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PTSD Diagnoses, Subsyndromal Symptoms, and Comorbidities Contribute to Impairments for Breast Cancer Survivors

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Abstract

The clinical importance of posttraumatic stress disorder (PTSD) symptomatology for cancer patients is unclear. The association between the magnitude of cancer-related PTSD symptoms, comorbidity, and functioning is tested. Breast cancer patients ($N = 74$) were assessed at diagnosis/surgery, followed, and screened for cancer-related PTSD 18 months later. Participants then completed diagnostic interviews and PTSD ($n = 12$), subsyndromal PTSD ($n = 5$), and no symptom ($n = 47$) patient groups were identified. Posttraumatic stress disorder cases were distinguished by having experienced violent traumas and anxiety disorders predating cancer, whereas subsyndromal cases were not. Also, longitudinal data show that PTSD covarys with poorer functioning and lower quality of life among breast cancer survivors. Both PTSD and subsyndromal PTSD were associated with employment absenteeism and the seeking of mental health services.

Studies of posttraumatic stress disorder (PTSD) in cancer patients find that diagnostic rates are low (3% to 14%), but symptomatology falling short of the diagnostic criteria of the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (*DSM-IV*; American Psychiatric Association [APA], 1994)—PTSD that is subsyndromal—may occur in upward of 50% of patients (Gurevich, Devins, & Rodin, 2002). How disabling subsyndromal PTSD may be for any individual is not fully known; however, the few data suggest that it is so. Stein, Walker, Hazen, and Forde (1997) using community survey data found that individuals with subsyndromal PTSD reported employment problems, social disruptions, and difficulties in the home. Similarly, Ciechanowski, Walker, Russo, Newman, and Katon (2004) found in a general survey of women in a health maintenance organization that quality of life was lower among those with subsyndromal PTSD compared to those with no symptoms. Finally, Marshall and colleagues (2001), using data from over 9,000 adults screened for anxiety disorders, reported that the presence of subsyndromal symptoms significantly raised the risk for suicidal ideation.

It is not known if similar disruptions occur for cancer survivors. The majority of the available data come not from studies determining patients' syndromal or subsyndromal PTSD diagnoses, but from patient self-reports of traumatic symptoms found to be correlated with poor quality of life and/or impaired physical functioning (e.g., Diemling, Kahana, Bowman, & Schaefer, 2002; Jacobsen et al., 1998; for a review, see Kangas, Henry, & Bryant, 2002). More persuasive are longitudinal data from the time of cancer diagnosis showing that the magnitude of cancer-

related intrusive and avoidant symptoms predict depressive symptoms (Golden-Kreutz & Andersen, 2004) and disrupted quality of life 2 years later (Golden-Kreutz et al., 2005).

Determination of PTSD “caseness” among cancer patients, particularly if distinguishing between syndromal and subsyndromal PTSD, requires clinical detail not readily obtained with questionnaires. From over 40 cancer-related PTSD studies (Gurevich et al., 2002; Kangas et al., 2002), only 8 studies used diagnostic interviews (e.g., SCID; First, Spitzer, Gibbon, & Williams, 1996). Across studies, 0 to 10 patients with PTSD were identified, for a total of 40 PTSD cases in the literature from over 700 patients assessed (Alter et al., 1996; Andrykowski & Cordova, 1998; Brewin, Watson, McCarthy, Hyman, & Dayson, 1998; Green et al., 1998; Kangas, Henry, & Bryant, 2005; Mehnert & Koch, 2007; Mundy et al., 2000; Palmer, Kagee, Coyne, & DeMichele, 2004; Pitman et al., 2001). Thus, a study of more cases of PTSD would be useful, but clarifying the clinical picture for those with subsyndromal PTSD would be of particular value.

Interest in subsyndromal PTSD is relatively recent, and as yet the APA has not specified diagnostic criteria. Stein and colleagues (1997) defined subsyndromal PTSD as having at least one symptom in each of the three *DSM-IV* PTSD symptom clusters, others required cases to meet criteria for any two of three clusters (Blanchard et al., 1996; Carlier & Gersons, 1995; Schutzwahl & Maerchler, 1999), and still others have used both criteria (Gillock, Zayfert, Hegel, & Ferguson, 2005; Weiss et al., 1992). Finally, Marshall et al. (2001) used a two-step procedure: patient's acknowledgement of a Criterion A trauma (actual or threatened death or serious injury, or a threat to the physical integrity of the self or others and a response involving intense fear, helplessness, or horror; APA, 1994) plus endorsements of four symptoms: reexperiencing, withdrawal/loss of interest, insomnia, and avoidance.

Diagnosis can be further complicated when PTSD symptomatology is only one component of a patient's psychopathology. Comorbidity is high for those with PTSD (66% to 98%; Keane & Kaloupek, 1997) as well as for those with subsyndromal PTSD (Marshall et al., 2001) and includes other anxiety disorders, depression, and substance use (Ozer, Best, Lipsey, & Weiss, 2003). To date, four cancer studies have reported comorbidity rates for PTSD cases. Green and colleagues (1998) reported 11%, Mundy et al. (2000) reported 28%, and Kangas et al. (2005) reported up to 71% of their PTSD cases had concurrent depression. Mehnert and Koch (2007) reported that women diagnosed with cancer-related PTSD or acute stress disorder were more likely (Odds Ratio [OR] = 22.2) to have a comorbid disorder.

