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Living with cancer-related uncertainty: associations with fatigue, insomnia, and affect in younger breast cancer survivors

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Abstract

Purpose—Uncertainty in cancer patients and survivors about cancer-related symptoms, treatment, and disease course has been related to poorer mental and physical health. However, little is known about whether cancer-related uncertainty relates with specific disease and treatment-related outcomes such as fatigue, insomnia, and affect disruptions. In this paper, we report these associations in younger survivors aged 50 years or less, a population increasing in prevalence.

Methods—Participants included 313 breast cancer survivors (117 African-Americans and 196 Caucasians) who were aged 24 to 50 years and were 2 to 4 years posttreatment. Self-reported cancer-related uncertainty (Mishel Uncertainty in Illness Scale–Survivor Version), fatigue (Piper Fatigue Scale–Revised), insomnia (Insomnia Severity Index), and negative and positive affect (Positive and Negative Affect Schedule (PANAS)) measures were collected upon study entry.

Results—Hierarchical regression analyses controlled for relevant sociodemographic variables including the following: race, age, years of education, number of children, employment status, marital status, monthly income, smoking status, family history of cancer, endorsement of treatment-induced menopause, and religiosity. Over and above these factors, higher cancer-related uncertainty was significantly associated with more self-reported fatigue ($\beta=.43$), insomnia ($\beta=.34$), negative affect ($\beta=.43$), as well as less positive affect ($\beta=-.33$), all $ps<.01$.

Conclusions—Younger breast cancer survivors who are 2–4 years posttreatment experience cancer-related uncertainty, with higher levels associated with more self-reported psycho-physiological disruptions. Cancer survivors who present in clinical settings with high uncertainty about recurrence or management of long-term effects of treatment may thus benefit from assessment of fatigue, insomnia, and affect.

Keywords

Uncertainty; Cancer survivorship; Fatigue; Insomnia; Affect

Breast cancer survivorship has increased almost 50 % in the last 50 years, resulting in more women adjusting to life post-treatment [1]. After treatment ends, survivors may struggle with cancer-related uncertainty about recurrence, treatment-related side effects, and their long-term health [2–4]. More-over, survivors live with cancer-related uncertainty that may continue for years after treatment ends [5–7].

However, little is known about cancer-related uncertainty and associated sequelae in younger breast cancer survivors, who are aged 50 years or less. This subgroup, comprising 25–30 % of breast cancer survivors in the USA, experiences survivorship differently than their older counterparts, reporting greater distress, more time lost from work, relationship and sexual difficulties, and struggles with child-rearing [1, 4, 5, 8–10]. The present study thus investigated the relationships between cancer-related uncertainty and several aspects of survivorship-related functioning in a diverse sample of younger breast cancer survivors 2–4 years posttreatment.

Cancer-related uncertainty is conceptualized to be a cognitive state generated by a patient or survivor's inability to determine the meaning or outcome of cancer-related stimuli (e.g., scars, absence of breast tissue, the attribution of symptoms to effects of treatment, the duration of treatment-related symptoms or sequelae) or events that trigger thoughts of recurrence (e.g., a mammogram) [11, 12]. Stimuli that trigger cancer-related uncertainty are complex, inconsistent, random, and/or unpredictable and may be generated by a lack of information [11, 13]. For instance, cancer-related uncertainty may be generated or exacerbated by having a family history of cancer, but it may be quelled by religiosity, which can offer structure and spiritually themed answers to unresolved questions [14]. In cancer patients and survivors, cancer-related uncertainty has been related to poorer physical health and psychological adjustment [6, 15–18]. For cancer survivors, long-term treatment side effects such as fatigue and cognitive changes may be accompanied by uncertainty about how long they will last, whether they will be permanent or may decrease over time, and why they persist.

Literature suggests that fatigue, insomnia, and mood disturbance are among the most persistent and deleterious psychophysiological concerns for all survivors, including those under age 50 [19–24]. In contrast to fatigue commonly experienced by noncancer individuals, fatigue after cancer treatment presents as physical weariness or tiredness not alleviated by rest, and it has been described as the most common cancer-related complaint and also the most poorly understood by physicians [23, 25]. Preliminary evidence by Mast [26] suggests that cancer-related uncertainty is positively associated with fatigue among older breast cancer survivors. However, in that study, fatigue was measured using one self-report item, and relevant sociodemographic variables were not controlled for in the analyses. Thus, assessing the association between cancer-related uncertainty and fatigue using reliable measures and covariates, in a sample of younger survivors, is needed.

