Marital Quality Affects Biobehavioral Outcomes

in Advanced and Recurrent Breast Cancer Patients

Dissertation

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By

Tammy Ann Schuler, M.A.

Graduate Program in Psychology

The Ohio State University
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Dissertation Committee:

Barbara L. Andersen, Ph.D., Advisor

Steven J. Beck, Ph.D.

Robert Cudeck, Ph.D.

Daniel R. Strunk, Ph.D.
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Abstract

Advanced and recurrent breast cancer patients experience negative biobehavioral sequelae following diagnosis. Poor marital quality has also been shown to worsen biobehavioral trajectories in earlier-stage cancer patients (e.g., Yang & Schuler, 2009; Schuler et al., under review). However, the contribution of poor marital quality among advanced or recurrent cancer patients coping with a health crisis remains unclear. This study tested the longitudinal covariation between poor marital quality and psychological distress, individual differences, health behaviors, endocrine and immune functioning, and physical health in advanced and recurrent breast cancer patients (N=98). Mixed-effects modeling compared trajectories for women in distressed marriages (n=23) to those in non-distressed marriages (n=75) at diagnosis and across a 12-month follow-up. Compared with patients in a non-distressed marriage, those in a distressed marriage showed significantly greater baseline total mood disturbance ($p<.001$) and differential rate of mood disturbance change across follow-up ($p=.018$). Immune differences were also present, with the Distressed group showing significantly higher Con A at baseline relative to the Non-Distressed group ($p=.052$), which persisted across 12-month follow-up. Clinical relevance and recommendations are described.
Dedication

This endeavor is dedicated to the study participants who have given their time and detailed information about their lives, with the hope that their contribution will improve post-diagnostic trajectories for others. I am humbled by the strength and generosity shown by these women and aspire to use their gift just as it was intended.
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Vita

Ph.D., Clinical Psychology ...........2011

*The Ohio State University*
Health psychology specialization
Quantitative psychology emphasis
Ph.D. advisor:
    Barbara Andersen, Ph.D.

Clinical Psychology Internship:
    Veterans Affairs Palo Alto Health Care System

M.A., Health Psychology ...............2006

*Northern Arizona University*
With distinction

B.A., Psychology .................2003

*Northern Arizona University*
Spanish minor
Summa cum Laude with honors

Publication


Wu, S.M., Schuler, T.A., Edwards, M.C., Yang, H-C., & Andersen, B.L. (under review). Factor analytic and item response theory analysis of the Penn State Worry Questionnaire when used with female cancer patients.


Fields of Study

Major Field: Graduate Program in Psychology
  Clinical psychology
  Health psychology specialization
  Quantitative psychology emphasis
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Chapter 1: Introduction

Psychological and physical sequelae of advanced and recurrent breast cancer

Diagnosis and treatment of advanced/recurrent breast cancer is a significant stressor associated with heightened psychological distress (Hotopf et al., 2002; Okamura et al., 2005), negative physical sequelae (Mahon, Cella, & Donovan, 1990), and poor prognosis. Psychological responses include mood disturbance and traumatic stress symptoms (Baider, Perez, & DeNour, 1989; Butler, Koopman, Classen, & Spiegel, 1999; Cella, Mahon, & Donovan, 1990; Carter & Carter, 1994; Classen, Koopman, Angell, & Spiegel, 1996; Derogatis, 1983; Mahon, Cella, & Donovan, 1990; Sarenmalm et al., 2008; Voogt et al., 2005), fear of death, difficulties with disability and lifestyle disruption (Gotay, 1984; Hilton, 1989; Mahon & Casperson, 1997; Munkres, Oberst, & Hughes, 1992; Weisman & Worden, 1985), and poor body image (Kullmer et al., 1999). Diagnosis of recurrent disease, specifically, is associated with psychological distress similar to that experienced at first diagnosis (Andersen et al., 2005). Like that experienced at first diagnosis, the level of cancer-specific stress and global stress is equivalent to that of patients seeking psychiatric treatment for anxiety disorders (Yang et al., 2008).

Physical sequelae include pain (Butler et al., 2003; Cella & Tross, 1986; Portenoy, Payne, & Jacobsen, 1999; Sarenmalm et al., 2008), appetitive difficulties (e.g., cachexia; Body, Lossignol, & Ronson, 1997) and declines in functional status (Yang et
Compared with early-stage cancer patients and their partners, advanced cancer patients and their partners report more physical symptoms of cancer and its treatment, greater restriction of activities, and that these problems persist across a lengthier span of time (Gotay, 1984; Yang et al.).

**Correlates of poor marital quality**

Factors such as positive social support may influence the psychological and physical difficulties listed above (Hann et al., 1995; Newsom, Knapp, & Schulz, 1996; Weisman & Worden, 1985). Supportive social environments facilitate coping (Lepore, 2001; Stein, Syrjala, & Andrykowski, 2008) and have been linked to improved psychological outcomes for cancer patients (Helgeson & Cohen, 1996). The marital relationship in particular has been cited as one of the most important forms of social support (Kiecolt-Glaser & Newton, 2001; Pistrang & Barker, 1995). Married individuals, on average, have better psychological and physical health than the non-married. Population-based studies have reliably shown that the married experience lower morbidity and mortality (e.g., Hu & Goldman, 1990; Jaffe et al., 2007; Osbourne et al., 2005; Robles & Kiecolt-Glaser, 2003) and these findings have been extended to those with cancer (Gore et al., 2005; House, 1988; Kradval, 2001; Krongrad et al., 1996; Nausheen et al., 2009; Wittenberg et al., 2010).

The mere presence of a spouse, however, may not be protective. The quality of the marriage, or subjective appraisal of one’s marital relationship (also referred to as marital satisfaction, marital adjustment, and marital happiness; Burman & Margolin, 1992; Lewis & Spanier, 1979), may drastically affect psychological and physical health. Research has suggested that negative aspects of social relationships often exist
independently of positive aspects (Kiecolt-Glaser & Newton, 2001; Rook, 1998). As such, the advantages conferred by having a partner may be constrained when marital quality is poor. Burman and Margolin’s (1992) social support-social strain hypothesis accounts for the buffering effects of positive marital relations, but suggests that marital strife may serve as a considerable source of stress. Thus, the benefits of marriage may not only be limited when the marriage is troubled, but the stress of a poor-quality marriage may be associated with numerous poorer psychological and physical health outcomes.

In illustration, our prior research suggested that women with Stage II/III breast cancer (N=100) in distressed marriages (i.e., who reported low marital satisfaction; n=28) had greater nurse-rated physical symptomatology immediately following primary surgical treatment than those in non-distressed marriages (n=72). Data also showed that, across a five-year follow-up, women in distressed marriages had greater psychological distress, poorer health behaviors, endocrine responses consistent with exposure to chronic stress, and worse nurse-rated functional status (Schuler et al., under review; Yang & Schuler, 2009). In this study, patients’ reports of marital distress remained stable (Yang & Schuler, 2009), which is in line with other reports of marital distress in cancer patients (Dorval et al., 1999; Dorval et al., 2005; Hinnen et al., 2008; Langer et al., 2010; Manne, 1998; Moreira et al., 2010).

Couples are generally able to adapt to a cancer diagnosis (Manne & Badr, 2008). Ratings of premorbid marital quality have been reliably shown to predict couples’ marital satisfaction following breast cancer diagnosis. Couples who report greater marital satisfaction prior to diagnosis have been shown to report higher levels of marital
satisfaction and experience more partner support and involvement following diagnosis (Lichtman, Taylor, & Wood, 1987). Likewise, couples who report premorbid conflict and tension in the marital relationship are at risk for poorer post-diagnosis marital adjustment (Lichtman, Taylor, & Wood, 1987; O’Mahoney & Carroll, 1997).

**Marital functioning in the healthy**

In those without serious illness, evidence suggests that marital distress may impact health via psychological distress. On average, unmarried individuals report better psychological well-being than maritally-distressed individuals (Glenn & Weaver, 1981). Among the married, day-to-day marital conflict has been shown to covary with daily mood more reliably than many other common stress experiences (Bolger et al., 1989). Regular marital strife is a consistent correlate of increased psychological distress. In fact, both depressive symptoms and syndromal depression are strongly associated with marital discord (Fincham et al., 1998). Epidemiological data indicate that amicable marital relations are linked to a moderate reduction in risk for developing depression while troubled marriages are related to a 25-fold increase in risk for both wives and husbands (Prince & Jacobson, 1995; Weissman, 1987). In 124 married couples with a child diagnosed with cancer, marital satisfaction was shown to covary with psychological distress six and 12 months following the child’s diagnosis (Hoekstra-Weebers et al., 1998).

A second pathway by which marital distress may influence health is through individual differences. For example, in the context of a brief (30-minute) laboratory-induced marital conflict situation with 90 newlywed couples, trait hostility was associated with greater degree of negative conflict behaviors among husbands and behavioral
withdrawal among wives (Newton et al., 1995). Karney and Bradbury’s (1995) meta-analysis demonstrated that neuroticism accounts for a significant amount of variance in marital quality. In the behavioral genetics literature, Spotts and colleagues found moderate heritability of marital quality in both Swedish (Spotts et al., 2004) and American (Spotts, Prescott, & Kendler, 2006) samples. In fact, Spotts et al. (2005) showed that 32% of the total variance in wives’ marital satisfaction was shared in common with a personality composite of optimism and aggression.

A third route occurs via interactions with health behaviors. Supportive relationships are hypothesized to impact health by through relations with increased good health behaviors and decreased poor health behaviors (Lewis, Rook, & Schwarzer, 1994). In illustration, higher marital adjustment has been cross-sectionally associated with less obesity and increased antihypertension medication compliance among hypertensive adults (Trevino, Young, Groff, & Jono, 1990). Marital strife, however, is related to decreased positive health behaviors and increased poor health behaviors. For example, a community sample of women who reported greater marital conflict was more likely to smoke and imbibe moderate to heavy volumes of alcohol (Cohen et al., 1991). Similarly, recent marital conflict covaried with greater anxiolytic use in a large, nationwide sample of Finnish women and men (Appelberg et al., 1993). Longitudinal data indicated that in women who underwent gastric restriction surgery to treat morbid obesity, marital dissatisfaction was associated with weight gain after the one-year follow-up (Hafner, Rogers, & Watts, 1990). Conversely, longitudinal data from a sample of rural men showed that positive marital interaction (both self-report and behavioral indices) reduced
the probability of poor health habits (i.e., poor dietary habits, substance use, and inadequate sleep; Wickrama, Conger, & Lorenz, 1995).

A fourth means by which marital distress may relate to health is through biological systems, such as endocrine and immune responses (Burman & Margolin, 1992; Robles & Kiecolt-Glaser, 2003; Uchino, Cacioppo, & Kiecolt-Glaser, 1996). For example, Kiecolt-Glaser and colleagues (e.g., Kiecolt-Glaser et al., 1993; Malarkey et al., 1994) found that in couples, hostile and negative behaviors during a brief (30-minute) laboratory-induced conflict situation were associated with increased adrenocorticotropin hormone (ACTH), epinephrine (EPI), and norepinephrine (NEPI) as well as down-regulated immune responses [e.g., lower natural killer cell cytotoxicity (NKCC); lower blastogenic response to phytohemagglutinin (PHA) and concanavalin A (Con A)] immediately following the conflict situation. Further, behavioral withdrawal by husbands predicted increased 24-hour composite NEPI and cortisol (CORT) levels in wives (Kiecolt-Glaser et al., 1996). In a different sample of married men, participants rated their marital quality over the previous six months. Poorer marital quality corresponded cross-sectionally with dampened antibody responses to Epstein-Barr virus and lower T-lymphocyte helpersuppressor ratios (Kiecolt-Glaser et al., 1988). Another cross-sectional study showed higher platelet levels of EPI and NEPI among women undergoing divorce or separation relative to women in stable relationships (Powell et al., 2002).

