the course of the previous week (Cohen et al., 1983). Each item was rated on a Likert-type scale ranging from 0 (never) to 4 (very often). Total PSS scores can range from 0 to 56. Its Cronbach's alpha was 0.85.

The 22-item Impact of Event Scale-Revised (IES-R) was used to measure cancer-related distress (Horowitz et al., 1979). 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 24 or greater indicate clinically meaningful post-traumatic symptomatology, and scores of 33 or greater indicate probable post-traumatic stress disorder (PTSD) (Creamer et al., 2003). The 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, the death of a loved one, a sexual assault) (Wolfe & Kimerling, 1997). 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 affected their life in the past year. These responses were summed to yield a mean "affected sum" score. In addition, a PTSD sum score was created based on the number of positively endorsed items (of 21) that reflect the *Diagnostic and Statistical Manual of Mental Disorders*, 4th edition, 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") (Campbell-Sills & Stein, 2007). Total scores range from 0 to 40, with higher scores indicative of higher self-perceived resilience. The normative adult mean score in the United States is 31.8 (SD = 5.4) (Campbell-Sills et al., 2009). Its Cronbach's alpha was 0.9.

The 28-item Brief COPE scale was designed to assess a broad range of coping responses among adults (Carver, 1997; Carver et al., 1989). Each item was rated on a Likert-type scale ranging from 1 (I have not been doing this at all) to 4 (I have been doing this a lot). Higher scores indicate greater use of the various coping strategies. 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.

### Data Analysis

As described previously (Calvo-Schimmel et al., 2022), LPA was used to identify unobserved subgroups of patients (i.e., latent classes) with distinct joint depression and sleep disturbance profiles over the six assessments, using the Center for Epidemiological Studies Depression Scale and GSDS scores. In brief, LPA was performed using MPlus, version 8.4 (Muthén & Muthén, 1998–2017). Estimation was carried out with full information maximum likelihood with standard errors and a chi-square test

that are robust to non-normality and nonindependence of observations (“estimator=MLR”). Model fit was evaluated to identify the solution that best characterized the unobserved latent class structure with the Bayesian information criterion, Vuong–Lo–Mendell–Rubin likelihood ratio test, entropy, and latent class percentages that were large enough to be reliable (Muthén & Muthén, 1998–2017; Nylund et al., 2007). Missing data were accommodated for with the use of the expectation–maximization algorithm (Muthén & Shedden, 1999).

**TABLE 1. Differences in Stress and Resilience Measures Among the Joint Depression and Sleep Disturbance Latent Classes at Enrollment**

| Measures <sup>a</sup>              | No Depression or Sleep Disturbance (0) (N = 285) |     | No Depression and Moderate Sleep Disturbance (1) (N = 430) |     | Subsyndromal Depression and Very High Sleep Disturbance (2) (N = 272) |      | Moderate Depression and Moderate Sleep Disturbance (3) (N = 235) |      | High Depression and Very High Sleep Disturbance (4) (N = 109) |      | Statistics   |
|------------------------------------|--|-----|--|-----|---|------|--|------|---|------|--|
|                                    | $\bar{X}$  | SD  | $\bar{X}$  | SD  | $\bar{X}$   | SD   | $\bar{X}$  | SD   | $\bar{X}$   | SD   |  |
| PSS total score (range = 0–56)     | 12.7   | 5.9 | 16   | 6.5 | 19.6  | 6.6  | 23.3   | 6.5  | 30.6  | 6.6  | F = 203.2, p < 0.001<br>0 < 1 < 2 < 3 < 4                            |
| IES-R total score (≥ 24)           | 10.2   | 7.5 | 15.1   | 9.5 | 20.7  | 10.8 | 24.1   | 11.6 | 40  | 16.2 | F = 180.05, p < 0.001<br>0 < 1 < 2 < 3 < 4                           |
| IES-R intrusion                    | 0.4  | 0.4 | 0.7  | 0.5 | 1   | 0.6  | 1.2  | 0.6  | 2   | 0.8  | F = 168.47, p < 0.001<br>0 < 1 < 2 < 3 < 4                           |
| IES-R avoidance                    | 0.7  | 0.6 | 0.8  | 0.6 | 1   | 0.6  | 1.2  | 0.7  | 1.6   | 0.8  | F = 46.32, p < 0.001<br>0 < 1 < 2 < 3 < 4                            |
| IES-R hyperarousal                 | 0.2  | 0.3 | 0.5  | 0.4 | 0.8   | 0.6  | 0.9  | 0.6  | 1.9   | 0.7  | F = 232.81, p < 0.001<br>0 < 1 < 2, 3, and 4;<br>2 and 3 < 4         |
| LSC-R total score (range = 0–30)   | 5  | 3.2 | 5.6  | 3.4 | 6.4   | 4    | 6.8  | 4.5  | 8.6   | 4.8  | F = 18.4, p < 0.001<br>0 and 1 < 3 and 4;<br>0 < 2; 2 and 3 < 4      |
| LSC-R affected sum (range = 0–150) | 8.2  | 7.8 | 9.8  | 8   | 12.4  | 10.2 | 15   | 13.9 | 21.9  | 14.1 | F = 36.97, p < 0.001<br>0 and 1 < 2, 3, and 4;<br>2 and 3 < 4        |
| LSC-R PTSD sum (range = 0–21)      | 2.1  | 2.4 | 2.7  | 2.5 | 3.4   | 3.2  | 3.7  | 3.4  | 5.2   | 3.7  | F = 22.51, p < 0.001<br>0 and 1 < 2, 3, and 4;<br>2 and 3 < 4        |
| CDRS total score (range = 0–40)    | 32.4   | 5.1 | 31.3   | 6.2 | 30.1  | 5.9  | 27.6   | 6.2  | 24.3  | 6.6  | F = 49.21, p < 0.001<br>0 > 2, 3, and 4;<br>1 and 2 > 3 and 4; 3 > 4 |

<sup>a</sup>Clinically meaningful cutoff scores or range of scores  
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

Data were analyzed using IBM SPSS Statistics, version 29.0. Differences among the joint depression and sleep disturbance classes in stress, resilience, and coping at enrollment were evaluated using parametric and nonparametric tests. A Bonferroni-corrected *p* value of less than 0.005 was considered statistically significant for the pairwise contrasts (i.e., 0.05/10 possible pairwise contrasts).