In addition to fatigue, cancer survivors commonly endorse symptoms of insomnia, which may include difficulty falling asleep, staying asleep, or waking from sleep [27]. Literature suggests that these symptoms are twice as prevalent among breast cancer survivors as those in the general population [28]. Symptoms of insomnia are associated with psychological, behavioral, and health disturbances in cancer survivors [27, 28]. To date, the association between cancer-related uncertainty and insomnia has not been reported in the literature.

Regarding emotional functioning, younger cancer survivors experience more chronic emotional distress than their older and healthy counterparts [4, 5, 8–10]. Among older breast cancer survivors, negative mood is related to cognitive processes, which include cancer-related uncertainty [29]. However, this association remains to be tested in younger survivors, for whom cancer-related uncertainty has been related to poorer quality of life and ratings of loss of social support [5, 9].

Sociodemographic variables may also contribute to cancer survivors' symptoms of fatigue, insomnia, and affect disturbance. Several factors known to relate directly or indirectly with survivors' psychophysiological functioning include their race, age, years of education, number of children, employment status, marital status, monthly income, and smoking status [19–24, 29]. Additionally, treatment-induced menopause is both common and associated with impaired emotional and health-related quality of life in younger breast cancer survivors [8].

Method

Study hypotheses

To advance our understanding of cancer survivorship in younger survivors, this study was designed to examine whether cancer-related uncertainty is positively associated with higher scores on self-report measures of fatigue, insomnia, and negative affect and is negatively associated with positive affect. We hypothesized that these relationships would persist after statistically controlling for the impact of literature-identified relevant sociodemographic factors.

Participants and procedure

Participants were enrolled in an uncertainty management intervention study approved by the Institutional Review Board at the University of North Carolina at Chapel Hill School of Nursing (M. Mishel, principal investigator). The Younger Breast Cancer Survivor Uncertainty Management Intervention (YS-UMI) was a randomized study conducted with Caucasian and African-American breast cancer survivors under age 50, as the latter subgroup has unique needs that have been historically understudied in clinical research [30]. Recruitment for this study was conducted throughout central, southern, and eastern sections of North Carolina and involved using multiple strategies tailored to participants' ethnicity and socioeconomic status, including use of recruitment booths at church and community events, posting flyers at cancer support groups and clinics, as well as targeted mailings to women identified in tumor registries [31]. Participants self-identified their ethnicity. Study criteria required participants to be English speaking, less than 50 years old at enrollment,

between 2 and 4 years posttreatment for breast cancer (stages 1, 2, 3, and 4), and not in treatment for any other forms of cancer. Data were collected in participants' homes at baseline, 4–6 months after baseline, and 8–10 months after baseline. This manuscript reports findings based on self-report data obtained at baseline. Compensation for completion of baseline data included a \$20 check, a magnet, and a community resource guide listing local free or income-based clinics with their eligibility criteria for getting follow-up care. These incentives were intended to show the women our appreciation for their participation in our study.

The final sample included 313 breast cancer survivors (117 African-Americans and 196 Caucasians), who were, on average, 3 years posttreatment. Study participants ranged in age from 24 to 50 years ($M=43.96$, $SD=(4.82)$) at time of assessment, and most were married ($n=212$, 67.70 %) and highly educated (years of education, $M=15.19$, $SD=2.35$).

Measures

Sociodemographic information—Information regarding race, age, years of education, number of children, employment status, marital status, monthly income, smoking status, family history of cancer, and endorsement of treatment-induced menopause was gathered using a demographic and health data form. Religiosity was assessed using the Participation in Religious Activities Scale, which measures frequency of participation in religious activities on a five-point Likert scale from 1 (“never”) to 5 (“very often”) [32]. Items are averaged to create a total score, with higher scores indicating a higher degree of religious participation. Internal reliability of total religiosity score in the current sample was good ($\alpha=.94$).

Cancer-related uncertainty—Cancer-related uncertainty was measured using the Mishel Uncertainty in Illness Scale–Survivor Version (MUIS-S), a 22-item scale adaption of the Uncertainty in Illness Scale [13, 33]. Participants rated their current agreement with statements on a five-point Likert scale of 1 (“strongly disagree”) to 5 (“strongly agree”). Sample items include: “I’m certain they will not find anything else wrong with me” and “The long-term effect of my treatment is clear to me.” Each item is scored and summed to create a total score. Higher total scores reflect greater cancer-related uncertainty. Cronbach’s alpha for total cancer-related uncertainty score in this sample was good ($\alpha=.84$).