This study aimed to clarify the nature, extent, and clinical importance of cancer-related PTSD diagnoses, both syndromal and subsyndromal. Breast cancer patients with node positive disease (stage II and III) were assessed at diagnosis/treatment and 18 months later screened for cancer-related PTSD symptoms using the PTSD Checklist-Civilian Version (PCL-C; Weathers, Litz, Herman, Huska, & Keane, 1991). The patients were potentially vulnerable to PTSD symptoms, as cure was not a certainty (estimated 5-year survival for stage II/III disease is 80%; American Cancer Society, 2007). As we were interested in detecting both syndromal and subsyndromal cases, a liberal cutoff on the PCL-C identified patients for further study as well as patients self-reporting no PTSD symptoms. Using SCID interviews, we identified and then compared three resultant groups: patients with no symptoms, patients with cancer-related subsyndromal PTSD, and patients with cancer-related PTSD. We anticipated that functioning would be significantly better for the no-symptom group than those with PTSD. We were particularly interested in the subsyndromal group, as the data are unclear on whether their current functioning would most closely resemble the no-symptom group or those with PTSD. Also of importance were comparisons of the two PTSD groups on risk factors (trauma and psychiatric histories; Brewin, Andrews, & Valentine, 2000) and psychiatric comorbidity.

Additionally, patients' longitudinal data from cancer diagnosis are used to predict quality of life and functional status at 18 months. Along with the entry of baseline functioning, the analyses include potentially important cofactors (younger age, extent of treatment, and time since diagnosis) identified from cancer studies assessing PTSD symptom reports (e.g., Jacobsen et al., 1998; Green et al., 2000). The PTSD literature suggests a history of psychiatric disorder and trauma as important (see Brewin, Andrews, & Valentine, 2000, for a meta-analysis). In summary, planned analyses detail the clinical picture for patients with a subsyndromal pattern or a PTSD diagnosis and test the importance of diagnostic and subsyndromal PTSD to quality of life impairments.

METHOD

Participants

All patients ($N = 74$) had been diagnosed with regional breast cancer (stage II, $n = 65$; stage III, $n = 9$) and surgically treated with breast-conserving surgery (segmental mastectomy; 53%) or modified radical mastectomy (47%). Most (92%) received adjuvant therapy: 7% received radiation therapy, 24% received chemotherapy, and 61% received both. The modal patient was 51-years-old (range = 31–84 years), Caucasian (95%; African American, 5%), married/partnered (75%), had some college (15 years), was employed (73%) at least part time, and half (56%) had an annual family income of $\geq \$50,000$.

Measures

PTSD symptoms and diagnoses—The PTSD Checklist–Civilian Version (PCL-C; Weathers et al., 1991) includes 17 items. Patients were instructed to consider their breast cancer experience, rating how much each symptom had bothered them in the last month using a 5-point scale (1 = *not at all*; 5 = *extremely*). Total scores range from 17 to 85. Internal consistency was .87.

The Structured Clinical Interview for DSM-IV, nonpatient version (SCID-NP; First et al., 1996) modules for anxiety disorders, mood disorders, and alcohol and drug abuse/dependence were used. Both past (precancer) and current symptoms were determined. Current symptoms were those present at the time of the interview. Precancer symptoms had to be (a) not present at the time of the interview, and (b) appearing/occurring prior to cancer diagnosis (i.e., longer than 18 months previously). Symptoms beginning after cancer diagnosis, but no longer present were noted. Patients' history of counseling/psychiatric treatment was also determined. Interviews were videotaped and reliability determined for 25%. Interrater kappa coefficients were as follows: mood disorders (precancer = .79, current = .88); anxiety disorders (precancer = .83, current = .89); alcohol and drug abuse/dependence (precancer = .83, current = .64); and current PTSD = .83. In cases of disagreement, a PhD clinical psychologist with extensive SCID experience was the criterion rater.

Using the SCID, interviewers assessed cancer-related PTSD symptoms including *DSM-IV* Criterion A and symptom clusters. According to the cluster criteria, to receive a PTSD diagnosis a patient must meet Criterion A, report at least one reexperiencing symptom, three avoidance/numbing symptoms, and two arousal symptoms. Current PTSD diagnoses were those continuing from the time of cancer diagnosis or those with delayed onset; there were no cases of symptoms that began but resolved.

Considering prior studies (see discussion above), in conjunction with meeting Criterion A, two strategies were used to identify subsyndromal PTSD cases. Patients were required to meet the symptom criteria for either the avoidance or hyperarousal clusters. With one exception (“foreshortened future”), the avoidance and hyperarousal clusters include symptoms with

lower frequencies of endorsements in cancer samples and unlike the reexperiencing cluster, multiple symptoms must be endorsed. Alternatively, patients who did not meet criteria for avoidance or hyperarousal were categorized as having subsyndromal PTSD if they had five or more symptoms across clusters. Factor analytic data with breast cancer patients show a mismatch between *DSM* assignment of symptoms to clusters and empirically determined assignment of symptoms to factors (Shelby, Golden-Kreutz, & Andersen, 2005). Thus, patients with multiple symptoms across the three clusters were included. For reference, these criteria are likely more stringent than criteria of Stein et al. (1997) and Marshall et al. (2001), similar to those of Weiss and colleagues (1992) and Gillock and colleagues (2005), and possibly less stringent than others (Blanchard et al., 1996; Carlier & Gersons, 1995; Schnurr, Lunney, & Sengupta, 2004; Schutzwohl & Maercher, 1999).