Harmonious marriages are also associated with better self-reported health and objective indicators of health, such as functional status (Ganong & Coleman, 1991; Prigerson, Maciejewski, & Rosenheck, 1999; Ren, 1997). For example, longitudinal data from 364 married couples showed that better initial marital quality was related to fewer
initial self-reported physical illness symptoms, while improvements in marital quality over the 4-year follow-up period were accompanied by decreased symptoms (Wickrama, Lorenz, & Conger, 1997). Moreover, osteoarthritic knee pain patients enrolled in a partner-assisted coping skills intervention who had improved marital adjustment from pre-to post-intervention had less physical disability and less pain behavior upon completion of intervention (Keefe et al., 1996) and at 12-month follow-up (Keefe et al., 1999).

Marital strife, in contrast, covaries with worse self-reported health, more physician visits, and poorer objective indicators such as functional status, physical symptomatology, and degree of recovery (Kiecolt-Glaser & Newton, 2001). In illustration, cross-sectional data from women with low back pain indicated that marital dissatisfaction related to greater self-reported pain as well as resultant disability (Saarjarvi, Rytokoski, & Karppi, 1990). Premature termination of a physically-demanding bicycling task occurred more frequently among male chronic back pain patients who first discussed a conflictual marital topic with their partners relative to those who discussed a neutral topic (Schwartz, Slater, & Birchler, 1994).

Marital conflict has been consistently associated with objective indicators, such as heightened blood pressure and heart rate (Kiecolt-Glaser & Newton, 2001). Simple recall of marital conflict has been shown to heighten systolic blood pressure and heart rate in maritally-distressed women (Carels et al., 1998). Hostile marital interactions, specifically, relate to significant increases in blood pressure among those with hypertension (Ewart et al., 1991). Regarding other physical symptomatology, chronic back pain showed elevated lumbar muscular reactivity during a conflict interaction (Flor et al., 1995). Data
from a nationwide, longitudinal study of Finnish women and men indicate that women who reported “considerable conflicts” with their partner and who also reported work conflicts had a 2.54-fold risk of physician-certified work disability related to a variety of health problems during the ensuing 6 years (Appelberg et al., 1996). Further, poorer marital quality covaries cross-sectionally with poorer periodontal health status and more dental caries in women and men (Marcenes & Sheiham, 1996) and longitudinal associations between peptic ulcer and marital strain were noted among women in the Alameda county epidemiological study (Levenstein, Ackerman, Kiecolt-Glaser, & Dubois, 1999).

**Marital functioning in cancer patients**

Our prior work (Schuler et al., under review; Yang & Schuler, 2009), in combination with other literatures, has shown that marital distress covaries cross-sectionally and longitudinally with increased psychological distress, individual differences (such as hostility and optimism), poorer health behaviors, altered endocrine and immune functioning, and worse physical health in those with cancer (Baider et al., 1998; Coyne & Anderson, 1999; Den Oudsten et al., 2010; Fang, Manne, & Pape, 2001; Hoskins, 1996; Manne et al., 1999; Nijboer et al., 1999; Pistrang & Barker, 1995; Schag et al., 1993; Viart et al., 1996; Weighs et al., 1999).

Regarding psychological distress related to poor marital quality, we found that in Stage II/III breast cancer survivors, clinically-significant (Horowitz, 1982a) cancer-specific stress and heightened (Cohen & Williamson, 1988) global stress were present at baseline assessment (which occurred following diagnosis and surgery but prior to adjuvant cancer treatment), for both maritally-distressed (i.e., low marital quality;
Distressed) and non-distressed (Non-Distressed) groups. Across follow-up, the rate of decline in cancer-specific stress for the Distressed group was significantly slower than that for the Non-Distressed group. Global stress decreased across time in the Non-Distressed group but increased in the Distressed group such that at five years, global stress was significantly higher in the Distressed group (Yang & Schuler, 2009). Thus, as in the previously-described literature (e.g., Hoekstra-Weebers et al., 1998) and consistent with the cancer-specific literature (e.g., Banthia et al., 2003), we found poor marital quality to relate to elevated psychological distress – across a five-year span.

We did not evaluate relations between marital distress and individual differences. However, Den Oudsten and colleagues (2010) conducted a 24-month longitudinal analysis of the effects of the Big Five personality traits on perceptions of availability of, and satisfaction with, social support in 609 Dutch, early-stage (0/I/II) breast cancer patients. Results of multiple linear regression showed that agreeableness predicted perceived availability of, and satisfaction with, social support at 12 and 24 months following diagnosis.

Our prior work tested longitudinal relations between marital distress and health behaviors -- specifically dietary habits and exercise. No significant group differences were found for baseline dietary habits. Subsequently, the Non-Distressed group showed significant changes in healthy dietary habits over time, and by five years, the Non-Distressed group showed significantly better dietary habits than the Distressed group. In particular, maritally-distressed women with heightened depressive symptomatology showed a constant decline in dietary habits with fewer improvements relative to the remaining women. This finding is in line with the prior research which showed that
positive marital interaction reduced the probability of poor dietary habits in healthy men (Wickrama, Conger, & Lorenz, 1995). With respect to exercise, the Non-Distressed group exercised significantly less than the Distressed group at baseline. However, while the Non-Distressed showed an increase in exercise during the first two years and then a gradual decrease, the Distressed group showed a stable level during the first 18 months and a rapid decrease thereafter. By five years, the groups did not significantly differ in their overall, lowered levels of exercise (Yang & Schuler, 2009).

In a follow-up study (Schuler et al, under review) with the same sample of women (N=100), we observed endocrine responses in the Distressed group consistent with those reported in marital distress and chronic stress research (e.g., Martí, 1993; Miller, Chen, & Zhou, 2007; Saxbe, Repetti, & Nishina, 2008). That is, the Non-Distressed group showed significantly higher baseline plasma cortisol than the Distressed group, a difference which was maintained across the five-year follow-up. For EPI, baseline values did not differ between groups but the patterns of change significantly differed. Specifically, the Distressed group showed an increase in EPI over time, relative to the Non-Distressed group. Of note, the clinical significance of HPA dysregulation in metastatic breast cancer has been demonstrated; flattening of the diurnal cortisol rhythm is predictive of early mortality, independent of other risk factors (Sephton et al., 2000). These endocrine changes could alter immune defense mechanisms and thus facilitate tumor progression (Antoni et al., 2006). Alternatively, direct endocrine effects on tumor metabolism, angiogenesis, oncogene expression, or DNA repair could explain some stress/depression effects on cancer progression (McGregor & Antoni, 2009; Sephton & Spiegel, 2003).
Health consequences may be of particular importance for individuals diagnosed with cancer. Thus, the health findings are of note. At baseline, all patients were recovering from surgery and anticipating the start of adjuvant chemotherapy and radiotherapy. There were no significant group differences in baseline nurse-rated functional status. The Distressed group showed improvement during the first three years and decrease thereafter. In contrast, the Non-Distressed group showed a more rapid improvement during the first three years and a plateau without any decline in functional status during the next two years. Thus, by five years, the Non-Distressed group was evaluated as having a significantly better functional status than the Distressed group (Yang & Schuler, 2009).

Regarding nurse-rated physical symptomatology from cancer and its treatment, the Distressed group had significantly more and/or more-severe symptoms at baseline than the Non-Distressed group. This difference remained significant for three years. Further, post hoc analyses suggested a moderation effect of depressive symptoms such that marital distress in combination with higher depressive symptoms was related to the most and/or more-severe symptoms (Yang & Schuler, 2009). Overall, findings align with those of the previously-described research which showed that poor marital functioning is longitudinally associated with worse objective (e.g., Appelberg et al., 1996) indicators of physical health.

Regarding pathophysiology outcomes, data from samples with and without serious illness indicate that poor marital functioning may be related to increases in disease morbidity and mortality (Kiecolt-Glaser & Newton, 2001). In a longitudinal review of medical records from women and men selected from among members of a
large HMO, amicable marriages and equality of decision-making were associated with a lower risk of death among married women (Hibbard & Pope, 1993). Zautra and colleagues (1998) found that women with rheumatoid arthritis who reported more positive spousal interaction patterns or less criticism/negativity showed less increase in clinician-rated disease activity than women who reported that their husbands were only supportive during disease flare-ups. Lower marital cohesion was associated with elevated nighttime blood pressure and 24-hour diastolic blood pressure among a population of early hypertensive men and women (Baker et al., 1999). Interview and observational measures of marital quality were predictors of 4-year mortality in men and women with congestive heart failure (Coyne et al., 2001). Follow-up analyses also showed effects on 8-year mortality, especially when the patient was a woman (Rohrbauch, Shoham, & Coyne, 2006). In another study, husbands who spoke more about the things that were important to them with their wives were less likely to be rehospitalized or die during the year following myocardial infarction, even when controlling for a biomedical index that is highly predictive of prognosis (Helgeson, 1991). For cancer patients enrolled in the Surveillance, Epidemiology and End Results (SEER) registry, Sprehn and colleagues (2009) reported spousal separation at the time of diagnosis to be associated with a significant decrement in 5- and 10-year survival compared with divorced and never married patients. In advanced or recurrent cancer specifically, retrospective data have shown that experiences with one or more stressful or traumatic life events (assessed in the posttraumatic stress disorder module of a structured clinical interview) were associated with significantly shorter disease-free intervals following diagnosis, relative to no stressful or traumatic life events (Palesh et al., 2007). While Palesh et al. did not
report on marital quality, per se, these data may relevant if poor marital quality is a chronic stressor (Burman & Margolin, 1992).

**Limitations in prior research**

Regarding relevant marital research, the larger proportion focuses on marital status rather than marital quality (Pistrang & Barker, 1995). Until recently, in fact, most social support literature emphasized the benefits of interpersonal relationships with less attention to relationship strain. Meanwhile, the adverse effects of troubled relationships may be more striking than the beneficial effects of amiable relationships (Coyne & Bolger, 1990). Concerning research methodology, validated instruments, such as the Dyadic Adjustment Scale (Spanier, 1976), are not routinely employed. Additional limitations include frequent cross-sectional and/or retrospective designs, and reliance on outcome data that are solely qualitative or self-report (Badr et al., 2010; O’Mahoney & Carroll, 1997).

Research which specifically tests the impact of poor marital functioning in cancer patients, especially those with advanced or recurrent disease, is limited. In a meta-analytic report, Hagedoorn and colleagues (2008) cautioned against applying generalizations from the literature, which focused largely on those with early-stage cancer, to those with advanced disease. Substantive differences in psychological and physical sequelae have been shown for recurrent compared with initial disease (Andersen et al., 2005; Helgeson & Tomich, 2005; Worden, 1989; Yang et al., 2008). Regarding advanced cancer, patients and their partners report more psychological distress and physical problems, relative to those with earlier-stage cancers (Lewis & Deal, 1995; Weitzner, McMillan, & Jacobsen, 1999). Moreover, though it is known that the sequelae
of advanced or recurrent cancer are different than that of early-stage cancer (e.g., 
Andersen et al., 2005; Yang et al., 2008), the full extent to which they are different 
remains unknown.