## Results

### LPA

As described previously (Calvo-Schimmel et al., 2022), five latent classes were identified and named no depression (DEP) or sleep disturbance (SLD) (21%, None); no depression and moderate sleep disturbance (32%, No DEP+Mod SLD); subsyndromal depression and very high sleep disturbance (20%, SubS DEP+Very High SLD); moderate depression and moderate sleep disturbance (18%, Both Moderate); and high depression and very high sleep disturbance (8%, Both High). Except for the Both High class, patients in the other four classes had both symptom scores increase slightly at the second and fifth assessments (i.e., following the administration of chemotherapy). For the Both High class, while depression scores increased slightly at the second and fifth assessments, sleep disturbance scores increased at the second assessment and remained high over time (see Supplemental Figure 1 online).

### Sample Characteristics

In terms of differences in demographic and clinical characteristics among the latent classes (Calvo-Schimmel et al., 2022), in brief, the overall sample (*N* = 1,331) was predominantly female, White, and college educated. Compared to the None class, patients in the other four classes were more likely to be female; less likely to be employed; more likely to self-report a diagnosis of depression; had lower functional status; and had a higher comorbidity burden (see Supplemental Table 1 online).

### Stress and Resilience

Significant differences were found among the five latent classes in PSS total, IES-R total, and IES-R intrusion and avoidance subscales scores at enrollment (i.e., None < No DEP+Mod SLD < SubS DEP+Very High SLD < Both Moderate < Both High). Compared to the None class, the other four classes reported higher IES-R hyperarousal subscale scores. Compared to the None and No DEP+Mod SLD classes, Both Moderate and Both High classes reported higher LSC-R total

scores. Compared to the None and No DEP+Mod SLD classes, the other three classes reported higher LSC-R affected sum and PTSD sum scores. In terms of resilience, compared to the None class, the SubS DEP+Very High SLD, Both Moderate, and Both High classes reported lower CDRS scores (see Table 1).

### Occurrence of SLEs

Significant differences were found among the classes in the occurrence of 54% of the SLEs listed on the LSC-R (see Table 2). Compared to the None class, the SubS DEP+Very High SLD, Both Moderate, and Both High classes reported higher occurrence rates for sexual harassment and forced to touch before the age of 16 years. Compared to the None class, Both Moderate and Both High classes reported higher occurrence rates for physical abuse at age 16 years or older, having a family member jailed, having serious money problems, and having a non-cancer-related serious physical or mental illness. Compared to the None class, the Both High class reported higher occurrence rates for forced to touch at age 16 years or older and being separated from a child. Compared to the None and No DEP+Mod SLD classes, the other three classes reported higher occurrence rates for emotional abuse. Compared to the None and No DEP+Mod SLD classes, Both Moderate and Both High classes reported higher occurrence rates for physical neglect and physical abuse before the age of 16 years. Compared to the None and No DEP+Mod SLD classes, the Both High class reported higher occurrence rates for having parents separated/divorced and caring for someone with a severe physical or mental handicap. Compared to the None, No DEP+Mod SLD, and SubS DEP+Very High SLD classes, the Both High class reported higher occurrence rates for family violence in childhood. Compared to the None class, the SubS DEP+Very High SLD class reported higher occurrence rates for forced sex before the age of 16 years.

### Effect of SLEs

Compared to the None class, the Both Moderate class reported higher effected scores for being separated/divorced, the sudden death of someone close, and being robbed/mugged (see Table 3). Compared to the None class, the Both High class reported higher effected scores for caring for someone with severe physical or mental handicap. Compared to the None and No DEP+Mod SLD classes, the Both Moderate and Both High classes reported higher effected scores for having serious money problems. Compared to the None and No DEP+Mod SLD classes, the Both High class reported higher effected scores for seeing

**TABLE 2. Differences Among the Joint Depression and Sleep Disturbance Latent Classes in the Percentage of Patients Exposed to Various Stressors on the Life Stressor Checklist–Revised at Enrollment**

| Stressful Life Event  | No Depression or Sleep Disturbance (0) (N = 285) |    | No Depression and Moderate Sleep Disturbance (1) (N = 430) |    | Subsyndromal Depression and Very High Sleep Disturbance (2) (N = 272) |    | Moderate Depression and Moderate Sleep Disturbance (3) (N = 235) |    | High Depression and Very High Sleep Disturbance (4) (N = 109) |    | Statistics   |
|---|--|----|--|----|---|----|--|----|---|----|--|
|   | n  | %  | n  | %  | n   | %  | n  | %  | n   | %  |  |
| <b>Interpersonal violence, abuse, and neglect stressors</b> |  |    |  |    |   |    |  |    |   |    |  |
| Family violence in childhood                                | 42   | 19 | 72   | 21 | 40  | 21 | 53   | 30 | 36  | 43 | $\chi^2 = 26.84, p < 0.001$<br>0, 1, and 2 < 4                   |
| Emotional abuse   | 30   | 13 | 51   | 15 | 53  | 27 | 51   | 28 | 39  | 47 | $\chi^2 = 59.33, p < 0.001$<br>0 and 1 < 2 and 3 < 4             |
| Physical neglect  | 6  | 3  | 6  | 2  | 8   | 4  | 19   | 11 | 11  | 13 | $\chi^2 = 35.85, p < 0.001$<br>0 and 1 < 3 and 4                 |
| Sexual harassment   | 22   | 10 | 56   | 16 | 43  | 22 | 38   | 21 | 27  | 34 | $\chi^2 = 27.99, p < 0.001$<br>0 < 2, 3, and 4; 1 < 4            |
| Physical abuse before the age of 16 years                   | 22   | 10 | 38   | 11 | 29  | 15 | 37   | 26 | 21  | 26 | $\chi^2 = 21.7, p < 0.001$<br>0 and 1 < 3 and 4                  |
| Physical abuse at age 16 years or older                     | 19   | 8  | 37   | 11 | 31  | 16 | 34   | 19 | 17  | 22 | $\chi^2 = 17.34, p = 0.002$<br>0 < 3 and 4                       |
| Forced to touch before the age of 16 years                  | 14   | 6  | 26   | 8  | 29  | 15 | 33   | 19 | 17  | 20 | $\chi^2 = 28.08, p < 0.001$<br>0 < 2, 3, and 4;<br>1 < 3 and 4   |
| Forced to touch at age 16 years or older                    | 7  | 3  | 14   | 4  | 15  | 18 | 16   | 9  | 10  | 12 | $\chi^2 = 14.41, p = 0.006$<br>0 < 4                             |
| Forced sex before the age of 16 years                       | 2  | 1  | 16   | 5  | 14  | 7  | 8  | 5  | 5   | 6  | $\chi^2 = 10.71, p = 0.03$<br>0 < 2                              |
| Forced sex at age 16 years or older                         | 9  | 4  | 16   | 5  | 19  | 10 | 13   | 7  | 9   | 11 | $\chi^2 = 10.16, p = 0.038$<br>No significant pairwise contrasts |
| <b>Other stressors</b>                                      |  |    |  |    |   |    |  |    |   |    |  |
| Been in a serious disaster                                  | 94   | 41 | 139  | 41 | 79  | 41 | 69   | 38 | 40  | 46 | $\chi^2 = 1.54, p = 0.82$  |
| Seen serious accident                                       | 70   | 31 | 122  | 36 | 62  | 32 | 51   | 28 | 33  | 38 | $\chi^2 = 4.36, p = 0.359$                                       |
| Had serious accident or injury                              | 49   | 22 | 73   | 22 | 49  | 25 | 50   | 28 | 27  | 31 | $\chi^2 = 6.28, p = 0.179$                                       |