Stressors, functioning; and quality of life—The Life Stressor Checklist-Revised (LSCL-R; Wolfe, Kimerling, Brown, Chrestman, & Levin, 1996) is an interviewer-administered measure assessing the occurrence of 30 stressful events. Two scoring methods are used: (a) one point is given to each positively endorsed event and events are summed for a total ranging from 0 to 30, which reflects the number of stressful events experienced, and (b) one point is given to each positively endorsed life event that meets the *DSM-IV* PTSD Criterion A and these events are summed for total reflecting the number of Criterion A events experienced.

Research nurses provided Karnofsky Performance Status (KPS; Yates, Chalmer, & McKegney, 1980) ratings after a patient interview and medical chart review. The KPS ranges from 100 (*Normal*) to 0 (*Dead*) with criteria for each interval (e.g., 90 = *Normal activity/minor symptoms*; 80 = *Normal activity with effort/some symptoms*). Interrater reliability ranges from .70 to .97.

The Medical Outcomes Study Short Form-36 item (SF-36; Ware, Snow, & Kosinski, 2000) documents quality of life disruption due to physical or mental health. Eight scales (general health, physical functioning, physical role limitations, pain, general mental health, vitality, emotional role limitations, and social functioning) are used and weighted differentially to calculate Physical Health Component Summary (PCS) and Mental Health Component Summary (MCS) scores. Each is standardized with a mean of 50 ($SD = 10$). Alpha reliability is .94 and .89, respectively.

Procedure

Consecutive, newly diagnosed breast cancer patients with regional disease treated at a university-affiliated cancer center were accrued for a clinical trial of a psychosocial intervention versus assessment only; description of eligibility, accrual, and randomization procedures are available (Andersen et al., 2004). The research was approved by the Institutional Review Boards of the cancer center and the university. Briefly, patients were accrued and assessed during postsurgery clinic visits. Quality of life and health data were collected by female research assistants and nurses. During the next 4 months, intervention arm patients received stress reduction treatments, though not ones focused on PTSD. All patients were then followed with repeated assessments.

Accrual for the cancer-related PTSD study began 30 months after the start of the trial and continued for 40 months. Of the 227 women accrued, 148 were enrolled during the PTSD study window. For them, the PCL-C was included with the routine 18-month assessment. We examined the distribution of PCL-C scores and used a liberal cutoff (scores >30 which characterized roughly the upper third of the distribution) to identify an n of 45. Search of the literature revealed that 30 was substantially lower than a recommended cutoff of 50 for breast cancer patients (Andrykowski, Cordova, McGrath, Sloan, & Kenady, 1998). Also,

Ciechanowski et al. (2004) found that scores of 30–45 were associated with impairment among women enrolled in a health maintenance organization. Patients in the lower third of the distribution (PCL-C score ≤ 22 ; $n = 47$) were also identified for enrollment.

Thirty-five of the 45 (78%) high and 39 of the 47 (83%) low PCL-C scorers were accrued ($N = 74$; 81%). Of the remainder, 16 (17%) refused and 2 (2%) could not be reached. Participant and nonparticipant groups did not differ on demographic, disease/treatment characteristics, or PCL-C scores (p -values $> .20$). For the 74, we confirmed that all were at least 6 months post all cancer treatments and had no evidence of disease. Following informed consent, master's-level research assistants blind to symptom status conducted the SCID in a clinic setting. Patients received a fee for participation.

Data Analysis

We conducted analyses in two steps. First, ANOVAs for continuous variables and the Freeman-Halton (1951) Fisher's exact test for categorical variables were performed to contrast the groups on variables related to risk (sociodemographics, disease/treatment, trauma history, precancer psychiatric diagnoses), psychiatric diagnoses, and disruption of routine activities. For pairwise comparisons, the Scheffé method was used for continuous variables and the Fisher's exact test, ORs, and 95% confidence intervals (CIs) were computed for categorical variables.

Second, the contribution of cancer-related PTSD symptoms to current (18 month) outcomes was tested. Correlations between demographic and disease/treatment variables and outcomes were examined and those with a significant trend ($p < .10$) were included as controls. Multiple linear regression models were used to predict three outcomes (functional status and physical and mental health-related quality of life). Each model included demographic/medical covariates, baseline/initial score of the outcome, and current psychiatric morbidity (other than PTSD) as control variables. Two dummy-coded variables were used to represent the three cancer-related PTSD symptom groups (PTSD, Subsyndromal PTSD, and No PTSD). The No PTSD group is the reference group.

In the preface, we note that group assignment and current functioning outcomes were not associated with the clinical trial arm (p -values $> .30$). We repeated the analyses detailed below with the trial arm as a control variable and also tested for interaction effects between the trial arm and PTSD symptoms. All results were unchanged; the trial arm (p -values $> .35$) and all interactions (p -values $> .20$) were not significant. Thus, the analyses below collapse across the trial arm.