Affect—Affect was measured using the Positive and Negative Affect Schedule (PANAS) [34]. The PANAS is a 20-item scale that consists of two subscales measuring positive and negative affect. Participants indicated the extent to which she or he has felt a particular emotion over the last month on a five-point Likert scale from 1 (“very slightly or not at all”) to 5 (“extremely”). The PANAS is one of the most widely used instruments; both subscales have demonstrated good reliability [34]. In this sample, reliabilities for both the negative affect and positive affect subscales were adequate ($\alpha=.90$ and $.89$, respectively).

Fatigue—Fatigue was measured using the revised Piper Fatigue Scale (R-PFS), a 22-numerical item scale on which participants rated the duration of their current fatigue as well as the severity, intrusiveness, extent, and unpleasantness of the fatigue they are currently

experiencing [35]. The measure assesses specific domains of fatigue (i.e., behavioral/severity, affective meaning, sensory, and cognitive/mood), which are used to create a total fatigue score. Each item is presented with a numerical scale from 0 to 10, with higher scores indicating greater fatigue. Scores from all items are averaged to create a total fatigue score (0=none, 1–3=mild, 4–6=moderate, and 7–10=severe) [35]. The scale has demonstrated good internal consistency, content validity, and concurrent criterion validity with adult cancer patients [20]. Cronbach's alpha for this sample was excellent ($\alpha=.98$).

Insomnia—Insomnia was measured using the Insomnia Severity Index [36]. This measure consists of seven items asking respondents to rate the degree to which several aspects of sleep (i.e., difficulty falling asleep) had been problematic over the past 2 weeks on a five-point Likert scale ranging from 0 (“not at all”) to 4 (“very much”). Scored items are summed to create a total score. Alpha values are .90–.91 in noncancer populations and .74 in cancer patients [37]. In this sample, Cronbach's alpha was good ($\alpha=.89$).

Analysis plan

Descriptive statistics were conducted on all study variables (see Table 1). To better understand the relations between cancer-related uncertainty and fatigue, insomnia, negative affect, and positive affect, four hierarchical linear regressions were conducted (see Table 2). Each regression modeled a separate outcome: step 1 included study covariates (demographic information and religiosity), and step 2 included MUIS-S scores. Standardized beta coefficients (β s) were calculated to allow for comparisons across covariates and psychophysiological outcomes.

Results

Sample characteristics

All 313 participants completed the self-report measures. As depicted in Table 1, the sample primarily comprised women who were working full-time, married, and nonsmoking. Participants varied in their religiosity, though on average, women endorsed some participation in religious activity. In our sample, 43.50 % of participants reported a family history of cancer, and 51.44 % reported to be experiencing treatment-induced menopause. The average cancer-related uncertainty score for this sample of younger survivors was 56.65 ($SD=11.96$). Additionally, on average, participants endorsed “mild-to-moderate” levels of fatigue ($M=3.48$, $SD=2.52$), using severity codes by Piper et al. [35]. Furthermore, insomnia symptoms on average ($M=9.61$, $SD=6.29$) were reflective of “sub-threshold insomnia” [36]. Regarding emotional state, mean scores for negative affect ($M=21.95$, $SD=7.89$) and positive affect ($M=35.63$, $SD=7.17$) were both slightly higher than reported averages for noncancer survivors [34].

Hypothesis testing

As previously described, a series of four hierarchical regression models tested whether cancer-related uncertainty was significantly associated with fatigue, insomnia symptoms, negative affect, and positive affect after controlling for covariates. Results of these regressions are presented in Table 2.

Step 1 of regression analyses determined the association of sociodemographic variables with fatigue, insomnia, negative affect, and positive affect. In total, covariates accounted for 8 % of the variance in fatigue scores. Higher fatigue scores were significantly associated with less self-reported income ($\beta = -.16, p < .05$) and being a smoker ($\beta = .15, p < .01$). No other covariates were related to fatigue scores. Covariates accounted for 13 % of the variance in insomnia scores. Higher insomnia scores were significantly related to not having full-time employment ($\beta = -.16, p < .01$), less religiosity ($\beta = -.15, p < .01$), and having treatment-induced menopause ($\beta = .12, p < .05$). Finally, covariates were more associated with the variance in scores of negative affect (12 %) than positive affect (5 %). Covariates significantly related to more negative affect included having less income ($\beta = -.24, p < .01$) and less religiosity ($\beta = -.24, p < .01$). More positive affect was related to having more formal education ($\beta = .16, p < .05$) and more religiosity ($\beta = .16, p < .05$).

Results of step 2 of the regression analyses supported our hypotheses, indicating that cancer-related uncertainty was positively associated with higher fatigue ($\beta = .43, p < .01$), insomnia ($\beta = .34, p < .01$), and negative affect ($\beta = .43, p < .01$) and was negatively associated with positive affect ($\beta = -.33, p < .01$), after accounting for covariates. The magnitude of these standardized coefficients reflects a medium effect size for each association ($\beta s > .3$).