*Continued on the next page*

**TABLE 2. Differences Among the Joint Depression and Sleep Disturbance Latent Classes in the Percentage of Patients Exposed to Various Stressors on the Life Stressor Checklist–Revised at Enrollment (Continued)**

| Stressful Life Event                                     | No Depression or Sleep Disturbance (0) (N = 285) |    | No Depression and Moderate Sleep Disturbance (1) (N = 430) |    | Subsyndromal Depression and Very High Sleep Disturbance (2) (N = 272) |    | Moderate Depression and Moderate Sleep Disturbance (3) (N = 235) |    | High Depression and Very High Sleep Disturbance (4) (N = 109) |    | Statistics  |
|--|--|----|--|----|---|----|--|----|---|----|---|
|  | n  | %  | n  | %  | n   | %  | n  | %  | n   | %  |   |
| <i>Other stressors (continued)</i>                       |  |    |  |    |   |    |  |    |   |    |   |
| Jail (family member)                                     | 33   | 14 | 69   | 20 | 38  | 19 | 46   | 26 | 26  | 30 | $\chi^2 = 13.77, p = 0.008$<br>0 < 3 and 4                      |
| Jail (self)  | 10   | 4  | 22   | 6  | 18  | 9  | 12   | 7  | 8   | 9  | $\chi^2 = 4.79, p = 0.309$                                      |
| Foster care or put up for adoption                       | 5  | 2  | 5  | 2  | 5   | 3  | 5  | 3  | 5   | 6  | $\chi^2 = 5.77, p = 0.217$                                      |
| Separated/divorced (parents)                             | 37   | 16 | 72   | 21 | 45  | 23 | 40   | 23 | 31  | 36 | $\chi^2 = 14.66, p = 0.005$<br>0 and 1 < 4                      |
| Separated/divorced (self)                                | 74   | 32 | 122  | 35 | 63  | 32 | 75   | 32 | 40  | 48 | $\chi^2 = 10.02, p = 0.04$<br>No significant pairwise contrasts |
| Serious money problems                                   | 31   | 13 | 51   | 15 | 43  | 22 | 44   | 24 | 37  | 44 | $\chi^2 = 44.17, p < 0.001$<br>0 < 3 < 4                        |
| Had serious physical or mental illness (not cancer)      | 28   | 12 | 56   | 16 | 40  | 21 | 45   | 25 | 28  | 32 | $\chi^2 = 23.09, p < 0.001$<br>0 < 3 and 4;<br>1 < 4            |
| Abortion or miscarriage                                  | 67   | 43 | 130  | 47 | 66  | 41 | 63   | 42 | 34  | 47 | $\chi^2 = 2.23, p = 0.693$                                      |
| Separated from child                                     | 1  | 1  | 5  | 2  | 5   | 3  | 5  | 3  | 5   | 6  | $\chi^2 = 11.05, p = 0.026$<br>0 < 4                            |
| Care for child with handicap                             | 6  | 3  | 16   | 5  | 6   | 3  | 4  | 2  | 7   | 9  | $\chi^2 = 7.83, p = 0.098$                                      |
| Care for someone with severe physical or mental handicap | 50   | 22 | 69   | 20 | 55  | 29 | 41   | 23 | 33  | 39 | $\chi^2 = 15.54, p = 0.004$<br>0 and 1 < 4                      |
| Death of someone close (sudden)                          | 111  | 49 | 171  | 50 | 91  | 47 | 79   | 45 | 51  | 60 | $\chi^2 = 5.46, p = 0.244$                                      |
| Death of someone close (not sudden)                      | 169  | 78 | 268  | 79 | 154   | 79 | 143  | 81 | 65  | 78 | $\chi^2 = 0.87, p = 0.929$                                      |

*Continued on the next page*

**TABLE 2. Differences Among the Joint Depression and Sleep Disturbance Latent Classes in the Percentage of Patients Exposed to Various Stressors on the Life Stressor Checklist–Revised at Enrollment (Continued)**

| Stressful Life Event        | No Depression or Sleep Disturbance (0) (N = 285) |    | No Depression and Moderate Sleep Disturbance (1) (N = 430) |    | Subsyndromal Depression and Very High Sleep Disturbance (2) (N = 272) |    | Moderate Depression and Moderate Sleep Disturbance (3) (N = 235) |    | High Depression and Very High Sleep Disturbance (4) (N = 109) |    | Statistics                 |
|-----------------------------|--|----|--|----|---|----|--|----|---|----|----------------------------|
|                             | n  | %  | n  | %  | n   | %  | n  | %  | n   | %  |                            |
| Other stressors (continued) |  |    |  |    |   |    |  |    |   |    |                            |
| Seen robbery/mugging        | 45   | 20 | 69   | 20 | 42  | 22 | 46   | 26 | 25  | 29 | $\chi^2 = 5.5, p = 0.239$  |
| Been robbed/mugged          | 59   | 26 | 82   | 24 | 55  | 28 | 50   | 28 | 27  | 33 | $\chi^2 = 3.59, p = 0.465$ |

a serious accident. Compared to the None and SubS DEP+Very High SLD classes, the Both High class reported higher effected scores for seeing a robbery/mugging. Compared to the None, No DEP+Mod SLD, and SubS DEP+Very High SLD classes, the Both Moderate and Both High classes reported higher effected scores for the death of someone close. Compared to the None, No DEP+Mod SLD, and SubS DEP+Very High SLD classes, the Both High class reported higher effected scores for emotional abuse, being in a serious disaster, being separated/divorced, and the sudden death of someone close. Compared to the None, No DEP+Mod SLD, and Both Moderate classes, the Both High class reported higher effected scores for having an abortion/miscarriage.