RESULTS

The SCID interviews classified patients ($N = 74$) based on current symptoms: no PTSD symptoms (No PTSD; $n = 47$), cancer-related subsyndromal PTSD (Subsyndromal; $n = 15$), and cancer-related PTSD diagnosis (PTSD; $n = 12$). Of the 12 PTSD cases, 9 had PCL-C scores in the elevated range and the remaining 3 cases scored in the lower range (< 22). Of the 15 subsyndromal cases, 7 patients met criteria for two clusters (six for reexperiencing and hyperarousal, one for avoidance and hyperarousal), 3 met criteria for avoidance/numbing only, 1 met criteria for hyperarousal only, and 4 patients had five or more symptoms across clusters. The PTSD symptoms were also assessed for other (noncancer) traumatic events that met criterion A. No patients met criteria for current subsyndromal PTSD or PTSD diagnosis related to other traumatic events.

Comparison of Groups

The groups were comparable on sociodemographic variables, but differed significantly in extent of disease (stage II vs. III), Freeman-Halton Fisher's exact test, $p < .05$, and extent of surgery (segmental vs. modified radical mastectomy), Freeman-Halton Fisher's exact test, $p < .01$. Twenty-five percent of PTSD patients were diagnosed with stage III disease compared to 7% (OR = 4.67, 95% CI = 0.42–52.00) of the Subsyndromal group and 6% (OR = 4.89, 95% CI = 0.85–28.24) of the No PTSD group. For type of surgery, 83% of the PTSD group received modified radical mastectomy versus 47% (OR = 5.71, 95% CI = 0.92–35.48) of the Subsyndromal group and 38% (OR = 8.06, 95% CI = 1.58–41.04) of the No PTSD group.

Regarding life events, patients reported having experienced an average of eight ($SD = 4$) stressful life events and an average of three ($SD = 3$) events that met Criterion A. The groups did not differ ($p > .10$) on total number of stressful events, but they significantly differed on the number of Criterion A events, $F(2, 71) = 3.85$, $p < .03$. Pairwise comparisons revealed that the PTSD group experienced significantly ($p < .05$) more Criterion A events than the No PTSD group, but the Subsyndromal group did not differ from the other two groups. For clinical detail, we inspected the frequencies of individual events, and a pattern was found for two. Half (50%) of the PTSD patients reported having been physically attacked/abused compared to 13% of the Subsyndromal group (OR = 6.50, 95% CI = 1.00–42.17) and 17% (OR = 4.88, 95% CI = 1.25–19.06) of the No PTSD group, Freeman-Halton Fisher's exact test, $p < .01$. Similarly, one third (33%) of patients with PTSD reported rape versus 13% (OR = 3.25, 95% CI = 0.48–92.04) of the Subsyndromal group and 11% (OR = 4.20, 95% CI = 0.92–19.14) of the No PTSD group, Freeman-Halton Fisher's Exact test, $p < .05$.

Across all disorders, the groups significantly differed, Freeman-Halton Fisher's exact test p -values $< .01$. Table 1 displays percentages of precancer (lifetime) psychiatric diagnoses within groups. Pairwise comparisons (see Table 1) revealed that patients with PTSD were distinguished by their history of anxiety disorders in contrast to the Subsyndromal (OR = 14.00, 95% CI = 1.37–142.90) and No PTSD groups (OR = 6.83, 95% CI = 1.65–28.25). The PTSD group was significantly more likely to have a history of PTSD (precancer) than the No PTSD group (OR = 7.68, 95% CI = 1.65–35.76), and there was a trend for the comparison between the PTSD and Subsyndromal groups (OR = 10.00, 95% CI = 0.97–102.90). The PTSD and No PTSD groups significantly differed in histories of mood (OR = 6.86, 95% CI = 1.61–29.23) and substance use/dependence diagnoses (OR = 5.38, 95% CI = 1.11–26.04). Here however, the rate for the Subsyndromal group was midway between the No PTSD and PTSD groups and not significantly different from either.

Overall, the percentage of patients with disorders increased with cancer-related PTSD symptom levels, Freeman-Halton Fisher's exact test, $p < .01$, with rates of 23%, 40%, and 75%, respectively (see Table 1). Overall, the rates for mood disorders were two to three times higher than rates for anxiety disorders. Compared to the No PTSD group, patients in the PTSD group were significantly more likely to have a current mood (OR = 8.44, 95% CI = 2.08–34.35) or anxiety disorder other than PTSD (OR = 7.33, 95% CI = 1.37–39.18). In all cases, rates for the Subsyndromal group were midway between the other groups and not significantly different from either. Current alcohol/substance use or dependence was largely not evident.

Interview queries assessed the daily impact of psychological distress. When asked if they, at times, felt emotionally unable to work, there were significant group differences, Freeman-Halton's Fisher exact test, $p < .01$. Forty-two percent of the PTSD group and 40% of the Subsyndromal group reported being unable to work in contrast to 11% of the No PTSD group (PTSD vs. No PTSD OR = 6.00, 95% CI = 1.37–26.24; Subsyndromal vs. No PTSD OR = 5.60, 95% CI = 1.40–22.44). When asked if stress due to cancer had been a cause to seek psychological treatment, the groups again significantly differed, Freeman-Halton Fisher's exact

test, $p < .001$, with 58% of the PTSD group and 33% of the Subsyndromal group acknowledging counseling in contrast to 11% of the No PTSD group (PTSD vs. No PTSD OR = 11.76, 95% CI = 2.69–51.42; Subsyndromal vs. No PTSD OR = 4.20, 95% CI = 1.02–17.35). Rates for the PTSD and Subsyndromal groups did not differ.