Most reports of marital distress in advanced or recurrent disease patients have 
assessments occurring months, or even years, after the cancer recurrence diagnosis, and 
utilize heterogeneous samples which include patients at different stages of illness, with 
different cancer sites, and at varying points in their recovery process. Cross-sectional 
designs are common (O’Mahoney & Carroll, 1997). Likewise, Manne (1998) noted that 
the majority of studies testing relations between marital variables and advanced and 
recurrent cancer, of which there are very few, rely on small sample sizes with high 
refusal and attrition rates.

**Summary**

To summarize, the current literatures suggest that poor marital functioning is a 
repeated, and more often, a chronic, social stressor. Adverse effects of poor marital 
functioning on psychological distress, health behaviors, endocrine and immune 
functioning, and physical health have been documented in those with and without serious 
ilness (Robles & Kiecolt-Glaser, 2003; Schuler et al., under review; Yang & Schuler, 
2009). For advanced and recurrent cancer patients, who already have considerable 
psychological and physical burdens, poor marital quality may worsen patients’ 
trajectories. If this is found to be the case, corresponding data will inform intervention 
strategies. Further, it is important to clarify potential correlates of both distress 
(including marital distress) and disease morbidity and mortality. Expanding this 
knowledge may be especially important for advanced or recurrent breast cancer patients.
Study aims and hypotheses

The current study tested relations between poor marital quality and psychological distress, individual differences, health behaviors, endocrine and immune functioning, and objectively-rated physical health in advanced and recurrent breast cancer patients. Women in distressed marriages were compared to those in non-distressed marriages at diagnosis and at three time points across a 12-month follow-up period using mixed-effects modeling.

Marital distress was determined by the Satisfaction Scale of the Dyadic Adjustment Scale (Spanier, 1989). Psychological distress outcomes included cancer-specific (Impact of Events Scale; Horowitz, Wilner, & Alvarez, 1979), global stress (Perceived Stress Scale – 10 Item Version; Cohen, Kamarck, & Mermelstein, 1983), hopelessness (Beck Hopelessness Scale; Beck et al., 1974), and total mood disturbance (Profile of Mood States – Short Form; Shacham, 1983). The individual difference variable tested was optimism (Life Orientation Test; Scheier & Carver, 1985). Health behaviors were measured via reports of monthly exercise frequency. Endocrine outcomes included plasma cortisol, plasma adrenocorticotropic hormone, and plasma catecholamines (epinephrine and norepinephrine). Immune outcomes included blastogenic response to concanavalin A, blastogenic response to phytohemagglutinin, and natural killer cell cytotoxicity. Finally, physical health outcomes included nurse-rated functional status (Karnofsky Performance Status Scale) and nurse-rated severity of cancer treatment toxicities and current signs/symptoms (Southwest Oncology Group criteria; Moinpour et al., 1989).

The following predictions were made:
Hypothesis I: Psychological Distress: Based on data from studies of marital distress in earlier-stage breast cancer patients (e.g., Yang & Schuler, 2009) and studies of sequelae in breast cancer recurrence (e.g., Andersen et al., 2005; Yang et al., 2008) it was hypothesized that marital distress would be associated with comparable, but clinically-elevated, reports of cancer-specific stress, significant global stress, hopelessness, and total mood disturbance at baseline. Further, trajectories would diverge over follow-up such that reports of psychological distress would be higher in the maritally-distressed relative to the non-distressed.

Hypothesis II: Individual Differences: Cross-sectional, longitudinal, and meta-analytic data have repeatedly shown covariation between marital distress and individual differences (e.g., Newton et al., 1995), neuroticism (e.g., Karney & Bradbury, 1995), agreeableness (e.g., Den Oudsten et al., 2010) and optimism (e.g., Spotts et al., 2005). As such individual differences tend to exhibit stability over time, the possibility that the two groups of women would show equivalence on a measure of optimism at baseline, even after the mutual stress of diagnosis, seemed unlikely. Thus, it was hypothesized that optimism would be lower in the maritally-distressed relative to the non-distressed at baseline and across the duration of follow-up.

Hypothesis III: Health Behaviors: Little research specifies patterns of exercise following diagnosis of advanced cancer or cancer recurrence. Lowered functional status among recurrent breast cancer patients (Yang et al., 2008) and more physical symptoms of cancer and treatment among advanced cancer patients (Gotay, 1984) would suggest that, in general, patients would not engage in as much physical activity as those with initial, earlier-stage cancer. However, since there are few data, it is difficult to estimate
how marital distress would interact with exercise outcomes. In the marital quality literature, marital distress has been repeatedly associated with fewer positive and more negative health behaviors. Thus, it was hypothesized that marital distress would covary with lower monthly exercise frequency at baseline and across the duration of the follow-up period compared to non-distress.

**Hypothesis IV: Endocrine Responses:** We previously reported endocrine responses in the Distressed group consistent with those shown in chronic stress research (Schuler et al., under review). Thus, it was hypothesized that, compared to non-distress, marital distress would be similarly associated with dysregulated endocrine responses consistent with exposure to chronic stress. These included: 1) consistently lower morning plasma cortisol at baseline and across follow-up; 2) comparable NEPI and EPI at baseline but higher NEPI and EPI across follow-up; and 3) comparable ACTH at baseline and across follow-up.

**Hypothesis V: Immune Responses:** Research has repeatedly linked chronic stress to down-regulated immune responses (e.g., Miller, Chen, & Zhou, 2007). Thus, it was hypothesized that marital distress would be associated with poorer immune responses at baseline and across follow-up relative to non-distress.

**Hypothesis VI: Physical Health:** Based on data from studies of marital distress in earlier-stage breast cancer patients (e.g., Yang & Schuler, 2009) and studies of sequelae in breast cancer recurrence (Andersen et al., 2005; Helgeson & Tomich, 2005; Yang et al., 2008), it was hypothesized that marital distress would be associated with lowered, but comparable, functional status at baseline relative to non-distress. However, patterns of group change would differ such that that marital distress would be associated with lower
functional status than non-distress across follow-up. In contrast, marital distress would covary with more baseline physical symptoms from cancer and treatment compared to non-distress. However, group symptom trajectories would vary such that they would converge during follow-up.
Chapter 2: Method

Design

A non-experimental, repeated-measures design was used. Two intact groups (maritally-distressed versus non-distressed) of women with advanced or recurrent breast cancer were studied with four assessments in a 12 month period.

Procedures

Potentially eligible patients were participants in longitudinal, prospective studies which described coping with diagnosis of advanced (i.e., Stage IV) or recurrent breast cancer. Stage IV breast cancer refers to disease with any tumor size, any lymph node involvement, but with distant metastasis – including that to ipsilateral supraclavicular lymph node(s) at the time of diagnosis. Breast cancer recurrence refers to clinical detection of metastatic breast disease in the same area, adjacent to, or distant from the original disease site (TNM staging system of the American Joint Committee on Cancer Staging and End Results Reporting; Lenhard, Osteen, & Gansler, 2001). Among these patients, only those with an intimate partner (i.e., married or cohabitating) at diagnosis and for the next 12 months remained eligible. Of those patients with an intimate partner, data from those with a change in partner status (e.g., married at baseline and divorced at 8-month follow-up) during the period of interest were not used. Figure 1 depicts participant eligibility.
Patients meeting eligibility criteria were identified from large samples (see Figure 1) accrued from two distinct psychosocial research studies at The Ohio State University-affiliated, National Cancer Institute–designated Comprehensive Cancer Center. Study group 1 (n=29) included patients with recurrence who had been former participants in a randomized clinical trial (RCT; N=227) which began following their diagnosis of Stage II/III breast cancer. RTC details of informed consent procedures, accrual, and randomization have been published (Andersen et al., 2004). Women diagnosed with breast cancer recurrence during the follow-up years were approached for accrual to a secondary study on coping with recurrence. Study group 2 (n=69) came from participants in a longitudinal study of coping with advanced or recurrent breast cancer (N=145); Study group 2 patients had not participated in the RCT.

Following completion of informed consent (IRB protocol 92C0350 and IRB protocol 1999C0068, respectively), women completed face-to-face interviews and questionnaires assessing marital distress, cancer stress, mood disturbance, health behaviors, and other areas prior to appointments with medical oncologists. In addition, a research nurse performed a health status assessment, utilizing medical chart inspection and physician consultation as needed, and took a 60 mL blood draw. Assessments were scheduled between 7 and 10 a.m. to minimize diurnal variability. All patients were followed and reassessed in person every 4 months. Participants were reimbursed for parking, and were paid $100.00 for the baseline assessment and $50.00 for each subsequent assessment.
Participants

Sociodemographic, disease/prognostic, and treatment characteristics are presented in Table 2. At baseline, 44% (43 of 98) had local metastases (e.g., residual breast tissue, chest wall) and 68% (67 of 98) had distant metastases. Metastatic sites were bone (43%), liver (20%), and lung (16%), with 66% of the sample having metastases at multiple sites. Women were assessed a median of 10 weeks following diagnosis, by which time the majority (84%) had begun treatment (surgery 28%, chemotherapy 54%, radiation 20%, and/or hormonal therapy 27%). Table 1 lists the proportion of patients assessed having receiving each cancer treatment since the previous assessment at each time point.

Subject attrition occurred during the 12-month follow-up period. Figure 2 delineates participant status at each time point. Twenty participants died (n=14) or withdrew (n=6) during follow-up. These individuals were compared to the women who remained in the study across follow-up (n=78) and the analyses suggested those who died or withdraw had risk characteristics for rapid disease progression. Women who died or withdrew had a significantly shorter disease-free interval between initial and recurrent cancer diagnoses (M=24.80; SD=14.13 months) compared with study completers (M=55.25; SD=48.53; p=.013). Additionally, women who died or withdrew were less likely to have received any type of surgical treatment (e.g., lumpectomy, mastectomy) at diagnosis of recurrent or advanced disease (p=.048).

Measures

Marital Distress

The level of marital distress among study participants was determined with the Satisfaction Scale (DASS) of the Dyadic Adjustment Scale (DAS; Spanier, 1989). The
DAS is a 32-item rating instrument used to assess relationship satisfaction and to characterize the quality of a dyadic relationship among married or cohabiting couples. The DAS is the most widely used and psychometrically-validated measure of relationship quality, having been used in over 1,000 studies (Coyne & Anderson, 1999). A DAS score of 100 (possible range 0-151) is routinely used to discriminate between distressed and non-distressed relationships (Heyman, Sayers, & Bellack, 1994; Hunsley et al., 1995; Eddy, Heyman, & Weiss, 1991; Kurdek, 1992; Spanier, 1976).

The Satisfaction subscale (DASS; 10 item-version; possible range 0-50) measures the amount of tension in the relationship as well as the participant’s commitment to continuing the relationship. The DASS is frequently used as a short form (Hunsley et al., 1995; Kurdek, 1992) with a cutoff of 33 to distinguish between maritally-distressed and non-distressed relationships. This cutoff corresponds proportionally to the cutoff for the full-scale DAS.