**Coping Strategies**

Significant differences were found among the five latent classes in the frequency of use of 64% of the coping strategies listed on the Brief COPE (see Table 4). Compared to the None class, the other four classes reported higher scores for self-distraction. Compared to the None class, the SubS DEP+Very High SLD class reported higher scores for using instrumental support and venting. Compared to the None and No DEP+Mod SLD classes, the Both High class reported lower scores for active coping. Compared to the None and No DEP+Mod SLD classes, the Both Moderate and Both High classes reported higher scores for substance use. Compared to the None, No DEP+Mod SLD, and SubS DEP+Very High SLD classes, the Both Moderate and Both High classes reported higher scores for denial, venting, and behavioral disengagement. Compared to the None, No DEP+Mod SLD, and

SubS DEP+Very High SLD classes, the Both High class reported lower scores for acceptance. Significant differences were found among the None, SubS DEP+Very High SLD, Both Moderate, and Both High classes for self-blame (i.e., None < SubS DEP+Very High SLD < Both Moderate < Both High).

**Discussion**

The current study extends the authors’ previous work that identified differences in demographic, clinical, and sleep characteristics, as well as co-occurring symptoms among five latent classes of patients with cancer with distinct joint depression and sleep disturbance profiles (Calvo-Schimmel et al., 2022). Specifically, the current study is the first to evaluate for differences in global, cancer-specific, and cumulative life stress, as well as resilience and use of coping strategies among these classes. The authors’ findings support their a priori hypothesis that patients with worst joint symptom profiles reported higher levels of all three types of stress; increased occurrence rates of and effects from a variety of SLEs; lower levels of resilience; and higher use of disengagement coping strategies. These findings are consistent with prior research that found associations between higher levels of depression and sleep disturbance as individual symptoms and higher levels of stress (Garvin et al., 2021; Goyal et al., 2018; Palesh et al., 2007). Table 5 provides a summary of these associations for the four higher classes compared to the None class.

One plausible explanation for the associations among depression, sleep disturbance, and stress in patients with cancer is that the two major neuroendocrine stress systems (i.e.,



**TABLE 3. Differences Among the Joint Depression and Sleep Disturbance Latent Classes in the Effect of Each of the Stressors on Life Over the Past Year**

| Stressful Life Event <sup>a</sup>                           | No Depression or Sleep Disturbance (0) (N = 285) |     | No Depression and Moderate Sleep Disturbance (1) (N = 430) |     | Subsyndromal Depression and Very High Sleep Disturbance (2) (N = 272) |     | Moderate Depression and Moderate Sleep Disturbance (3) (N = 235) |     | High Depression and Very High Sleep Disturbance (4) (N = 109) |     | Statistics                               |
|---|--|-----|--|-----|---|-----|--|-----|---|-----|--|
|   | $\bar{X}$  | SD  | $\bar{X}$  | SD  | $\bar{X}$   | SD  | $\bar{X}$  | SD  | $\bar{X}$   | SD  |  |
| <b>Interpersonal violence, abuse, and neglect stressors</b> |  |     |  |     |   |     |  |     |   |     |  |
| Family violence in childhood                                | 1.8  | 1.1 | 1.7  | 1.1 | 1.7   | 1.1 | 2.2  | 1.4 | 2.3   | 1.1 | KW = 13.56, p = 0.009<br>1 < 4           |
| Emotional abuse   | 2.2  | 1.3 | 2.3  | 1.3 | 2.5   | 1.4 | 2.8  | 1.3 | 3.3   | 1.1 | KW = 19.98, p < 0.001<br>0, 1, and 2 < 4 |
| Physical neglect  | 2.5  | 1.8 | 2.2  | 1.3 | 2.5   | 1.5 | 2.9  | 1.1 | 3.3   | 1.3 | KW = 3.16, p = 0.531                     |
| Sexual harassment   | 1.5  | 1.3 | 1.4  | 0.9 | 1.5   | 0.9 | 1.6  | 1   | 1.7   | 1   | KW = 4.08, p = 0.396                     |
| Physical abuse before the age of 16 years                   | 1.8  | 1.2 | 1.4  | 0.8 | 2.2   | 1.3 | 2.2  | 1.5 | 2.2   | 1.3 | KW = 12.91, p = 0.012<br>1 < 3           |
| Physical abuse at age 16 years or older                     | 1.9  | 1.2 | 1.4  | 0.9 | 1.9   | 1.2 | 2.1  | 1.3 | 2.4   | 1.4 | KW = 8.72, p = 0.069                     |
| Forced to touch before the age of 16 years                  | 1.6  | 1.2 | 1.6  | 1   | 2.2   | 1.4 | 2.1  | 1.4 | 2.7   | 1.5 | KW = 9.42, p = 0.051                     |
| Forced to touch at age 16 years or older                    | 1.3  | 0.5 | 1.9  | 1.3 | 1.7   | 1   | 2.1  | 1.5 | 2.3   | 1.4 | KW = 2.69, p = 0.611                     |
| Forced sex before the age of 16 years                       | 1  | -   | 1.6  | 1   | 2.2   | 1.5 | 2.4  | 1.3 | 2.6   | 1.5 | KW = 4.4, p = 0.354                      |
| Forced sex at age 16 years or older                         | 1.7  | 1.3 | 1.9  | 1.3 | 1.6   | 0.8 | 1.7  | 1.3 | 2.1   | 1.7 | KW = 0.74, p = 0.946                     |
| <b>Other stressors</b>                                      |  |     |  |     |   |     |  |     |   |     |  |
| Been in a serious disaster                                  | 1.2  | 0.6 | 1.2  | 0.6 | 1.4   | 0.9 | 1.5  | 1   | 1.8   | 0.9 | KW = 28.49, p < 0.001<br>0, 1, and 2 < 4 |
| Seen serious accident                                       | 1.4  | 0.8 | 1.4  | 0.8 | 1.4   | 0.8 | 1.6  | 1   | 1.9   | 1.2 | KW = 11.53, p = 0.021<br>0 and 1 < 4     |