Prediction of Functioning

Table 2 displays multiple linear regression results testing the association between cancer-related PTSD groups and functional performance status and physical and mental health-related quality of life. In summary, all models accounted for significant variance in functional performance status (total $r^2 = 33\%$), $F(7, 65) = 4.57$, $p < .001$, physical health-related quality of life (total $R^2 = 48\%$), $F(7, 65) = 8.63$, $p < .001$, and mental health-related quality of life (total $R^2 = 50\%$), $F(7, 65) = 9.18$, $p < .001$. First, the presence of a current psychiatric disorder other than PTSD contributed to significantly lower mental health-related quality of life scores ($p < .01$), but was not associated with functional performance status or physical health-related quality of life scores. Second, compared to patients in the No PTSD group, patients with PTSD had significantly lower functional performance status, physical health-related quality of life, and mental health-related quality of life scores (p -values $< .05$). Third, the Subsyndromal group did not differ from the No PTSD group on functional performance status, physical health-related quality of life, or mental health-related quality of life scores.

DISCUSSION

New data on PTSD among cancer patients is provided. Novel contributions include a clinical study of cancer-related subsyndromal PTSD, the provision of current and lifetime comorbidity data, and longitudinal data showing the contribution of cancer-related PTSD and comorbid conditions to impaired physical and mental health outcomes and employment absenteeism among breast cancer survivors.

Contrasting diagnostic groups suggested unique patterns of clinical presentation, risk, and psychiatric comorbidity. Half of the PTSD patients met criteria for anxiety disorders prior to cancer diagnosis, a history unlike that of the subsyndromal group. A history of trauma also distinguished the PTSD cases. As one patient noted, “Cancer is *not* the most difficult thing that has ever happened to me.” In the PTSD literature, the relationship between prior trauma and PTSD is estimated to be .17, a statistically significant, but small, effect size (Ozer et al., 2003). However, the estimate jumps to .27 when the type of trauma is that reported here, namely assault, rape, and/or domestic violence. These data are consistent with questionnaire findings from Green and colleagues (2000). Other difficulties for patients with PTSD were also identified. Rates of prior mood (75%) and substance use disorders (33%) were high, a pattern similar to that found among head and neck and lung cancer patients with PTSD (Kangas et al., 2005; Kugaya et al., 2000). Both classes of disorders can be a sequelae of posttraumatic stress (Ozer et al., 2003). We do not know, but these disorders, having occurred for 75% of the patients, may have heightened risk not only for PTSD, but also for a depressive episode when cancer was diagnosed. What did not reemerge for these particular women at the time of diagnosis was significant substance abuse.

Inclusion of the subsyndromal group is novel for the cancer literature. Unlike PTSD cases, subsyndromal patients did not have a significant trauma history. Nevertheless, their risk for PTSD symptoms was heightened, a circumstance possibly related to prior mood disorders and/or substance use, as the rates for both classes of disorders were midway between the levels of the No PTSD and PTSD groups. In the regression analyses, the subsyndromal PTSD group did not differ from the No PTSD group in current impairment; a similar finding as been reported for veterans with subsyndromal PTSD (Grubaugh et al., 2005). Yet, it was clear that women with subsyndromal symptoms were struggling day to day, as their levels of occupational

impairment equaled that of the PTSD group and by 18 months postdiagnosis, 33% had sought psychological treatment. Although a modest assessment, these data bring to light the real-life impact of the cancer stressor. Gillock et al. (2005) found similar, significantly higher rates of healthcare utilization among syndromal and subsyndromal cases compared to no symptom patients from a primary care clinic. Similarly, Walker and colleagues (2003) studied women in a health maintenance organization and reported those with moderate PCL-C scores (30–44) had healthcare costs 38% higher and those with high PCL-C scores (≥ 45) had costs 104% higher than women with low/no symptoms (< 30). Taken together, the costs—psychological, occupational, financial, and others—are significant for cancer patients with PTSD, but they appear considerable for those with subsyndromal PTSD as well.

Our findings need to be viewed within the particular circumstances of this study. There was no effect (or interaction) of trial outcome on these findings, but readers are reminded of this context for data collection. Like the majority of the PTSD cancer literature, only breast cancer patients were enrolled. We do not know the generalizability of these findings to patients with other disease sites or samples with greater ethnic/racial diversity. As the focus was on clarification of subsyndromal symptoms, the liberal cutoff on the PCL-C was used and the two clinical groups were contrasted to the referent, a no symptom group, as has been done previously (e.g., Walker et al., 2003). For the SCID phase, we excluded the group scoring in the middle of the PCL-C distribution. This choice does not limit the validity of the findings, but it does preclude determination of PTSD incidence. To aid in future research, we conducted power analyses on variables for which the comparison of the PTSD and Subsyndromal groups was not significant. For example, the rates of precancer psychiatric diagnoses between the Subsyndromal ($n = 15$) and PTSD ($n = 12$) groups were 47% versus 75%, respectively (*ns*). To achieve a power of .80 with a two-tailed alpha of .05, a sample size of 104 patients would be needed. Multicenter accrual appears needed for future studies.