Patients completed 4 assessments in total (baseline, 4-, 8-, and 12-month assessments). To obtain a reliable DASS score for each woman, the mean of a woman’s 4 DASS assessments were calculated. Guided by previous research procedures (Schuler et al., under review; Yang & Schuler, 2009), two groups were defined using the DASS cutoff of 33: women who reported, on average, relationship distress during the 12-month period (Distressed; n=25; DASS grand mean = 27.86, SD = 5.89; range = 23.33) and women who did not (Non-Distressed; n=73; DASS grand mean = 39.55, SD = 3.35; range = 17.00). Using 33 as a cutoff, 25.5% (25 of 98) of the sample scored within the distressed range. This estimate is similar to that of prior reports of Stage II/III breast cancer patients (25%; N=100; Yang & Schuler, 2009). The average DASS score for the
sample did not vary, with the mean being 36.72 ($SD = 7.65$) at baseline and 36.43 ($SD = 5.32$) at 12 months. Figure 3 plots the data.

A recent meta-analysis of studies using the DAS reported an average Cronbach’s alpha of .92 for the full DAS and .85 for the Satisfaction subscale (Graham, Liu, & Jeziorski, 2006). Internal consistency estimates for the current study sample ranged from .78 to .83 across assessments, also comparable to those in the DAS literature for intervals from weeks to months (e.g., .69 to .96; Belsky, Lang, & Rovine, 1983; Stein, Girodo, & Dotzenroth, 1982; Weihs et al., 1999).

Psychological Distress

Impact of Events Scale. The Impact of Events Scale (IES; Horowitz, Wilner, & Alvarez, 1979) is a 22-item self-report questionnaire used to assess reactions to cancer diagnosis and treatment. Factor analytic studies indicate that the measure examines three factors: intrusive thoughts (i.e., “I had dreams about being a cancer patient”), avoidant thoughts/behaviors (e.g., “I tried not to talk about it”), and hyperarousal (e.g., ”I was jumpy and easily startled”). Individuals rate the frequency of these feelings or events during the previous week, using a 5-point Likert scale ranging from 0 = not at all to 4 = extremely. Items are summed for a total score that ranges from 0 to 88, with higher scores reflecting greater cancer-related distress. Coefficient alpha reliabilities of .78 to .83 have been reported (Cordova et al., 1995; Horowitz, Wilner, & Alvarez, 1979, Schwartz et al., 1995). The two-week test-retest is between .79 and .89 (Horowitz, Wilner, & Alvarez, 1979). Internal consistency estimates for the current study sample ranged from .99 to 1.0 across assessments.
Perceived Stress Scale – 10 Item Version. The Perceived Stress Scale – 10 Item Version (PSS-10; Cohen, Kamarck, & Mermelstein, 1983) assesses an individual’s appraisal of life as stressful (i.e., unpredictable, uncontrollable, and overloading). The 10-item PSS was used for its improved internal reliability and factor structure over other versions of the PSS (Cohen & Williamson, 1988). Example items include, “How often have you felt nervous or stressed?” and “How often have you felt confident about your ability to handle your personal problems?” Women rated how often they experienced these feelings in the past month on a 5-point Likert scale from 0 = never to 4 = very often. Total scores range from 0 to 40, with higher scores indicating greater overall distress. This measure has been shown to predict psychological distress beyond that attributable to depression (Cohen & Williamson, 1988) and normative data are available for middle- and older-aged adults. Internal consistency estimates for the current study sample ranged from .85 to .90 across assessments.

Beck Hopelessness Scale. The Beck Hopelessness Scale (BHS; Beck et al., 1974) is a 20-item scale which measures negative attitudes about the future. Items were rated by a true-false format with 9 items keyed false and 11 items keyed true. Examples of items are "I might as well give up because I can't make things better for myself," and "I have enough time to accomplish the things I most want to do." Scores range from 0 to 20 with higher scores indicating a greater degree of hopelessness. Scores ranging from 0 to 3 are minimal/normal, 4 to 8 are mild, 9 to 14 are moderate, and scores greater than 14 represent severe hopelessness (Beck & Steer, 1988). Alpha reliability coefficients have ranged from 0.83 to 0.93 in the general population and samples of recurrent breast cancer patients (Beck et al., 1974; Northouse, Dorris, & Charron-Moore, 1995; Northouse, Laten,
The BHS was only given at baseline and 12-month follow-up. Internal consistency estimates were .81 and .84, respectively.

The Profile of Mood States (Short Form) – Total Mood Disturbance. The Profile of Mood States – Short Form (Shacham, 1983) is a 37-item self-report inventory on which women reported how they have felt during the past week, yielding six mood subscales: Tension-Anxiety, Depression-Dejection, Anger-Hostility, Vigor-Activity, Fatigue-Inertia, and Confusion-Bewilderment and one Total Mood Disturbance Score. Each item was rated on a 5-point scale from 0 = not at all to 4 = extremely. Higher scores on each subscale indicate greater levels of each type of mood. The Total Mood Disturbance Score (POMS-TMD) is the sum of the Tension, Depression, Anger, Fatigue, and Confusion subscales minus the Vigor subscale. The Anxiety subscale scores can range from 0 to 24, the Depression from 0 to 32, the Anger from 0 to 28, the Vigor from 0 to 24, the Fatigue from 0 to 20, and the Confusion from 0 to 20. The Total Mood Disturbance score ranges from -24 to 124 with higher scores representing greater total mood disturbance. Reliability and validity are well-established (Curran, Andrykowski, & Studts, 1995; Shacham, 1983). Internal consistency estimates for the current study sample ranged from .84 to .89 for the Tension-Anxiety subscale, .81 to .92 for the Depression-Dejection subscale, .82 to .88 for the Anger-Hostility subscale, .90 to .93 for the Vigor-Activity subscale, .90 to .94 for the Fatigue-Inertia subscale, and .78 to .84 for the Confusion-Bewilderment subscale.

Individual Differences

Life Orientation Test. The Life Orientation Test (LOT; Scheier & Carver, 1985) is an 8-item measure of optimism. The instrument is composed of 8 items (with 4 filler
items) using a 5-point Likert scale from 0 = *strongly disagree* to 4 = *strongly agree*. Four items are counterbalanced for desirability and, therefore, are reversed-scored. Examples of items include: "*In uncertain times I expect the best*" and "*I'm always optimistic about the future.*" Total scores range from 0 to 32 with higher scores reflecting higher optimism. Alpha reliability coefficients ranging from .76-.87 have been reported (Carver et al., 1993; Scheier & Carver, 1985; Given et al., 1993) and test-retest reliabilities have ranged from .74 over a 12-month interval (Carver et al., 1993) to .79 over a 4-week interval (Scheier & Carver, 1985). The LOT was only given at baseline and 12-month follow-up, and internal consistency estimates were .87 and .88, respectively.

**Health Behaviors**

**Exercise Frequency per Month.** An item from an inventory which assesses use of complementary treatments allowed respondents to identify whether they used exercise as a form of complimentary treatment at baseline and again at 12-month follow-up. For those who responded affirmatively, the patient identified which form(s) of exercise were used. Examples include walking, swimming, stretching, yoga, tai-chi, and dance. Subsequently, women specified their average frequency of exercise per month. Higher scores indicate greater exercise frequency. Baseline exercise frequency ranged from 2 to 40 times per month in study participants who responded affirmatively (the case for 41 out of 98 women).

**Endocrine Responses**

**Plasma cortisol.** Plasma cortisol (CORT) determinations were made using the Cortisol Coat-A-Count RIA (Diagnostic Products Corporation, 5700 West 9th Street, Los
Angeles, CA 90045). Intra-assay coefficient of variation is 4.3% and inter-assay coefficient of variation is 5.2%. Sensitivity is 0.2 ug/dl. All RIA assays were counted and calculated on the Packard Cobra II Gamma Counter (Packard Instrument Company, 800 Research Parkway, Meriden, CT 06450).

**Plasma catecholamines norepinephrine and epinephrine.** Plasma norepinephrine (NEPI) and epinephrine (EPI) determinations were made by HPLC with Electro Chemical Detection using Standards and Chemistry [Alumina extraction] purchased from ChromSystems, Munich, Germany (U.S. affiliate Thermo-Alko, 500 Cummins Center, Beverly, Ma. 01915). C-18 Columns were purchased from the Waters Corporation (Waters Corporation, 34 Maple Street, Milford, MA 01757). Intra-assay variation for NEPI is 3%. Inter-assay variation for NEPI is 6%. Intra-assay variation for EPI is 6%. Inter-assay variation for EPI is 13%. Sensitivity for NEPI is 15 pg/ml and 6 pg/ml for EPI. HPLC Pump and detector manufactured by ESA (ESA, Inc., 22 Alpha Road, Chelsford, MA 01824). A Waters 717 plus Autosampler was used to make injections (Waters Corporation, 34 Maple Street, Milford, MA 01757).

**Plasma adrenocorticotropic hormone.** Plasma adrenocorticotropic hormone (ACTH) was measured using the Immulite 1000 with reagents manufactured specifically for this instrument (Diagnostic Products Corporation, 5700 West 9th Street, Los Angeles, CA 90045). Intra-assay variation is 5.6% and inter-assay variation is 7.8%. Sensitivity is 9 pg/ml. This assay was read and calculated with the System Luminometer 400 (Nichols Institute, 1311 Calle Batido, San Clemente, CA 92673).

**Immune Responses**
**Blastogenic response to PHA (PHA) and Con A (Con A).** The concentrations for PHA and Con A used were 2.5, 5.0, and 10.0µg/ml. For both assays isolated peripheral blood leukocytes (PBLs) seeded in triplicate at 0.5 x 10^5/wells were incubated for 68 hours at 37°C in 96-well flat-bottom plates, and then labeled for 4 hours with MTS (Promega) to measure proliferative response. Briefly, the MTS procedure is a non-radioactive calorimetric procedure which labels metabolically active cells via reduction of a colored substrate. The amount of proliferation as determined by optical density (OD) of the suspension in the well. OD determinations were performed using a Titertek Multiscan MCC microplate reader at a determination wavelength of 492nm, and a reference wavelength of 690nm as has been noted (Gieni et al., 1995; Shobitz, 1994). As previously described (Carson et al., 2004; Schuler et al., under review), blastogenic response was expressed as the mean of standardized scores using the three dilutions of PHA and Con A. A z-score was calculated for the three dilutions of PHA and Con A, and then the three z-scores were averaged.

**Natural killer cell cytotoxicity (NKCC).** PBLs were isolated from 60 ml of venous blood by use of Ficoll gradients (Pharmacia Biotech, Inc., Piscataway, NJ). The isolated leukocytes were then washed in calcium- and magnesium-free phosphate-buffered saline and counted on a Coulter counter (Coulter Corp., Miami, FL). Aliquots of 8 x 10^6 isolated PBLs were suspended again in 0.8ml of RPMI-1640 medium supplemented with 10% fetal bovine serum, 0.75% sodium bicarbonate, 2mM l-glutamine, and 10 µg/ml of ciprofloxacin. Quantification of conjugated to either fluorescein isothiocyanate or rhodamine according to the cell surface marker being studied: total T cells (CD3, fluorescein isothiocyanate), T4 subset (CD4, rhodamine), T8
subset (CD8, fluorescein isothiocyanate), and NK cells (CD56, rhodamine). All Mabs were purchased from Coulter Corp. Briefly, 0.5 x 10^6 cells were incubated with the Mab for 15 minutes at room temperature. After the incubation, the cells were fixed, and the red blood cells were lysed with Optilyse C, a buffered solution containing 1.5% formaldehyde, according to the manufacturer’s instructions (Coulter Corp.). Samples were analyzed with the use of a Coulter EPICS Profile II flow cytometer as described previously (Kiecolt-Glaser, Dura, Speicher, Trask, & Glaser, 1991).