*Continued on the next page*

**TABLE 3. Differences Among the Joint Depression and Sleep Disturbance Latent Classes in the Effect of Each of the Stressors on Life During the Past Year (Continued)**

| Stressful Life Event <sup>a</sup>                        | No Depression or Sleep Disturbance (0) (N = 285) |     | No Depression and Moderate Sleep Disturbance (1) (N = 430) |     | Subsyndromal Depression and Very High Sleep Disturbance (2) (N = 272) |     | Moderate Depression and Moderate Sleep Disturbance (3) (N = 235) |     | High Depression and Very High Sleep Disturbance (4) (N = 109) |     | Statistics   |
|--|--|-----|--|-----|---|-----|--|-----|---|-----|--|
|  | $\bar{X}$  | SD  | $\bar{X}$  | SD  | $\bar{X}$   | SD  | $\bar{X}$  | SD  | $\bar{X}$   | SD  |  |
| <i>Other stressors (continued)</i>                       |  |     |  |     |   |     |  |     |   |     |  |
| Had serious accident or injury                           | 1.5  | 0.9 | 1.5  | 0.9 | 1.7   | 1.1 | 1.6  | 1.1 | 2   | 1.2 | KW = 7.35, p = 0.119                                       |
| Jail (family member)                                     | 1.6  | 1.2 | 1.7  | 1.2 | 1.8   | 1.2 | 2.1  | 1.6 | 2.3   | 1.6 | KW = 5.37, p = 0.251                                       |
| Jail (self)  | 1.7  | 1.3 | 1.5  | 0.9 | 1.7   | 1.2 | 2.3  | 1.3 | 1.9   | 1.6 | KW = 5.85, p = 0.211                                       |
| Foster care or put up for adoption                       | 2  | 1.4 | 2.8  | 2.1 | 2.2   | 0.8 | 2  | 1.7 | 2.6   | 1.7 | KW = 0.89, p = 0.926                                       |
| Separated/divorced (parents)                             | 1.4  | 0.9 | 1.5  | 0.9 | 2   | 1.2 | 2.2  | 1.3 | 1.8   | 1.3 | KW = 11.78, p = 0.019<br>No significant pairwise contrasts |
| Separated/divorced (self)                                | 1.7  | 1.2 | 1.9  | 1.3 | 2.1   | 1.4 | 2.3  | 1.4 | 2.8   | 1.4 | KW = 23.42, p < 0.001<br>0, 1, and 2 < 4; 0 < 3            |
| Serious money problems                                   | 2  | 1.6 | 2.1  | 1.4 | 2.7   | 1.7 | 3.1  | 1.6 | 3.6   | 1.6 | KW = 24.92, p < 0.001<br>0 and 1 < 3 and 4                 |
| Had serious physical or mental illness (not cancer)      | 2  | 1.3 | 2.3  | 1.4 | 2.4   | 1.4 | 2.7  | 1.4 | 2.9   | 1.3 | KW = 10.06, p = 0.039<br>No significant pairwise contrasts |
| Abortion or miscarriage                                  | 1.4  | 0.9 | 1.4  | 0.8 | 1.7   | 1.1 | 1.5  | 1   | 2.2   | 1.4 | KW = 17.95, p < 0.001<br>0, 1, and 3 < 4                   |
| Separated from child                                     | 1  | -   | 2.2  | 1.3 | 2   | 1.7 | 3.8  | 1   | 4   | 1.4 | KW = 7.85, p = 0.097                                       |
| Care for child with handicap                             | 3.3  | 1.5 | 3.4  | 1.3 | 3   | 1.7 | 2.8  | 1.5 | 3.5   | 1.4 | KW = 1.4, p = 0.845  |
| Care for someone with severe physical or mental handicap | 2  | 1.3 | 2.5  | 1.3 | 2.6   | 1.7 | 2.9  | 1.4 | 3.2   | 1.5 | KW = 13.86, p = 0.008<br>0 < 4                             |
| Death of someone close (sudden)                          | 1.9  | 1.3 | 2.1  | 1.2 | 2   | 1.2 | 2.5  | 1.4 | 2.8   | 1.6 | KW = 20.48, p < 0.001<br>0, 1, and 2 < 4;<br>0 < 3         |

*Continued on the next page*

**TABLE 3. Differences Among the Joint Depression and Sleep Disturbance Latent Classes in the Effect of Each of the Stressors on Life During the Past Year (Continued)**

| Stressful Life Event <sup>a</sup>   | No Depression or Sleep Disturbance (0) (N = 285) |     | No Depression and Moderate Sleep Disturbance (1) (N = 430) |     | Subsyndromal Depression and Very High Sleep Disturbance (2) (N = 272) |     | Moderate Depression and Moderate Sleep Disturbance (3) (N = 235) |     | High Depression and Very High Sleep Disturbance (4) (N = 109) |     | Statistics                                     |  |
|-------------------------------------|--|-----|--|-----|---|-----|--|-----|---|-----|--|--|
|                                     | $\bar{X}$  | SD  | $\bar{X}$  | SD  | $\bar{X}$   | SD  | $\bar{X}$  | SD  | $\bar{X}$   | SD  |  |  |
| Other stressors (continued)         |  |     |  |     |   |     |  |     |   |     |  |  |
| Death of someone close (not sudden) | 1.8  | 1.2 | 2  | 1.2 | 2.1   | 1.2 | 2.6  | 1.4 | 3.2   | 1.4 | KW = 66.76, p < 0.001<br>0, 1, and 2 < 3 and 4 |  |
| Seen robbery/mugging                | 1.2  | 0.7 | 1.6  | 1   | 1.4   | 1.1 | 1.6  | 1   | 2   | 1.3 | KW = 14.74, p = 0.005<br>0 and 2 < 4           |  |
| Been robbed/mugged                  | 1.4  | 0.8 | 1.6  | 1   | 1.5   | 1   | 2  | 1.3 | 2   | 1.4 | KW = 13.42, p = 0.009<br>0 < 3                 |  |

<sup>a</sup> Range = 1 (not at all) to 5 (extremely)

KW—Kruskal–Wallis

**Note.** These data are reported for patients who reported the occurrence of the stressor (see Table 2).

hypothalamus–pituitary–adrenal axis and sympathetic nervous system) are activated in response to a cancer diagnosis and associated treatments (Irwin et al., 2016; Pariante & Lightman, 2008; Smith & Mong, 2019; Young & Singh, 2018). Stimulation of the hypothalamus–pituitary–adrenal axis induces a dysregulation in responsiveness to glucocorticoids (e.g., cortisol) and an increase in the expression of pro-inflammatory cytokines (e.g., interleukin-6, tumor necrosis factor- $\alpha$ ) with resultant sympathetic nervous system hyperactivity (Smith, 2015; Smith & Mong, 2019).