Results of the regression analyses also revealed the unique contribution of cancer-related uncertainty to variance in scores of each psychophysiological outcome. This information is reflected in R^2 change scores in step 2 of the regressions. Cancer-related uncertainty accounted for the greatest variance in fatigue and negative affect scores (17 % each), followed by insomnia and positive affect scores (10 % each).

Discussion

To our knowledge, this is the first study to document an association between cancer-related uncertainty and symptoms of fatigue, insomnia, and affect changes in younger breast cancer survivors. These findings are based on a racially diverse sample of 313 survivors between ages 24 and 50, suggesting that cancer-related uncertainty is a salient experience for these populations and is related to poorer posttreatment psychophysiological functioning.

Our findings indicate that younger survivors' cancer-related uncertainty levels relate to concurrent and elevated symptoms of fatigue, sleep disturbance, and disrupted mood, underscoring the significance of cancer-related uncertainty years after treatment ends.

Descriptive analyses indicated that the average cancer-related uncertainty score was slightly higher (within 0.5 standard deviation) than what has been previously reported for younger breast cancer survivors [5]. For the similar Managing Uncertainty in Illness-Adult Scale, three data sets obtained from current breast cancer patients had average cancer-related uncertainty scores that were higher than those found in our sample of younger survivors [38]. As the women in our study completed treatment between 2 and 4 years prior to study entry, it would be expected that survivors have less cancer-related uncertainty than do current patients.

Study participants reported levels of fatigue between the “mild” and “moderate” categories suggested by Piper et al. [35]. This finding supports the literature describing cancer-related fatigue as a persistent concern for survivors, which may last for years after treatment ends [39]. In our sample, fatigue was significantly related to cancer-related uncertainty. We extend the previous findings linking fatigue with cancer-related uncertainty in older survivors [12] to younger breast cancer survivors, using the well-validated revised Piper Fatigue Scale measure of fatigue.

Women in our study also reported elevated symptoms of insomnia. A score of 10 on the Insomnia Severity Index was recently posited as a sensitive and specific indicator of clinically impairing insomnia [40]. Alarming, the current study participants averaged a score of 9.61 on this measure, which is just below the clinical cutoff. These results support the literature reporting sleep difficulties as a major concern for cancer survivors [41]. To our knowledge, we are the first to report an association between self-reported insomnia severity and the experience of cancer-related uncertainty.

In spite of the younger survivors’ difficulties indicated by these findings, scores of negative affect and positive affect in our sample were similar to those in a healthy sample [34]. These results reflect findings that 2 years after treatment ends, many breast cancer survivors report age-normative emotional distress levels [42, 43]. However, we also found that women in our sample with more cancer-related uncertainty had significantly less positive affect and more negative affect. These findings indicate that emotional disturbance can worsen when survivors’ uncertainty levels are elevated, and suggest that monitoring of cancer-related uncertainty throughout survivorship may be important for maintenance of emotional well-being.

We also report several significant associations between sociodemographic sample characteristics and self-reported fatigue, insomnia, and affect. Within fatigue, having less income and being a smoker were associated with higher fatigue scores, which is consistent with prior literature on correlates of cancer-related fatigue [21, 22]. Regarding insomnia, higher scores were related to having less than full-time employment, having treatment-induced menopause, and less religiosity. Prior research suggests that survivors experiencing elevated insomnia have more difficulty working full-time and tend to be unemployed or take sick leave [28]. In our study, women with treatment-induced menopause had more difficulty with insomnia symptoms, which could be due to experiencing hot flashes, night sweats, general aches and pains, or psychological distress [8]. We also found that several sociodemographic variables were associated with survivors’ affect. Greater income related to less negative affect and more education was positively related to greater positive affect. These results emphasize the protecting role of socioeconomic status in the mental health of long-term cancer survivors.

Finally, in our sample, religiosity was related to less insomnia and negative affect as well as more positive affect. These findings are supported by the literature relating religious coping to better quality of life in long-term breast cancer survivors [29]. These associations may be mediated by less cancer-related uncertainty, though this remains to be examined in future studies.