To determine natural killer cell activity, a microtiter ⁵¹Cr-release cytotoxicity assay was used as described previously (Andersen et al., 1998) to assess NK cell lysis (killing). The target cells used were K-562 cells, and NK cell-sensitive human myeloid cell line. Target cells, labeled overnight for 16 hours with ⁵¹Cr were placed triplicate wells of 96-well V-bottom plates, and PBLs were added, resulting in four effector-to-target (E:T) cell ratios of 100:1, 50:1, 25:1, and 12.5:1. As previously (Carson et al., 2004; Schuler et al., under review), NKCC was also expressed as the mean of standardized scores using the four E:T ratios.

Physical Health

Symptoms/Signs of Illness and Treatment Toxicities. The Southwest Oncology Group (SWOG; Moinpour et al., 1989) criteria were used to document types and severity of cancer treatment toxicities and current signs/symptoms. Signs/symptoms were provided for twenty-two body systems (e.g., hematologic gastrointestinal, neurosensory, pain, neurologic/neurocentral, immunologic) comprised of 4-6 items each. Each item is rated for severity on a 5-point scale (0=none to 4=life threatening) unique to each item. In illustration, the severity scale for gastritis/ulcer (a gastrointestinal item) includes 0 =
none; 1 = antacid required; 2 = requires vigorous medical mgmt, no surgery; 3 = requires surgery for ulcer; and 4 = perforation, bleeding. Subscale scores are the average of sign/symptom severity for each body system. Subscale scores range from 0 to 4, with higher scores indicating more life-threatening symptoms. The subscale scores are summed to obtain an overall toxicity score. This total score ranges from 0 to 76, with a score of 76 indicating life-threatening symptoms in each of the body systems. Project nurses with advanced training in oncology and toxicity screening conducted this assessment. If needed, supporting information was obtained through consultation with medical staff or chart review.

Karnofsky Performance Status Scale. The Karnofsky Performance Status Scale (KPS; Karnofsky & Burchenal, 1949) was used to assess functional status. Nurses provided Karnofsky ratings following completion of the sign/symptom interview and evaluation. It is the most widely used evaluator-rated measure of functional status in cancer studies. The scale ranges from 100 (Normal, no complaints, no evidence of disease) to 0 (Dead) with 10 point intervals each containing differential criteria (e.g., 90 = able to carry on normal activity, minor signs/symptoms of disease; 80 = normal activity with effort, some signs/symptoms of disease). The lower the score, the more restricted the patient is in the performance of daily and self-care activities. Across cancer studies, inter-rater reliability for the scale ranges from .70 to .97 (Mor et al., 1984; Yates et al., 1981) and studies have demonstrated predictive validity for cancer endpoints (e.g. death, treatment toxicities; Ganz et al., 1988, Maltoni et al., 2005).

Depression
Depressive symptoms have been shown to covary with marital distress in those with (Wellisch et al., 1983; Yang & Schuler, 2009) and without (Prince & Jacobson, 1995) cancer. The relationship between depressive symptoms and marital distress is hypothesized to be bidirectional, with poor marriages enhancing depressive symptoms and depression promoting poorer marital quality (Fincham & Beach, 1999). As such, study analyses controlled for baseline levels of depressive symptomatology using the Center for Epidemiological Studies Depression Scale (CES-D; Comstock & Helsing, 1976; Radloff, 1977). Unlike other measures of depressive symptoms, the CES-D is relatively unaffected by physical symptoms and is, therefore, commonly used in research with medical patients (Devins et al., 1988). The CES-D consists of 20 items (e.g. “I felt everything I did was an effort,” “I felt sad”) rated on a 4-point Likert scale from 0 = hardly ever or never to 3 = most or all of the time. Women are asked to respond based on their feelings during the previous week. Following reverse scoring of positively-valenced items, all items are summed with total scores ranging from 0 to 60. Higher scores reflect greater depressive symptoms, with a well-established cutoff of ≥16 indicating significant depressive symptomatology among cancer patients (Edgar, Rosberger, & Nowlis, 1992; Gritz, Wellisch, & Landsverk, 1988; Lewis & Deal, 1995; Weissman et al., 1977). Internal consistency reliability at baseline assessment for the current study sample was .81, consistent with prior research (Himmelfarb & Murell, 1983).
Chapter 3: Results

Preliminary Analyses

Ninety-eight participants were eligible for the four assessments, for a total of 392 possible data points. Of the 98 participants, 96 were assessed at baseline, 79 at 4-month follow-up, 76 at 8-month follow-up, and 72 at 12-month follow-up (depicted in Figure 4). Thus, 323 of 392 (82%) data points were available. Of the missing data, 47% was due to patient death, 33% due to missed assessments, and 20% from patient withdrawal (dropout).

For the 323 available data points, missing data percentages ranged from 2.17%-8.33% for psychological distress outcomes (i.e., IES = 4.95%, PSS-10 = 2.79%, POMS-TMD = 2.17%, BHS = 8.33%), it was 13.69% for optimism, and it was 0% for functional status and physical symptoms of disease/treatment outcomes. The rates of missing data were higher for biologic variables. With time, blood draws often became more difficult (e.g., collapsed veins) and/or counts were too low for all assays to be performed. Missing data estimates for endocrine and immune responses ranged from 27.24% - 35.60% (i.e., CORT = 27.86%, ACTH = 35.60%, EPI = 27.24%, NEPI = 27.24%, Con A = 28.17%, PHA = 28.17%, NKCC = 30.65%).

Sociodemographic, disease/prognostic, and treatment characteristics for the Distressed and Non-Distressed groups are provided (Table 2). Chi-square, Fisher’s Exact Probability Test, or ANOVAs were used as appropriate to compare the groups. There
were no significant group differences ($ps>.06$). Additional comparisons tested for group differences in occurrences of death or withdrawal from the study during the follow-up period and there were none ($ps>.17$).

Descriptive statistics for the outcome variables at baseline and at 12-month follow-up are listed in Table 3. As expected, ANOVA group comparisons showed a significant group difference in baseline depressive symptoms with the Distressed group having a higher level of depressive symptoms compared to the Non-Distressed group ($p = .029$). Further ANOVA comparisons showed significant differences in baseline PSS-10 and baseline POMS-TMD with the Distressed group having higher stress and greater POMS-TMD relative to the Non-Distressed group ($ps<.01$), and baseline Con A, with the Distressed showing a greater blastogenic response to Con A ($p = .018$).

Baseline correlations among the outcome variables ranged in magnitude from $- .003$ to $.714$. As expected, moderate correlations ($r = .40 - .70$) were found between conceptually similar measures: psychological distress/optimism (e.g., IES and PSS-10 = $.488$; POMS-TMD and BHS = $.465$; BHS and optimism = $-.509$), blastogenic response (Con A and PHA = $.684$), and physical health (KPS and SWOG = $-.460$). Moderate correlations were also found between measures of psychological distress and physical health (e.g., POMS-TMD and KPS = $-.561$). Baseline correlations are presented in Tables 4 – 6.

**Primary Analyses**

Mixed-effects modeling (Raudenbush & Bryk, 2002) was used to test for group differences at baseline and differential change across time for each outcome. Mixed-effects models are advantageous for analyzing longitudinal data in that the procedure
accounts for the correlations among repeated assessments within an individual and allows the number of repeated assessments to vary across individuals. Both fixed (group average effects) and random effects (within-individual variability) were estimated. Fixed effects for Group, Time, and the Group x Time interaction were included in all models. The Group effect tested differences between the Distressed and Non-Distressed at baseline (intercept). The Time effect tested whether the outcome changed during the follow-up for the Non-Distressed group. The Group x Time interaction determined if the rate of change in the Distressed group was significantly different from that of the Non-Distressed.

The models were constructed in the following manner: 1) Form of change, linear versus quadratic, was determined through examination of the Bayesian Information Criterion for unconditional growth models containing only fixed effects. 2) Intercept (baseline) and linear change were tested as random effects for all models. To determine if including one or both random effects would further improve model fit, BIC and negative 2 log likelihood (-2LL) were examined. 3) To test the effects of marital distress beyond effects of depression, baseline depressive symptoms (continuous CES-D) and baseline depressive symptoms (continuous CES-D) x Time effects were included in all models with the exception of POMS-TMD, since a scale measuring depressive symptoms is used to calculate total mood disturbance (Shacham, 1983). In addition, the following were considered as controls: age (continuous), cancer diagnosis (recurrent or Stage IV), surgical treatment at baseline or during follow-up (yes or no), receiving chemotherapy at baseline or during follow-up (yes or no), receiving radiation at baseline or during follow-up (yes or no), participation in the intervention arm of the RCT (yes or no), died during
follow-up (yes or no). All main effects and two-way interactions with Time were entered into the model.

A backward elimination process (i.e., inclusion of all possible relevant sociodemographic, disease, and treatment control variables in each linear or quadratic unconditional growth model; and elimination of non-significant sociodemographic, disease, and treatment control variables to create a final, parsimonious model for each outcome) was employed in which terms ($P > .20$) were eliminated from each model until a final solution was reached (Cnaan, Laird, & Slasor, 1997). For the immune outcomes percentage of lymphocytes consisting of T-cells for the PHA and Con A models, and NK cell counts for the NKCC model, were included regardless of significance to control for cell numbers in determining functional responses.

All statistical tests were two-sided. The Statistical Package for the Social Sciences: Release 18.0 was used. Effect sizes were calculated using the formula $r = \sqrt{t^2 / (t^2 + df)}$ (Snijders & Bosker, 1999). All available data from the 6 patients who withdrew and from the 15 (15.31% of 98) women who died during the follow-up period were included.

**Primary Analyses Results**

Linear models provided significantly better fit than quadratic for all fixed outcomes excepting the models for IES and Con A. Table 7 summarizes results. Random effects included for intercept did improve model fit for IES, PSS-10, POMS-TMD, CORT, ACTH, NEPI, PHA, NKCC, and SWOG. Random effects covariance matrices and residual variance coefficients are presented for the models with improved fit in Table 8. Random effects included for intercept did not improve model fit for BHS.
LOT, exercise frequency, EPI, or KPS. Random effects included for linear change did not improve fit for any models. When random effects did not improve model fit, it was likely due to restricted variability of scores at intercept and/or little variability of scores across time. All covariance matrices presented in Table 8 are size 1 x 1, since random effects for linear change did not improve fit for any model. Fixed effects, but not random effects, were estimated for BHS, LOT, exercise frequency, EPI, and KPS since random effects did not improve fit for these models.

For psychological distress, the Group POMS-TMD effect was significant with the Distressed group showing greater baseline total mood disturbance ($p<.001$). There was no significant Time effect ($p=.398$). However, there was a significant Group x Time effect ($p=.018$) with the Distressed group showing a steeper decline in total mood disturbance over time than the Non-Distressed group (Figure 7).