For the current study, women were required to meet *DSM-IV* Criterion A and exhibit PTSD symptoms related to cancer to be classified as having PTSD or subsyndromal PTSD, but a specific trauma event was not required. Establishing the index event for cancer is difficult, as the experience includes numerous threatening events. For some cancer patients, no single index event may occur as it does for the individual who is in a car accident, raped, or terrorized at gunpoint. Instead, for the cancer patient, stress can be prolonged due to continued physical symptoms, life disruption, and the possibility of cancer recurrence and death. Here, we collapsed PTSD symptoms associated with events during the diagnostic period, treatment, and recovery. Future research clarifying the relationship between index events and symptoms would be important, as traumatic stress symptoms with cancer could reflect prolonged distress/stress rather than PTSD.

Finally, the longitudinal analyses showed that across outcomes, PTSD diagnosis related to poorer status. This was an excess burden, beyond that occurring with other disorders, such as depression. Of the findings, the functional performance status data are particularly important as the ratings were made by research nurses, and they lend credence to those from a national survey of female veterans. Namely, veterans with PTSD had more health problems and poorer quality of life (Frayne et al., 2004). These data focus on patients' difficulties, but an analysis of patients' resilience is similarly important, as that is the path for the majority. Such combined study could be an avenue to understand broadly the anxiety-provoking aspects of cancer that are considerable, and for some, enduring.

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REFERENCES

- Alter CL, Pelcovitz D, Axelrod A, Goldenberg B, Harris H, Meyers B, et al. Identification of PTSD in cancer survivors. *Psychosomatics* 1996;37:137–143. [PubMed: 8742542]
- American Cancer Society. *Cancer facts and figures, 2007*. Author; Atlanta, GA: 2007.
- American Psychiatric Association. 4th ed.. Author; Washington, DC: 1994. *Diagnostic and statistical manual of mental disorders*.
- Andersen BL, Farrar WB, Golden-Kreutz DM, Glaser R, Emery CF, Crespin T, et al. Psychological, behavioral, and immune changes following a psychological intervention. *Journal of Clinical Oncology* 2004;22:3570–3580. [PubMed: 15337807]
- Andrykowski MA, Cordova MJ. Factors associated with PTSD symptoms following treatment for breast cancer: Test of the Andersen model. *Journal of Traumatic Stress* 1998;11:189–203. [PubMed: 9565911]
- Andrykowski MA, Cordova MJ, McGrath PC, Sloan DA, Kenady DE. Stability and change in posttraumatic stress disorder symptoms following breast cancer treatment. *Psycho-Oncology* 2000;9:69–78. [PubMed: 10668061]
- Andrykowski MA, Cordova MJ, Studts JL, Miller TW. Posttraumatic stress disorder after treatment for breast cancer. *Journal of Consulting and Clinical Psychology* 1998;66:586–590.
- Blanchard EB, Hickling EJ, Barton KA, Taylor AE, Loos WR, Jones-Alexander J. One year prospective follow-up of motor vehicle accident victims. *Behavior Research & Therapy* 1996;34:775–786.
- Brewin CR, Andrews B, Valentine JD. Meta-analysis of risk factors for posttraumatic stress disorder in trauma-exposed adults. *Journal of Consulting and Clinical Psychology* 2000;68:748–766. [PubMed: 11068961]
- Brewin CR, Watson M, McCarthy S, Hyman P, Dayson D. Memory processes and the course of anxiety and depression in cancer patients. *Psychological Medicine* 1998;28:219–224. [PubMed: 9483699]
- Carlier IV, Gersons BP. Partial posttraumatic stress disorder (PTSD). *Journal of Nervous and Mental Disorders* 1995;183:107–109.
- Ciechanowski ES, Walker EA, Russo JE, Newman E, Katon WJ. Adult health status of women HMO members with posttraumatic stress disorder symptoms. *General Hospital Psychiatry* 2004;26:261–268. [PubMed: 15234820]
- Diemling GT, Kahana B, Bowman KE, Schaefer ML. Cancer survivorship and psychological distress in later life. *Psycho-Oncology* 2002;11:479–494. [PubMed: 12476430]
- First, MB.; Spitzer, RL.; Gibbon, M.; Williams, J. *Structured Clinical Interview for DSM-IV Axis I Disorders—Patient Edition (SCID-I/P, Version 2.0)*. New York State Psychiatric Institute, Biometrics Research Department; New York: 1996.
- Frayne SM, Seaver MR, Loveland S, Christiansen CL, Spiro A, Parker VA, et al. Burden of medical illness in women with depression and posttraumatic stress disorder. *Archives of Internal Medicine* 2004;164:1306–1312. [PubMed: 15226164]
- Freeman GH, Halton JH. Note on an exact treatment of contingency, goodness of fit and other problems of significance. *Biometrika* 1951;38:141–149. [PubMed: 14848119]
- Gillock KL, Zayfert C, Hegel MT, Ferguson RJ. Posttraumatic stress disorder in primary care: prevalence and relationships with physical symptoms and medical utilization. *General Hospital Psychiatry* 2005;27:392–399. [PubMed: 16271653]
- Golden-Kreutz D, Andersen BL. Depressive symptoms after breast cancer surgery: Relationships with stress. *Psycho-Oncology* 2004;13:211–220. [PubMed: 15022156]
- Golden-Kreutz DM, Thornton LM, Wells-DiGregorio S, Frierson GM, Jim HS, Carpenter KM, et al. Traumatic stress, perceived global stress, and life events: Predicting quality of life in breast cancer patients. *Health Psychology* 2005;24:288–296. [PubMed: 15898865]