### Stress and Resilience

As shown in Table 1, global (i.e., PSS score) and cancer-specific (i.e., IES-R total score; IES-R intrusion, avoidance, and hyperarousal scores) stress measures exhibited a dose–response effect in that the levels of these two types of stress increased significantly as the joint depression and sleep disturbance profiles worsened. The current findings are consistent with previous studies of the general population that found a dose–response relationship between depression (Overstreet et al., 2016; Steine et al., 2017) and sleep disturbance (Steine et al., 2017), as single symptoms, and the number and/or impact of past SLEs. For example, in a study of adult caretakers of twins (Overstreet et al., 2016), depressive symptoms worsened as the number

of traumatic events (e.g., feared death) increased. In another study of adult survivors of sexual abuse (Steine et al., 2017), a dose–response relationship was found between depression and insomnia scores and cumulative childhood maltreatment scores.

### Global Stress

Although the PSS lacks a clinically meaningful cutoff score, patients in the two worse depression and sleep disturbance profiles reported PSS scores (i.e., 23.3 and 30.6) that were slightly higher than those scores reported by patients with ovarian cancer (i.e., 17.9) (Liu et al., 2017); patients with cancer receiving radiation therapy (i.e., 22.1) (Ravindran et al., 2019); and patients with gynecologic cancer undergoing their third cycle of chemotherapy (i.e., 22.3) (Yeh, 2021). The current findings are consistent with previous studies of patients with heterogeneous types of cancer that found positive associations between depression (Li et al., 2021; Yuan et al., 2020) and sleep disturbance (Ban et al., 2022; Lv et al., 2023) as individual symptoms and patients' perceptions of global stress.

### Cancer-Specific Stress

Patients in the Both Moderate and Both High classes had average IES-R scores that indicate clinically meaningful levels of post-traumatic symptomatology. In addition, 21% of the patients in the Both Moderate

**TABLE 4. Differences in Brief COPE Subscale Scores Among the Joint Depression and Sleep Disturbance Latent Classes at Enrollment**

| Subscale <sup>a</sup>                  | No Depression or Sleep Disturbance (0) (N = 285) |     | No Depression and Moderate Sleep Disturbance (1) (N = 430) |     | Subsyndromal Depression and Very High Sleep Disturbance (2) (N = 272) |     | Moderate Depression and Moderate Sleep Disturbance (3) (N = 235) |     | High Depression and Very High Sleep Disturbance (4) (N = 109) |     | Statistics   |
|--|--|-----|--|-----|---|-----|--|-----|---|-----|--|
|  | $\bar{X}$  | SD  | $\bar{X}$  | SD  | $\bar{X}$   | SD  | $\bar{X}$  | SD  | $\bar{X}$   | SD  |  |
| <b>Engagement coping strategies</b>    |  |     |  |     |   |     |  |     |   |     |  |
| Active coping                          | 6.2  | 1.7 | 6.1  | 1.7 | 5.9   | 1.6 | 6  | 1.6 | 5.5   | 1.6 | F = 3.87, p = 0.004<br>0 and 1 > 4                             |
| Planning                               | 5  | 1.9 | 5.2  | 1.9 | 5.4   | 1.7 | 5.4  | 1.6 | 5.6   | 1.7 | F = 2.58, p = 0.036<br>No significant pairwise contrasts       |
| Positive reframing                     | 5.4  | 2   | 5.5  | 2   | 5.5   | 2   | 5.4  | 1.9 | 5.1   | 1.8 | F = 0.91, p = 0.459  |
| Acceptance                             | 6.8  | 1.3 | 6.9  | 1.3 | 6.7   | 1.3 | 6.5  | 1.4 | 6.2   | 1.5 | F = 8.12, p < 0.001<br>0, 1 and 2 > 4; 1 > 3                   |
| Humor                                  | 4.1  | 2   | 4.5  | 2   | 4.5   | 1.9 | 4.1  | 1.8 | 4.3   | 2.1 | F = 3.28, p = 0.011<br>No significant pairwise contrasts       |
| Religion                               | 5.1  | 2.4 | 4.9  | 2.3 | 5   | 2.4 | 5.1  | 2.1 | 5.3   | 2.3 | F = 0.76, p = 0.551  |
| Using emotional support                | 6.2  | 1.8 | 6.4  | 1.7 | 6.4   | 1.6 | 6.3  | 1.6 | 6   | 1.8 | F = 1.66, p = 0.158  |
| Using instrumental support             | 5  | 1.9 | 5.3  | 1.8 | 5.5   | 1.8 | 5.4  | 1.6 | 5.4   | 1.8 | F = 3.5, p = 0.008<br>0 < 2                                    |
| <b>Disengagement coping strategies</b> |  |     |  |     |   |     |  |     |   |     |  |
| Self-distraction                       | 5.1  | 1.9 | 5.5  | 1.7 | 5.6   | 1.6 | 5.7  | 1.6 | 5.8   | 1.5 | F = 5.01, p = 0.001<br>0 < 1, 2, 3, and 4                      |
| Denial                                 | 2.3  | 0.8 | 2.3  | 0.8 | 2.4   | 1   | 2.7  | 1.3 | 3.3   | 1.8 | F = 25.53, p < 0.001<br>0, 1 and 2 < 3 and 4;<br>3 < 4         |
| Venting                                | 3.4  | 1.5 | 3.7  | 1.6 | 4   | 1.6 | 4.5  | 1.5 | 5.2   | 1.5 | F = 33.72, p < 0.001<br>0, 1, and 2 < 3 and 4;<br>0 < 2; 3 < 4 |
| Substance use                          | 2.1  | 0.6 | 2.2  | 0.6 | 2.2   | 0.8 | 2.4  | 0.9 | 2.5   | 1   | F = 6.1, p < 0.001<br>0 and 1 < 3 and 4                        |
| Behavioral disengagement               | 2.1  | 0.4 | 2.1  | 0.5 | 2.2   | 0.8 | 2.4  | 0.9 | 2.9   | 1.4 | F = 35.25, p < 0.001<br>0, 1, and 2 < 3 and 4;<br>3 < 4        |
| Self-blame                             | 2.4  | 0.9 | 2.5  | 0.8 | 2.8   | 1.2 | 3.4  | 1.3 | 4.4   | 1.8 | F = 85.26, p < 0.001<br>0 < 2 < 3 < 4                          |

<sup>a</sup> Each item was rated on a 4-point Likert-type scale ranging from 1 (“I have not 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.

and 69% of the patients in the Both High classes had total IES-R scores of 33 or greater, which suggests PTSD. The current findings are supported by prior studies of patients with cancer that found associations between worse depression (Goyal et al., 2018; Thekdi et al., 2015) and sleep disturbance (Goyal et al., 2018; Weng et al., 2021), as single symptoms, and higher IES-R scores.