For those participants who used exercise as a form of complementary treatment at baseline and/or 12-month follow-up ($n=41$), the average frequency of exercise sessions per month was specified. Of the 41 participants, 31% ($n=18$) reported exercising at baseline and at 12-month follow-up; 17.2% ($n=10$) reported exercising only at baseline; 29.3% ($n=17$) reported exercising only at 12-month follow-up; and 22.4% ($n=13$) reported exercising at baseline but could not be assessed at 12-month follow-up due to non-compliance ($n=3$), withdrawing from the study ($n=2$), or death ($n=8$). For those who completed an assessment, but responded that they did not use exercise as a form of complementary treatment, exercise frequency of zero sessions per month was assumed. There was no significant Group effect for the Non-Distressed ($n=30$) compared to the Distressed ($n=11$) group ($p=.724$). There was a significant Time effect ($p=.014$) with the
Non-Distressed group showing an increase in physical activity. The Group x Time effect was non-significant \( (p=.379; \text{Figure 9}) \).

Regarding the immune Con A assay, there was a significant Group Con A effect with the Distressed group showing greater blastogenic response to Con A at baseline \( (p=.052) \). Regarding trajectories, there was a significant quadratic Time effect \( (p=.003) \) with the Non-Distressed group showing a quadratic increase in blastogenic response to Con A across follow-up. The Group x Time effect was non-significant \( (p=.253; \text{Figure 14}) \).

In regard to endocrine responses, the Group effect for ACTH was non-significant \( (p=.536) \). The Time effect was significant \( (p=.006) \) such that the Non-Distressed group showed a linear increase over time. The Group x Time effect was non-significant \( (p=.496; \text{Figure 11}) \). This pattern was also observed for both EPI and NEPI. The Group effects were non-significant \( (ps=.845 \text{ and } .771 \text{ respectively}) \). Regarding trajectories, there were significant Time effects \( (ps=.045 \text{ and } .037 \text{ respectively}) \). For EPI, the Non-Distressed group showed a gradual decrease through 4-month follow-up and a relatively stable trajectory through the remainder of follow-up. For NEPI, the Non-Distressed group showed a gradual increase between baseline and 4-month follow-up, followed by a gradual decrease through 12-month follow-up. The Group x Time effects were non-significant \( (ps=.568 \text{ and } .383 \text{ respectively}; \text{Figures 12 and 13}) \).

The Group, Time, and Group x Time effects were non-significant for the IES \( (ps>.065; \text{Figure 4}) \), PSS-10 \( (ps>.092; \text{Figure 5}) \), BHS \( (ps>.311; \text{Figure 6}) \), LOT \( (ps>.164; \text{Figure 8}) \), CORT \( (ps>.096; \text{Figure 10}) \), PHA \( (ps>.111; \text{Figure 15}) \), NKCC \( (ps>.333; \text{Figure 16}) \), KPS \( (ps>.085; \text{Figure 17}) \), and SWOG \( (ps>.095; \text{Figure 18}) \).
Post-Hoc Analyses

Post-hoc analyses were of two types. First, post-hoc power analyses were conducted to provide additional clarity of the contributors to the non-significant results reported above. In particular, sample sizes necessary to achieve significance with the observed effects were considered. Post-hoc power estimates for differences between/within two independent groups were calculated for each outcome using the G-Power program. The determination of adequate power was based on the standard of ≥.80 (Cohen, 1992). Table 9 lists effect size estimates and power achieved for Group and Group x Time effects, as these are the effects most relevant to study hypotheses. Additionally, Table 9 describes sample size required to detect a significant result, if present, for each effect when the corresponding power estimate was less than .80.

As indicated, power estimates were, on average, largest for psychological distress outcomes (e.g., .99 for the POMS-TMD Group effect) and smallest for endocrine/immune outcomes (e.g., .15 for the NKCC Group x Time effect). These post-hoc power estimates were consistent with the a priori power estimates for these variables. Effect sizes for biologic variables were smaller compared with other variables (e.g., -.04 for the NEPI Group effect compared with -.29 for the POMS-TMD Group effect). The magnitude of these estimates was likely influenced by sample size and differential rates of missing data (see Results). However, the calculated effect sizes and required sample sizes to detect significant results indicate that group differences for some of the variables studied are unlikely to exist (e.g., -.02 and N=3,966 for the BHS Group x Time effect).

Second, mixed-effects modeling was used to test for Group, Time, and Group x Time differences for each outcome using continuous DASS as time-varying. This was
done as statistical tests of continuous variables tend to achieve greater power than those of discrete or grouped variables (Selvin, 1987). Method to determine linear versus quadratic form of change, random effects included, control variables entered, and backward elimination procedures were the same as those used above. However, since these models do not include dichotomous marital distress groups, the baseline DASS effect determined whether baseline DASS significantly covaried with baseline outcomes. The Time and DASS x Time interaction effects determined significant covariation between time-varying DASS and outcomes across follow-up. Data are presented in Appendix A.

Findings were largely consistent with those for dichotomous marital distress groups excepting three cases. First, for psychological distress, the Group effect for the dichotomous PSS-10 analyses was non-significant ($p=.094$). However, the Group effect for the time-varying PSS-10 model was significant ($p=.004$) with the Distressed group reporting higher global stress at baseline compared with the Non-Distressed group. Additionally, the dichotomous POMS-TMD analyses showed a significant Group x Time effect ($p=.018$) with the Distressed group showing a steeper decline in total mood disturbance over time than the Non-Distressed group. However, for the time-varying POMS-TMD analyses, the DASS x Time effect was non-significant ($p=.271$), meaning that the significant baseline difference also persisted across time.

Second, the dichotomous Con A analyses showed a significant Group effect ($p=.052$) with the Distressed group showing greater blastogenic response to Con A at baseline and a significant quadratic Time effect ($p=.003$) with the Non-Distressed group showing a quadratic increase in Con A across follow-up. For the time-varying model, the
covariation of greater baseline marital distress with higher baseline Con A approached significance ($p=.084$) and the Time effect was non-significant ($p=.942$).

Third, in terms of endocrine responses, the dichotomous ACTH model showed a significant Time effect ($p=.006$) such that the Non-Distressed group showed a linear increase over time. The Time effect was non-significant for the time-varying model ($p=.100$). In addition, the dichotomous EPI and NEPI analyses showed significant Time effects ($ps=.045$ and .037 respectively). The Non-Distressed group showed a decrease in EPI between baseline and 8-month follow-up with an increase thereafter, and a gradual increase in NEPI between baseline and 4-month follow-up, followed by a gradual decrease through 12-month follow-up. However, the Time effects were non-significant ($ps>.173$ respectively) for the time-varying EPI and NEPI models.
Chapter 4: Discussion

The study aim was to test relations between marital quality and psychological distress, health behaviors, endocrine and immune functioning, and objectively-rated physical health in advanced or recurrent breast cancer patients at diagnosis and across a 12-month follow-up. Compared with the Non-Distressed group, the Distressed group showed significantly greater baseline total mood disturbance and differential rate of change across follow-up. Immune differences were also present, with the Distressed group showing significantly higher Con A at baseline relative to the Non-Distressed group, which persisted across 12-month follow-up.

Primary Analysis Findings

As hypothesized, marital distress covaried significantly with psychological distress outcomes. The Distressed group showed significantly greater total mood disturbance at baseline and groups differed significantly for rate of change over time. These findings align with existing literature, including our prior findings for Stage II/III breast cancer patients (Yang & Schuler, 2009). For the time-varying analyses, higher baseline marital distress did covary significantly with higher baseline global stress. The effect persisted across follow-up.

Although the Distressed group reported heightened levels of both cancer-specific and global stress (Cohen, 1988; Horowitz, 1982) at baseline, group trajectories did not diverge significantly. This result contrasts with hypotheses. It is possible that there may
have been no differential effect of marital distress. As previously-described, differences in stress trajectories have been shown for patients with recurrent disease compared with earlier-stage disease (Yang et al., 2008). Thus, the difficulties of adjustment to coping with advanced and recurrent cancer may have nullified the effect of marital distress on stress trajectories. Conversely, the follow-up period for the current study was, by necessity, shorter compared with our prior work (Yang & Schuler, 2009) due to patients’ disease severity and mortality rates. This shorter follow-up period may not have been substantial time for group differences to emerge. Moreover, the rate of unavailable data increased across assessments, also due to patients’ disease severity and mortality rates. Though mixed effects models remain robust in the presence of missing data, this may have reduced the likelihood of detecting rate of change differences, if present. The above possibilities may also explain the non-significant findings for hopelessness. Of note, hopelessness was the only psychological distress outcome which showed a (non-significant) increase from baseline to 12-months for both groups and may illustrate the challenge progressive disease poses.

The significant total mood disturbance (POMS-TMD) outcomes were consistent with the larger literature. Compared with the other psychological distress measures, power estimates and effect sizes were largest for total mood disturbance outcomes. As the POMS assesses negative mood and is a composite of mood subscales (i.e., Tension-Anxiety, Depression-Dejection, Anger-Hostility, Vigor-Activity, Fatigue-Inertia, and Confusion-Bewilderment), it likely contains one or more psychological distress constructs that covary with marital distress for this sample.
Baseline depressive symptomatology was not originally considered as a covariate for the total mood disturbance model since one of the measure’s composite subscales is a depression subscale. Thus, one possibility could have been that depressive symptomatology was affecting group differences, given what is known about the strong relations between marital distress and depressive symptomatology (Prince & Jacobson, 1995; Yang & Schuler, 2009; Wellisch et al., 1983). To follow-up, baseline depressive symptomatology was entered into the total mood disturbance model. The Group effect remained significant ($p=.009$). The Group x Time effect was non-significant ($p=.080$).

As reported, when baseline depressive symptomatology was not entered, the Group x Time effect was significant ($p=.018$). This finding suggests that marital distress was related to increased negative moods above and beyond the influence of depressive symptoms.

Significant findings were observed for some psychological distress variables (e.g., POMS-TMD) but not others (e.g., IES, BHS). These results suggest that, although the majority of the psychological distress variables were correlated (see Table 4), the constructs behaved in a heterogeneous manner in this sample of patients. This statement is further supported by the range of within-individual variability across variables at diagnosis and over time, as well as differing group trajectories for each variable. These results are likely related to qualitative differences in the constructs examined. For example, one might expect total mood disturbance, as compared with hopelessness, to operate differentially in the context of cancer diagnosis and/or marital distress.

No significant results were shown for optimism, which is inconsistent with the literature describing relations between optimism and marital distress (e.g., Kiecolt-Glaser...
Again, effect sizes were quite small, suggesting that group differences may be unlikely to have existed. It is noted that prior literature focused on relations between marital distress and optimism in healthy populations and early-stage (0/I/II) breast cancer patients. Again, the difficulties of adjustment to/coping with advanced and recurrent cancer may have nullified the effect of marital distress on optimism.

Furthermore, it could be argued that controlling for baseline depression in the optimism model influenced effects of marital distress on optimism, as the correlation between optimism and depression is moderate (e.g., \( r = -.42 \); Scheier, Carver, & Bridges, 1994). For the present sample, the correlation between baseline optimism and baseline depressive symptoms was moderate \( (r = -.40) \). To test this argument, baseline depression symptomatology was entered as a covariate for the optimism model. However, the effects remained null \( (ps>.152) \).

No significant effects of interest were observed for exercise frequency. Again, effect sizes were small which may suggest that marital distress does not strongly affect exercise frequency in advanced and recurrent cancer patients. The literature has shown lowered functional status among recurrent breast cancer patients (Yang et al., 2008) and an older study showed that more physical symptoms of disease/treatment and restriction of activities among advanced cancer patients compared in patients with early stage disease (Gotay, 1984). The implication, which corresponds with study findings, is that later-stage cancer patients would not engage in as much physical activity as those with earlier-stage cancer. In fact, less than half of the current sample reported engaging in any physical activity at baseline \( (41.84\%; \ n=41 \text{ out of the original } 98) \) and approximately half
were engaging in physical activity at the 12-month follow-up (48.61%; n=35 out of the remaining 72).