- Green BL, Krupnick JL, Rowland JH, Epstein SA, Stockton P, Spertus I, et al. Trauma history as a predictor of psychological symptoms in women with breast cancer. *Journal of Clinical Oncology* 2000;18:1084–1093. [PubMed: 10694561]
- Green BL, Rowland JH, Krupnick JL, Epstein SA, Stockton P, Stern NM, et al. Prevalence of posttraumatic stress disorder in women with breast cancer. *Psychosomatics* 1998;39:102–111. [PubMed: 9584535]
- Grubaugh AL, Magruder KM, Waldrop AE, Elhai JD, Knapp RG, Frueh C. Subthreshold PTSD in primary care: Prevalence, psychiatric disorders, health care use, and functional status. *The Journal of Nervous and Mental Disorders* 2005;193:658–664.
- Gurevich M, Devins GM, Rodin GM. Stress response syndromes and cancer. *Psychosomatics* 2002;43:259–281. [PubMed: 12189252]
- Jacobsen PB, Sadler IJ, Booth-Jones M, Soety E, Weitzner MA, Fields KK. Predictors of posttraumatic stress disorder symptomatology following bone marrow transplantation for cancer. *Journal of Consulting and Clinical Psychology* 2002;70:235–240. [PubMed: 11860050]
- Jacobsen PB, Widows MR, Hann DM, Andrykowski MA, Kronish LE, Fields KK. Posttraumatic stress disorder symptoms after bone marrow transplantation for breast cancer. *Psychosomatic Medicine* 1998;60:366–371. [PubMed: 9625227]
- Kangas M, Henry JL, Bryant RA. Posttraumatic stress disorder following cancer. *Clinical Psychology Review* 2002;22:499–524. [PubMed: 12094509]
- Kangas M, Henry JL, Bryant RA. The course of psychological disorders in the 1st year after cancer diagnosis. *Journal of Consulting and Clinical Psychology* 2005;73:763–768. [PubMed: 16173866]
- Keane, TM.; Kaloupek, DG. Comorbid psychiatric disorders in PTSD. Implications for research.. In: Yehuda, R.; McFarlane, AC., editors. *Psychobiology of posttraumatic stress disorder*. New York Academy of Sciences; New York: 1997. p. 24–34.
- Kugaya A, Akechi T, Okuyama T, Nakano T, Mikami I, Okamura H, et al. Prevalence, predictive factors, and screening for psychologic distress in patients with newly diagnosed head and neck cancer. *Cancer* 2000;88:2817–2823. [PubMed: 10870066]
- Marshall RD, Olfson M, Hellman F, Blanco C, Guardino M, Struening EL. Comorbidity, impairment, and suicidality in subthreshold PTSD. *American Journal of Psychiatry* 2001;158:1467–1473. [PubMed: 11532733]
- Mehnert A, Koch U. Prevalence of acute and posttraumatic stress disorder and comorbid mental disorders in breast cancer patients during primary cancer care: A prospective study. *Psycho-Oncology* 2007;16:181–188. [PubMed: 16856147]
- Mundy EA, Blanchard EB, Cirenza E, Gargiulo J, Maloy B, Blanchard CG. Posttraumatic stress disorder in breast cancer patients following autologous bone marrow transplantation or conventional cancer treatments. *Behaviour Research & Therapy* 2000;38:1015–1027. [PubMed: 11004740]
- Ozer EJ, Best SR, Lipsey TL, Weiss DS. Predictors of posttraumatic stress disorder and symptoms in adults: A meta-analysis. *Psychological Bulletin* 2003;129:52–73. [PubMed: 12555794]
- Palmer SC, Kagee A, Coyne JC, DeMichele A. Experience of trauma, distress, and posttraumatic stress disorder among breast cancer patients. *Psychosomatic Medicine* 2004;66:258–264. [PubMed: 15039512]
- Pitman RK, Lanes DM, Williston SK, Guillaume JL, Metzger LJ, Gehr GM, et al. Psychophysiologic assessment of posttraumatic stress disorder in breast cancer patients. *Psychosomatics* 2001;42:133–140. [PubMed: 11239126]
- Schnurr PP, Lunney CA, Sengupta A. Risk factors for the development versus maintenance of posttraumatic stress disorder. *Journal of Traumatic Stress* 2004;17:85–95. [PubMed: 15141781]
- Schutzwahl M, Maercher A. Effects of varying diagnostic criteria for posttraumatic stress disorder are endorsing the concept of partial PTSD. *Journal of Traumatic Stress* 1999;12:155–165. [PubMed: 10027149]
- Shelby RA, Golden-Kreutz DM, Andersen BL. Mismatch of PTSD symptoms and DSM-IV symptom clusters in a cancer sample: Exploratory factor analysis of the PTSD Checklist-Civilian Version. *Journal of Traumatic Stress* 2005;18:347–357. [PubMed: 16281232]
- Stein MB, Walker JR, Hazen AL, Forde DR. Full and partial posttraumatic stress disorder: A community survey. *American Journal of Psychiatry* 1997;154:1114–1119. [PubMed: 9247398]