Although the SubS DEP+Very High SLD class had an average IES-R total score that was below the clinically meaningful cutoff for post-traumatic symptomatology (i.e., 20.7), 36% of these patients had an IES-R total score that suggests post-traumatic symptomatology and 13% had scores indicative of probable PTSD. It is possible that patients in this class were receiving treatment for depression. Although some classes of antidepressants improve sleep, others (e.g., tricyclic antidepressants, selective serotonin reuptake inhibitors) may cause sleep disturbance (Hutka et al., 2021; Mayers & Baldwin, 2005). Of note, the mean GSDS total score of this class was about 1.65 times higher than the GSDS cutoff score, similar to scores reported by parents of newborn infants (Gay et al., 2004) and shift workers (Lee, 1992). Given that 13% of the U.S. population (Pratt et al., 2017) and 30% of women after a diagnosis of breast cancer (Burgess et al., 2005) use antidepressants, clinicians need to evaluate for sleep disturbance, determine if alternative treatments for depression are warranted, and teach patients routine practices to improve sleep.

### Cumulative Life Stress

As shown in Table 2, compared to the None class, the Both Moderate and Both High classes reported the occurrence of 32% and 50% of the 28 SLEs evaluated, respectively. Some of the highest occurrence rates for these two classes were for emotional abuse, having serious money problems, and sexual harassment. These findings are consistent with a study of healthy individuals with and without sleep disturbance (Park et al., 2020) that reported a positive correlation ( $r = 0.51$ ) between depression severity scores and the number of non-cancer-related SLEs (e.g., divorce, death of a family member) in individuals with sleep disturbance. One plausible explanation for this association is that exposure to and the cumulative impact of past SLEs, along with cancer-related stress, have synergistic effects. In the current study, eight SLEs reported by the Both Moderate and Both High classes are considered PTSD stressors (e.g., emotional abuse, sexual harassment); that may explain the higher rates of PTSD in these classes.

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### KNOWLEDGE TRANSLATION

- Almost 50% of the patients receiving chemotherapy reported clinically meaningful levels of depression and sleep disturbance.
  - The co-occurrence of both symptoms was associated with clinically meaningful levels of global stress and cancer-specific stress.
  - Almost 90% of the patients receiving chemotherapy reported cancer-specific stress scores that suggest significant post-traumatic distress symptomatology.
- 

In terms of adverse childhood experiences (ACEs) specifically, 43% of the patients in the Both High class reported family violence during childhood; 26% reported being physically abused before the age of 16 years; and 20% reported being forced to touch before the age of 16 years. Similarly, compared to the None class, the Both Moderate class reported higher occurrence rates for physical abuse (26%) and forced to touch (19%) before the age of 16 years. Patients in the SubS DEP+Very High SLD reported higher occurrence rates for being forced to touch and have sex before the age of 16 years. The current findings are consistent with a population-based study that found an association between a higher number of ACEs and an increased odds in later life of reporting depressive symptoms, particularly in cases of abuse, neglect, and household dysfunction (Von Cheong et al., 2017). In terms of sleep disturbance, as noted in two systematic reviews (Kajeepeeta et al., 2015; Yu et al., 2022), patients who experience ACEs are at increased risk for sleep disturbance during adulthood. Although SLEs and ACEs are not preventable, clinicians can assess for them prior to the initiation of chemotherapy and make referrals to mental health professionals who can provide tailored interventions that focus on cognitive behavioral well-being (Abbas et al., 2022).

### Resilience

Resilience refers to the flexibility one has in responding to changing environmental demands to recover mental health from negative SLEs (Ban et al., 2022). In the current sample, compared to the None class, the other four classes had resilience scores that were below the normative score for the United States (Campbell-Sills et al., 2009). This finding is consistent with prior studies that found a negative correlation between depressive symptoms and resilience in patients with cancer (Lee, Lin, et al., 2019; Ristevska-Dimitrovska et al., 2015).

**TABLE 5. Stress, Resilience, and Coping Characteristics Associated With Membership in the 4 Highest Joint Depression and Sleep Disturbance Classes Compared to the Joint No Depression or Sleep Disturbance Class**

| Characteristic  | SubS DEP+          |                  |                  |              |
|---|--------------------|------------------|------------------|--------------|
|   | No DEP+<br>Mod SLD | Very High<br>SLD | Both<br>Moderate | Both<br>High |
| <b>Stress characteristics</b>                             |                    |                  |                  |              |
| 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        |                    | ●                | ●                | ●            |
| <b>Higher occurrence of life stressors</b>                |                    |                  |                  |              |
| Family violence in childhood                              |                    |                  |                  | ●            |
| Emotional abuse   |                    | ●                | ●                | ●            |
| Physical neglect  |                    |                  | ●                | ●            |
| Sexual harassment   |                    | ●                | ●                | ●            |
| Physical abuse before the age of 16 years                 |                    |                  | ●                | ●            |
| Physical abuse at age 16 years or older                   |                    |                  | ●                | ●            |
| Forced to touch before the age of 16 years                |                    | ●                | ●                | ●            |
| Forced to touch at age 16 years or older                  |                    |                  |                  | ●            |
| Forced sex before the age of 16 years                     |                    | ●                |                  |              |
| Jail (family member)                                      |                    |                  | ●                | ●            |
| Separated/divorced (parents)                              |                    |                  |                  | ●            |
| Serious money problems                                    |                    |                  | ●                | ●            |
| Had serious physical or mental illness (not cancer)       |                    |                  |                  | ●            |
| Separated from child                                      |                    |                  |                  | ●            |
| Care for someone with severe physical or mental handicap  |                    |                  |                  | ●            |
| <b>Higher effect of life stressors</b>                    |                    |                  |                  |              |
| Emotional abuse   |                    |                  |                  | ●            |
| Been in a serious disaster                                |                    |                  |                  | ●            |