Despite the null findings for Group and Group x Time effects, the Non-Distressed group showed an increase in exercise frequency across follow-up, rather than the decrease that would be expected given sequelae of advanced/recurrent cancer diagnosis. One argument could be that women who engaged in less exercise had more severe disease and died during follow-up. Thus, as data became unavailable for these women, average exercise frequency for the Non-Distressed group appeared to increase. However, this is an unlikely explanation since death during follow-up was entered as a possible covariate.

For endocrine responses, no significant Group or Group x Time differences between the Distressed and Non-Distressed groups were observed. Some null findings were expected, and aligned with meta-analytic data and our prior work (e.g., for ACTH; Miller, Chen, & Zhou, 2007; Schuler et al., under review). Others were unexpected and contrasted with our previous data (e.g., for CORT, EPI, NEPI; Schuler et al.). As CORT responses and depressive symptoms are well-known to covary (e.g., Miller, Chen, & Zhou, 2007), baseline depressive symptomatology was removed from the CORT model in a follow-up analysis. The Group and Group x Time effects remained non-significant (ps>.228).

As was the case for other study findings, effect sizes for endocrine responses tended to be small, suggesting that marital distress may not impact endocrine functioning for this sample. An explanation is that typical sequelae of advanced or recurrent cancer/treatment offset the effects of marital-distress, such that group endocrine
responses remained equivalent. In illustration of the possible effects of advanced or recurrent cancer/treatment on cortisol, prior reports have indicated that metastatic breast cancer patients in general tend to show blunted morning cortisol (Giese-Davis et al., 2006) as well as compromised cortisol responses to acute stressors (Spiegel et al., 2006).

Notably, Time effects were significant with the Non-Distressed group showing an increase in ACTH across follow-up. The Time effect for EPI was also significant with the Non-Distressed group showing a decrease between baseline and 8-month follow-up with an increase thereafter. Again, one argument might be that ACTH and EPI levels appeared to change as women with more severe disease died across follow-up. However, as death during follow-up was entered as a possible control variable, this remains an unlikely explanation. It is possible that these increasing trajectories also reflect typical biologic sequelae of disease/treatment.

Decades of research link chronic stress and down-regulated immune responses (e.g., Miller, Chen, & Zhou, 2007). Thus, it was hypothesized that marital distress would be associated with poorer immune responses (i.e., lower NKCC and poorer blastogenic response to PHA and Con A) at baseline and across follow-up relative to non-distress. Unexpectedly, the Distressed group showed a significantly higher baseline blastogenic response to Con A, which persisted across time. The Non-Distressed group did show a quadratic increase across follow-up suggesting that blastogenic response improved for the Non-Distressed group as time progressed. However, these effects contrast with the literature, and mechanisms by which marital distress would be associated with an improved immune response relative to non-distress are uncertain.
In contrast with current study hypotheses (although similar to our previous findings; Schuler et al., under review), effects for PHA and NKCC were non-significant. Immune marker levels were comparable to those of patients with Stage II/III disease (Andersen et al., 2004). It is possible that these null effects relate to processes of disease and treatment. Patients with advancing breast cancer often demonstrate reduced immune capabilities (Baxevanis et al., 1993; Caras et al., 2004; Konjevic and Spuzic, 1993; Liyanage et al., 2002; Schule et al., 2002; Wolf et al., 2003). NKCC in particular is low in Stage IV breast cancer patients relative to early-stage patients and healthy controls (Baxevanis et al., 1993; Konjevic and Spuzic, 1993). Overall, it is again possible that sequelae of advanced or recurrent cancer/treatment offset the effect of marital-distress level such that these immune responses remained equivalent across the sample, or the impact of chronic stress on immunity may not be evident in the measures used here.

Relevant to the above are data on inflammatory immune processes. This literature is important since cancer is described as a chronic inflammatory condition (Mantovani et al., 2008). Moreover, marital distress and inflammation may covary. In an analogue study of marital conflict in healthy couples, couples with high hostility demonstrated increased inflammation (e.g., increased proinflammatory cytokines) in response to a laboratory-induced conflictual interaction relative to those with lower hostility Kiecolt-Glaser et al., 2005). Meta-analytic data have linked increases in inflammation (e.g., C-reactive protein; interleukin-6) to heightened psychological distress and endocrine changes in cancer patients (Howren et al., 2009) – which are also biobehavioral correlates of marital distress (Yang & Schuler, 2009; Schuler et al., under
review). Thus, inflammation may be an important piece of the paradigm for the effects of marital distress in cancer patients.

Study of the interaction of inflammatory processes and cancer progression is an area of current and rapidly-expanding research activity, although the picture remains complex. To illustrate, some cancer therapies aim to reduce inflammation while other therapy-induced inflammatory responses are used as antitumor treatments (Grivennikov et al., 2010). In fact, inflammation often precedes and may modulate the quality and strength of the adaptive immune response. Since preliminary findings (e.g., Kiecolt-Glaser et al., 2005) suggest that inflammation may covary with marital distress, a modulating effect such as this one may partially explain the higher blastogenic response to Con A in the Distressed group. However, this modulatory response is generally thought to occur in the context of acute inflammation, rather than the chronic inflammation that would be expected in cancer patients such as the ones studied here (Scambato & Cittadini, 2010).

As was the case for the psychological distress variables, although some biologic variables were correlated as expected (see Table 5), the pattern of significant versus non-significant findings suggests that the behavior of many of the variables was heterogeneous in this sample. As before, this statement is also supported by the range of within-individual variability across variables at diagnosis and over time, as well as differing group trajectories for each variable. For some biologic variables, differential behavior would be consistent with normal biological processes (e.g., ACTH compared with NKCC). Regarding other variables, the reason for this pattern of results remains unclear. For example, a significant Group effect was found for one indicator of
blastogenic response (Con A), but not for the other indicator (PHA). Once again, it is possible that these differential observations are related to underlying disease processes, and/or the influence of related responses such as inflammation.

For nurse-rated physical health, it was hypothesized that there would be no group differences in functional status (KPS) at baseline, though both groups would show lowered functional status. However, patterns of group change would differ such that that marital distress would be associated with lower functional status than that for the non-distressed. Indeed, the current sample’s range (range=70-80) was lower compared to newly-diagnosed, earlier-stage breast cancer patients from our prior report (range=80-90; Yang & Schuler, 2009), showing greater impairment of these patients compared to that for patients with Stage II/III disease. As expected, baseline level of impairment did not differ for the Distressed group relative to the Non-Distressed, but the group trajectories did not significantly diverge thereafter. It was also hypothesized that marital distress would covary with more baseline physical symptoms from cancer and treatment (SWOG) compared to non-distress but that group symptom trajectories would vary such that they would converge during follow-up. However, the physical symptom findings were similar to those for functional status in that there were no significant group differences in baseline level or rate of change.

The null physical health findings are likely explained by the severity of participants’ disease and demanding treatments. As before, sequelae of advanced or recurrent cancer/treatment may have offset the effect of marital-distress level such that physical health remained equivalent across the sample.

Post-hoc Analyses
The effects from continuous, time-varying marital distress models were largely consistent with effects from dichotomous marital distress models. It is the case that data analyzed as continuous is advantageous for increasing power. However, the consistency of study findings suggests that the risk of error did not increase when the marital distress variable was dichotomized. That dichotomous and continuous outcomes predicted similar outcomes provides additional support for the clinical value of the DASS cut-off score. For example, both models showed that heightened marital distress covaried with higher mood disturbance at baseline. In this case, the dichotomous marital distress grouping appeared to accurately consist of individuals with higher mood disturbance which covaried with marital distress.

Summary

The current study provides new, longitudinal data regarding the covariation of psychological distress with marital distress in newly-diagnosed advanced and recurrent breast cancer patients. Information regarding longitudinal psychological distress, individual difference, health behavior, endocrine/immune response, and nurse-rated physical health trajectories in married advanced and recurrent breast cancer patients is also offered. The data suggest that women in distressed marriages experience greater psychological distress at diagnosis and that these difficulties persist. Descriptive statistics demonstrated that the maritally-distressed experienced clinically-relevant levels of cancer-specific stress, global stress, and hopelessness (Cohen, 1988; Horowitz, 1982; Beck & Steer, 1988) during the follow-up period. Moreover, though not an original study goal, it was also observed that for non-maritally-distressed women who remained
in the study, physical activity increased, and changes occurred for endocrine responses (e.g., increased ACTH), and immune responses (e.g., increased Con A).

Considering the shortened life expectancy following diagnosis of advanced or recurrent breast cancer, it is noteworthy that heightened psychological distress was present at diagnosis and persisted for the maritally-distressed. Psychological symptoms such as increased hopelessness have been shown to predict depressive symptoms in cancer patients experiencing recurrence (Brothers & Andersen, 2009). Moreover, the effects of psychological distress on outcomes in cancer patients have been repeatedly-demonstrated (e.g., Andersen et al., 1998).

**Clinical Summary**

For baseline CES-D, 31.90% of the sample scored above the ≥16 cutoff for significant depressive symptomatology. This percentage is lower than that of other studies of recurrent breast cancer patients which have reported baseline estimates of 48-49% scoring above the ≥16 cutoff (n=252, Gotay et al., 2007). Thus, effects of marital distress on psychological distress may have been more difficult to detect for this sample of women compared to other samples because of the lower levels of depressive symptoms. It is also a possible explanation as to why effects from some models (e.g., POMS-TMD) did not appear to change based on presence or absence of baseline depressive symptoms as a covariate.

In total, 56.4% of the sample met IES criteria for high cancer-related distress at baseline. The Distressed group’s mean cancer-specific stress remained above the clinical cutoff of 19 at 4 (M=20.62) and 8 months (M=21.44), whereas the Non-Distressed group’s mean cancer-specific stress dropped below the clinical cutoff by 4 months.
and did not rise above the cutoff thereafter. By 12 months, group mean levels of cancer-specific stress were comparable with 39.70% of the sample scoring above the clinical cutoff.

For global stress, the baseline estimates for both groups were above that of normative data, with the baseline estimate for the Distressed group 1.0 SD higher than the national average (M=13.5, SD=6.4; Cohen, 1988). The Distressed group’s mean global stress remained above the national average at 4 (M=14.21) and 8 months (M=15.53), whereas the Non-Distressed group’s mean global stress dropped below the national average (Cohen, 1988) by 4 months (M=12.62) and did not rise above thereafter. By 12 months, the trajectory of the Distressed group had declined to that of the national average such that there were no significant group differences.

The percentage of the Distressed group endorsing symptoms of hopelessness at baseline was 26.1%, and was 21.7% for the Non-Distressed group (Beck & Steer, 1988). Group means were comparable to baseline hopelessness scores for recurrent breast cancer patients in the control arm (n=88) of a randomized trial examining the effects of a family-based intervention for patients and family caregivers (M=2.98, SD=4.00; Northouse et al., 2004). More women reported mild symptoms of hopelessness at baseline compared with moderate/severe symptoms.