Several important limitations should also be noted. The cross-sectional design of this study precludes causal inferences about relations among study variables. Theoretically, cancer-related uncertainty is posited to precipitate psychological disturbance, such as affect disturbance, as the survivor struggles to resolve uncertainty-generating stimuli [11, 12]. Cancer-related uncertainty may also precipitate symptoms of fatigue and insomnia by initiating a psychophysiological stress response impairing daytime energy and sleep quality. Recently, cancer-related fatigue, sleep disturbance, and depressive symptoms have been related to hypothalamus-pituitary-adrenal (HPA) axis dysfunction as well as circulating inflammation [44]. Research is needed to determine the extent to which cancer-related uncertainty triggers dysregulated cortisol output from the HPA axis and potential downstream effects on energy and sleep. However, fatigue and insomnia may also generate cancer-related uncertainty in survivors who struggle to understand and treat these persistent symptoms. Thus, longitudinal studies are needed to elucidate causality of the relations reported in this paper. In addition to causality, longitudinal designs can test potential mediators of the relationships we report. Our models accounted for between 15 and 29 % of the variances in scores of fatigue, insomnia, negative affect, and positive affect, suggesting that additional factors need to be evaluated to better explain these outcomes. For instance, Von et al. [24] found that mood disturbance, interleukin-1 β , and morning cortisol were strongly associated with breast cancer patients' fatigue. Literature on cancer survivorship also implicates neuroimmune (i.e., cortisol secretion and inflammation) dysfunction as a predictor of fatigue, insomnia, and disturbed affect [29, 41, 44]. Future studies would thus benefit from the measurement of these biological data to better inform symptom management in younger cancer survivors. Additionally, self-report questionnaires were used to measure survivors' fatigue and insomnia levels. Physiological measures of energy and sleep disturbance, such as an ATP profile test or the use of an actometer, could have provided more objective information about survivors' physiological activity throughout the day and evening.

Findings from this study could be useful for physicians and other health-care professionals caring for cancer survivors. Survivors with cancer-related uncertainty will present with concerns about the ambiguity, complexity, or unpredictability of survivorship and/or treatment-related symptoms or may feel that they lack information about these symptoms and their treatments [11, 12]. Clinicians can inquire about these uncertainties and offer information, referrals when appropriate, and support. Uncertainty management interventions offering similar approaches have proven successful at improving aspects of survivors' mental health [30, 45]. Furthermore, our data suggest that illness uncertainty places cancer survivors at higher risk for disturbed psychophysiological and emotional functioning. Thus, survivors expressing cancer-related uncertainty concerns may benefit from clinical assessment of these domains.

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Table 1

Summary of demographic and psychological/adjustment-related variables

Variable	Range	Mean (SD)/N (%)
Demographic		
Race (African-American)		117 (37.38 %)
Age (years)	24–51	43.96 (4.82)
Education (years)	10–25	15.19 (2.35)
Number of children	0–5	1.66 (1.14)
Employment status (full-time)		190 (60.70 %)
Marital status (married)		212 (67.70 %)
Monthly income (\$4,000+)		143 (45.69 %)
Smoking status (smoker)		30 (9.58 %)
Religiosity	1.00–5.00	3.64 (1.02)
Family Hx of cancer (yes)		136 (43.50 %)
Treatment-induced menopause (yes)		161 (51.44 %)
Psychological/adjustment-related		
Cancer-related uncertainty	26–92	56.65 (11.96)
Fatigue	.00–9.41	3.48 (2.52)
Insomnia	0–26	9.61 (6.29)
Negative affect	10–49	21.95 (7.89)
Positive affect	12–50	35.63 (7.17)

N=313. Range refers to the range of scores obtained in current study sample

Table 2

Hierarchical regressions relating cancer-related uncertainty to fatigue, insomnia, and affect

	Fatigue	Insomnia	Negative affect	Positive affect
Step 1	$R^2=.08^*$	$R^2=.13^{**}$	$R^2=.12^{**}$	$R^2=.05$
Race (AA)	.01	.02	<-.00	-.02
Age (years)	<-.00	.09	-.01	.06
Education (years)	.11	-.09	.02	.16*
No. of children	.06	.06	.02	-.05
Employed (full-time)	-.11	-.16^{**}	-.04	.01
Marital status	-.04	.01	-.07	-.03
Income	-.16*	-.11	-.24^{**}	-.02
Smoking status	.15*	.02	.06	-.05
Religiosity	-.01	-.15*	-.24^{**}	.16*
Family Hx of Ca	-.07	-.09	-.05	<.00
Treatment-induced menopause	.03	.12*	.10	-.05
Step 2	$R^2=.17^{**}$	$R^2=.10^{**}$	$R^2=.17^{**}$	$R^2=.10^{**}$
CRU	.43^{**}	.34^{**}	.43^{**}	-.33^{**}

N=313. Coefficients are standardized betas (β s)

CRU cancer-related uncertainty

* $p<.05$;** $p<.01$