- Walker EA, Katon W, Russo J, Ciechanowski P, Newman E, Wagner AW. Health care costs associated with posttraumatic stress disorder symptoms in women. *Archives of General Psychiatry* 2003;60:369–374. [PubMed: 12695314]
- Ware, JE.; Snow, KK.; Kosinski, M. SF-36 Health Survey: Manual and interpretation guide. Quality Metric Inc; Lincoln, RI: 2000.
- Weathers, FW.; Litz, BT.; Herman, DS.; Huska, JA.; Keane, TM. The PTSD Checklist-Civilian Version. Boston Veterans Affairs Medical Center, National Center for PTSD; Boston: 1991.
- Weiss DS, Marmar CR, Schlenger WE, Fairbank JA, Jordan BK, Hough RL, et al. The prevalence of lifetime and partial post-traumatic stress disorder in Vietnam theater veterans. *Journal of Traumatic Stress* 1992;5:365–376.
- Wolfe, JW.; Kimerling, R.; Brown, PJ.; Chrestman, KR.; Levin, K. Psychometric review of The Life Stressor Checklist-Revised.. In: Stamm, BH., editor. *Measurement of stress, trauma, and adaptation*. Sidran Press; Lutherville, MD: 1996. p. 5
- Yates JW, Chalmer B, McKegney EP. Evaluation of patients with advanced cancer using the Karnofsky Performance Status Scale. *Cancer* 1980;53:2002–2007.

Table 1

Type and Percentage of Lifetime (Pre cancer) and Current Psychiatric Diagnoses Within Cancer-Related PTSD Groups

Period of diagnosis	Diagnosis type	No PTSD (<i>n</i> = 47)	Subsyndromal PTSD (<i>n</i> = 15)	PTSD (<i>n</i> = 12)	Total sample (<i>N</i> = 74)
Lifetime (pre-cancer)					
	Mood disorder (%)	30 _a	43 _{a,b}	75 _b	37
	Anxiety disorder (%)	13 _a	7 _a	50 _b	18
	PTSD (%)	9 _a	7 _{a,b}	42 _b	14
	Alcohol/substance abuse or dependence (%)	9 _a	20 _{a,b}	33 _b	15
	All disorders (%)	36 _a	47 _{a,b}	75 _b	45
Current					
	Mood disorders (%)	19 _a	33 _{a,b}	67 _b	30
	Anxiety disorders (excluding PTSD) (%)	6 _a	13 _{a,b}	33 _b	12
	Alcohol/substance abuse or dependence (%)	2	7	0	3
	All disorders (excluding PTSD) (%)	23 _a	40 _{a,b}	75 _b	35

Note: Pairwise comparisons were conducted using Fisher's exact test. Common subscripts for a variable across groups indicate no significant differences, whereas different superscripts for a variable indicate a significant difference ($p < .05$).

Table 2
Multiple Linear Regression Analyses Testing the Association between Cancer-Related PTSD Symptom Groups and Current Functional Status and Quality of Life

Variables	<i>B</i>	<i>SE B</i>	β
Karnofsky Performance Status			
Employment status ^a	4.86	1.50	.34**
Surgical treatment ^b	2.42	1.76	.19
Initial Karnofsky score	0.19	0.10	.21
Radiation therapy ^c	3.26	1.77	.24
Comorbid psychiatric diagnosis ^d	-1.65	1.50	-.12
Cancer-related PTSD diagnosis (C ₁) ^e	-4.99	2.07	-.29*
Cancer-related subsyndromal PTSD (C ₂) ^f	-1.96	1.76	-.12
Quality of Life—Physical Health Component (PCS)			
Employment status	3.60	1.89	.18
Surgical treatment	5.44	2.21	.30*
Initial physical health component score (PCS)	0.55	0.11	.49**
Radiation therapy	6.10	2.21	.32**
Comorbid psychiatric diagnosis	-1.20	1.86	-.06
Cancer-related PTSD diagnosis (C ₁)	-8.24	2.58	-.34**
Cancer-related subsyndromal PTSD (C ₂)	-2.37	2.17	-.10
Quality of Life—Mental Health Component (MCS)			
Age in years	0.10	0.09	.10
Disease stage ^g	-4.01	3.21	-.12
Surgical treatment	3.05	1.89	.16
Initial mental health component score (MCS)	0.28	0.09	.33**
Comorbid psychiatric diagnosis	-6.68	2.03	-.33**
Cancer-related PTSD diagnosis (C ₁)	-5.86	2.79	-.23*
Cancer-related subsyndromal PTSD (C ₂)	-1.83	2.33	-.08

Note:

^aEmployment status: 0 = not employed outside of home, 1 = employed

^bSurgical treatment: 0 = segmental mastectomy, 1 = modified radical mastectomy

^cRadiation therapy: 0 = no, 1 = yes

^dComorbid psychiatric diagnosis (other than PTSD): 0 = no, 1 = yes

^eDummy coded variable C₁ with PTSD diagnosis coded as 1

^fDummy coded variable C₂ with Subsyndromal PTSD coded as 1

^gDisease stage: 0 = II, 1 = III.

* $p < .05$.

** $p < .01$.