*Continued on next page*

**TABLE 5. Stress, Resilience, and Coping Characteristics Associated With Membership in the 4 Highest Joint Depression and Sleep Disturbance Classes Compared to the Joint No Depression or Sleep Disturbance Class (Continued)**

| Characteristic  | SubS DEP+          |                  |                  |              |
|---|--------------------|------------------|------------------|--------------|
|   | No DEP+<br>Mod SLD | Very High<br>SLD | Both<br>Moderate | Both<br>High |
| <b>Higher effect of life stressors (continued)</b>  |                    |                  |                  |              |
| Seen serious accident   |                    |                  |                  | ●            |
| Separated/divorced (self)   |                    |                  | ●                | ●            |
| Serious money problems  |                    |                  | ●                | ●            |
| Abortion or miscarriage   |                    |                  |                  | ●            |
| Care for someone with severe physical or mental handicap  |                    |                  | ●                | ●            |
| Death of someone close (sudden)   |                    |                  | ●                | ●            |
| Death of someone close (not sudden)   |                    |                  | ●                | ●            |
| Seen robbery/mugging  |                    |                  |                  | ●            |
| Been robbed/mugged  |                    |                  | ●                |              |
| <b>Use of coping strategies</b>   |                    |                  |                  |              |
| Lower use of active coping  |                    |                  |                  | ●            |
| Lower use of acceptance   |                    |                  |                  | ●            |
| Higher use of instrumental support  |                    | ●                |                  |              |
| Higher use of self-distraction  | ●                  | ●                | ●                | ●            |
| Higher use of denial  |                    |                  | ●                | ●            |
| Higher use of venting   |                    | ●                | ●                | ●            |
| Higher use of substance use   |                    |                  | ●                | ●            |
| Higher use of behavioral disengagement  |                    |                  | ●                | ●            |
| Higher use of self-blame  |                    | ●                | ●                | ●            |
| Both High—high depression and very high sleep disturbance; Both Moderate—moderate depression and moderate sleep disturbance; No DEP+Mod SLD—no depression and moderate sleep disturbance; PTSD—post-traumatic stress disorder; SubS DEP+Very High SLD—subsyndromal depression and very high sleep disturbance |                    |                  |                  |              |

Similarly, in a study of patients with breast cancer (Lai et al., 2020), worse sleep quality was associated with lower levels of resilience. Given that higher levels of resilience may represent a protective factor against stress in patients who experience joint depression and sleep disturbance, clinicians should recommend interventions that boost resilience (e.g., psychological resilience training [Loprinzi et al., 2011]) and reduce stress (e.g., yoga [Loprinzi et al., 2011]).

### Coping Strategies

The use of disengagement coping, characterized by avoidance, withdrawal, and denial, is viewed as maladaptive. Of note, these strategies are associated with greater stress and negative health outcomes in patients with cancer (Merluzzi et al., 2019). Compared to the None class, patients in the Both Moderate and Both High classes reported a higher use of all the disengagement coping strategies evaluated using the Brief COPE (see Table 4). This finding

is not unexpected given that in previous studies of patients with cancer the use of disengagement strategies was associated with higher levels of depression (Stanton et al., 2018) and sleep disturbance (Hoyt et al., 2009; Thomas et al., 2010; Trudel-Fitzgerald et al., 2017).

Although findings are inconsistent, one plausible explanation for the association between higher levels of depression and sleep disturbance and an increased use of disengagement coping strategies is gender. For example, in a study of gender differences in the use of coping strategies (Wolanin, 2021), women with breast cancer were more inclined than men with prostate cancer to use disengagement coping strategies that altered their emotional reactions to stressful circumstances (i.e., venting). In another study of patients with gastrointestinal and lung cancer (Oppegaard et al., 2020), compared to men, women had higher scores for self-distraction, denial, and venting. These strategies are associated with decreased self-esteem, fewer functional social relationships, decreased meaning in life, and delays in seeking adequate treatment. Given that 86% of the patients in the Both Moderate and 85% in the Both High classes who reported the use of disengagement coping strategies were women, additional studies are needed to confirm these gender differences.

An equally plausible hypothesis for a higher use of disengagement coping strategies among the worse joint depression and sleep disturbance profiles is a reduction in the capacity to use active coping strategies. This reduced capacity may be related to increases in demands from the disease, a higher number and/or severity of treatment-related symptoms, and/or lower levels of resilience (Merluzzi et al., 2019; Popa-Velea et al., 2017; Schuurhuizen et al., 2018). Because the use of coping strategies is modifiable, additional research is needed to evaluate the relationships among various demographic and clinical characteristics, as well as social determinants of health, and the use of disengagement coping strategies in patients with cancer who experience high levels of joint depression and sleep disturbance.

Of note, the SubS DEP+Very High SLD class was the only subgroup who reported a higher use of the engagement coping strategy of instrumental support. The use of instrumental support is characterized by seeking the help and information required to improve a situation (e.g., significant stress) from caregivers other than a spouse or parents (Cai et al., 2021; Priscilla et al., 2011). In patients with cancer, this behavior is associated with lower levels of depression (Priscilla et al., 2011) and sleep disturbance (Oh et al., 2020), as well as higher

levels of resilience (Zhou et al., 2022). This finding is not entirely unexpected because patients in this class may have received treatment for depression prior to the start of chemotherapy, increasing their ability to use engagement coping strategies (Sadek & Bona, 2000).

### Limitations

Several limitations warrant consideration. Given that this sample was relatively homogenous in terms of self-reported race and ethnicity, education, and socioeconomic status, these results need to be replicated with more diverse samples. In addition, these findings warrant replication in patients receiving other types of cancer treatment (e.g., radiation therapy). Because patients were recruited during their first and second cycles of chemotherapy, pretreatment levels of depression, sleep disturbance, and stress were not evaluated. Equally important, because the stress measures were completed only once, causal relationships between the symptom profiles and stress cannot be evaluated. Given that the major reason for refusal to participate in this study was being overwhelmed by the cancer treatment, these findings may underestimate the co-occurrence of both symptoms and levels of stress.

### Implications for Research and Practice

Despite these limitations, the current findings suggest that patients with worse depression and sleep disturbance profiles experience multiple types of stress (i.e., global, cancer-specific, cumulative life stress). In addition, the current study is the first to describe a dose-response effect in two different types of stress in patients with cancer. These findings warrant additional evaluation because unrelieved stress can lower resilience and increase the use of disengagement coping strategies. In addition, given the positive associations among depression, sleep disturbance, and stress, the molecular mechanisms (e.g., neuroendocrine) that underlie these relationships warrant careful examination.

Clinicians need to conduct routine assessments of depression, sleep disturbance, SLEs, and ACEs among patients with cancer. Equally important, to improve the management of these symptoms and decrease stress, clinicians need to refer patients for psychological interventions aimed to reduce stress, promote resilience, and enhance the use of engagement coping strategies.

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