By 12 months, both groups’ means had risen above the clinical cutoff for mild symptoms of hopelessness (Beck et al., 1974); 42.9% of the Distressed group and 27.1% of the Non-Distressed group endorsed symptoms (Beck & Steer, 1988). The 12-month group means were comparable to BHS scores for the recurrent breast cancer patients in the control arm of the trial described above at their 6-month follow-up (M=3.89,
SD=4.60; Northouse et al., 2004). These percentages suggest that symptoms of hopelessness actually increased, rather than decreased, across follow-up.

The Distressed group had elevated total mood disturbance at baseline (M=29.54, SD=21.60), showing greater total mood disturbance than metastatic breast cancer patients from prior literature (M=23.2; SD=28.0; Giese-Davis et al., 2000). However, for the Non-Distressed group total mood disturbance was lower. By 4 months, both groups’ scores were lower than the aforementioned mean from prior literature and remained so for the duration of follow-up. These findings suggest that, although a decline occurred over time, marital distress was associated with total mood disturbance that may exceed what would be expected at the time of advanced or recurrent cancer diagnosis.

The sample average KPS score fell in the 70-80 range at baseline and remained so through follow-up (grand mean=78.97), which corresponds to an impaired performance status (i.e., “caring for self; not capable of normal activity or work” through “normal activity with some difficulty; some signs/symptoms”). As expected, the current sample’s range was lower than that for newly-diagnosed breast cancer patients from our prior report (range=80-90; Yang & Schuler, 2009), showing greater impairment than patients with Stage II/III disease.

KPS scores below 80 generally confer impaired physical functioning. This reference is often used as an eligibility criterion for research studies of oncology patients (with a score of 80 and above needed for eligibility). At baseline, 42% of participants’ scores fell within the 60-70 range (i.e., “requires occasional assistance, but is able to care for most needs” through “for self; not capable of normal activity or work”) and 2% fell below 60 (i.e., “hospitalization necessary; very sick; active supportive treatment
necessary” and “disabled, requires special care and assistance”). Thirty-eight percent of the Distressed group had scores ranging from 60-70, and 4% had scores below 60. Forty-four percent of the Non-Distressed group had scores ranging from 60-70, and 1% had scores below 60.

At 12-month follow-up, a larger percentage of the remaining sample had a score within the 80-100 range at 12-month follow-up (70%) relative to baseline (56%). This was likely due to women with lower baseline KPS having died, having withdrawn from the study, or having missed the 12-month follow-up assessment. Twenty-nine percent of the remaining sample had scores within the 60-70 range, and 1% had a score below 60. Forty percent of the Distressed group had scores ranging from 60-70 whereas 26% of the Non-Distressed group had scores ranging from 60-70, and 1% had a score below 60.

For symptoms/signs of illness and treatment toxicities (SWOG), possible severity ratings include none, mild, moderate, severe, and life-threatening. With the exception of one person, no woman received an average rating of severe, or life-threatening for any of the body system subscales at any time point. The exception was a woman in the Non-Distressed group who showed severe mucosal symptoms (e.g., dysphagia; unable to eat solids) at 4-month follow-up. On average, all participants showed mild levels of endocrine symptoms/signs (e.g., difficulties with hot flashes; irregular menses) at each time point, but did not show average mild/moderate symptoms for any of the other body systems.

**Implications for Intervention**

Intervention strategies to address the vulnerabilities of female patients and their partners are considered. First, a large number of randomized clinical trials have
demonstrated that couple therapy in general, particularly behavioral approaches, lead to substantial improvements in relationship quality in healthy couples (Shadish & Baldwin, 2005; Snyder, Castellani, & Whisman, 2006). Improvements in marital quality have been shown to persist for six months to a year after treatment (Christensen & Heavey, 1999). Follow-up data from Christensen et al. (2006) showed that two-thirds of couples treated with behavioral therapies reported significantly improved marital quality relative to pretreatment at two-year follow-up. Approximately half continued to show improvement at five-year follow-up (Christensen et al., 2010).

For medically-ill populations specifically, research has shown that assisting patients and spouses with improving communication and coping may improve marital quality. Poor communication appears to increase marital distress. To illustrate, lung cancer patients and spouses who were maritally-distressed reported less-frequent relationship talk [talking about the nature and state of one’s relationship, what one needs from the relationship (and/or one’s partner), and the relationship implications of a shared stressor] than the Non-Distressed (Badr, Acitelli, & Carmack Taylor, 2008). Disclosure to one’s partner, however, has been shown to relate to better psychosocial adaptation to early-stage cancer (Figueriedo, Fries, & Ingram, 2004; Manne et al., 2004b; Porter, Keefe, Hurwize, & Faber, 2005).

Some models of coping may be especially appropriate when treating medically-ill patients. Coyne and Smith (1991) have suggested utilizing a “relationship focused coping” model, which conceptualizes the interdependent process of coping that occurs within the relationship that involves balancing one’s own needs with the needs of the partner and the relationship. With this paradigm, coping by active engagement or
involving the partner in the illness experience contributed to higher relationship satisfaction in couples following myocardial infarction, while coping by protective buffering, or hiding concerns and worries from one’s partner, was associated with more relationship conflict (Coyne and Smith, 1991). Female cancer patients (Hinnen et al., 2008) and diabetic patients (Kenny, Kashy, & Cook, 2006) evaluated their relationships as more satisfying when partners were perceived as more actively-engaged (i.e., involving one’s partner in discussions, asking how the person feels, and other problem- and emotion-focused coping strategies; Coyne & Smith, 1991). For the diabetic patients, active engagement moderated the association between protective buffering (i.e., less-supportive behavior, characterized by denying fears and worries; Coyne & Smith, 1991) and relationship satisfaction. A negative association was present only when levels of active engagement were low (Schokker et al., 2010). Badr et al. (2010) showed that common positive dyadic coping was associated with better dyadic adjustment for female metastatic breast cancer patients and spouses, underscoring that the spouse’s needs should be addressed along with the patient’s.

**Limitations**

Limitations regarding study findings are noted. First, the generalizability of the findings beyond samples like the one studied here is unknown. The sample was homogeneous: primarily Caucasian, middle-class, middle-aged, and seen at a university-affiliated comprehensive cancer center. The data may thus underestimate any impact of marital distress when it occurs among couples who also have fewer socioeconomic resources, for example. Moreover, the data may not generalize to other racial or ethnic groups, males, gay/lesbian relationships, or those who divorce following cancer diagnosis.
Secondly, this is an observational study. Women were not, of course, randomly assigned to Distressed or Non-Distressed groups, nor were marital satisfaction ratings obtained prior to the women’s diagnoses. The prior literatures suggesting that marital distress is usually a chronic phenomena, our prior reports (e.g., Yang & Schuler, 2009), and the stability of patients’ satisfaction reports during the 12 months after diagnosis, do, taken together, suggest that the classification of patients, albeit imperfect, was likely accurate for the majority. The size and homogeneity of the sample led to the identification of two groups which were equivalent on virtually all demographic, disease, and treatment characteristics. For the purpose of identifying a sample evidencing chronic, clinical levels of marital distress, having four assessments increased the reliability of the score which was compared with the clinical cutoff to make group assignments. The reasoning was that identifying a martially-distressed group would provide the opportunity to describe their clinical characteristics because of the hypothesis that they might be a group at risk for poorer biobehavioral outcomes. When mixed-effects models were analyzed post-hoc with marital distress as a time-varying, continuous variable, findings remained largely consistent.

Third, the missing data did not occur randomly. The rate of missing endocrine/immune data was higher than that for other outcomes since, over time, blood draws often became more difficult and the serum samples were smaller. Moreover, many became too ill for study participation or died. Even so, these occurrences do not differ from those of other studies of advanced and recurrent breast cancer patients. Manne (1998), for example, noted that the majority of studies testing relations between marital
variables and advanced and recurrent cancer, of which there are very few, rely on samples with high attrition rates.

As above, post-hoc analyses were performed to estimate power, effect size, and required sample size to detect group differences, if present, for effects with power of less than .80. The magnitude of these estimates indicated that some null findings may be due to the sample size and/or missing data. However, these estimates also indicate that for certain outcomes, group differences may not exist (e.g., EPI Group effect).

The biologic variable effect size estimates were consistent with meta-analytic data, which has suggested that the effect sizes of the relationship between stress and immune cell function are smaller for chronic stressors (e.g., spousal caregiving) than for brief stressors (e.g., academic examinations). Meta-analytic data have also suggested that effect sizes for immune outcomes are also smaller for subjective assessments of stress (e.g., marital quality) than for objective assessments (e.g., the presence or absence of an ill spouse; Segerstrom & Miller, 2004). Results for biologic variables varied substantially, with required Ns ranging from 162 (CORT Group effect) to 13,076 (EPI Group effect) to detect Group differences in the endocrine measures, if present. These results are consistent with research with metastatic breast cancer patients from other groups which have noted difficulties detecting relations between psychological constructs and biological indicators (e.g., cortisol) due to low power (Sephton et al., 2009).

Length of marriage tends to predict couple adjustment to first-time cancer diagnoses, with more established marriages believed to provide a buffer to the initial stress (Lichtman et al., 1987; Northouse & Swain, 1987). Data on length of marriage were not collected for the purposes of the original studies, and thus length of marriage...
was not included as a covariate in the mixed-effects models. However, the effects of age and length of marriage are correlated (O’Mahoney & Carroll, 1997) and age was included as a covariate.

**Future Directions**

Several future directions are possible. First, similar biobehavioral outcomes could be examined in other populations of interest. For example, it is theorized that social support variables may have less of an impact on certain outcomes in those with more aggressive malignancies than breast (Gore et al., 2005). Thus, the longitudinal covariates of marital distress should be explored in such individuals. Also, as prior research has shown differences between later-stage and earlier-stage breast cancer patients across physical and psychological trajectories (e.g., Yang et al., 2008), statistical comparison of these two groups across marital distress trajectories would be informative. Moreover, marital distress covariates appear to be affected by gender (Kiecolt-Glaser & Newton, 2001). Thus, future research examining these relations in male cancer patients would be useful.

A second direction would be to study the marital unit. Cross-sectional and longitudinal psychosocial adjustment and QoL indicators have been shown to be highly-correlated between woman with breast cancer and their partners (Hagedoorn et al., 2008; Douma et al., 2011; Ezer, Rigol Chachamovich, & Chachamovich, 2011; Northouse et al., 2007). One relevant modeling approach would be the Actor Partner Interdependence Model (APIM; Kenny, Kashy, & Cook, 2006). APIM uses a multi-level modeling approach in which data from two dyad members are treated as nested scores within the sample group (i.e., couple) to estimate within-person and between person main effects, as
well as interaction effects. In addition, APIM can be used for moderation/mediation
analyses. As current study analyses indicated variable covariation, not relationship
directionality, this method could be particularly useful. The use of this modeling
approach is illustrated by Dorros and colleagues (2010), who studied 95 dyads containing
a female Stage I-III cancer patient. In the study, APIM revealed a pattern of influence
whereby the interaction of high levels of depression together with high levels of stress in
women was associated with lowered physical health and well-being in their partners.

A third direction would be to examine the longitudinal covariation of marital
distress with additional biobehavioral outcomes in advanced and recurrent breast cancer
patients. Collecting diurnal endocrine markers (e.g., CORT, ACTH) and other immune
markers (e.g., markers of inflammation) may assist in substantiating this research. A
recent meta-analysis showed that collecting diurnal endocrine markers across the span of
the day produces larger effect sizes (Stetler & Miller, 2011). Moreover, CORT effect
sizes were found to be larger when it was measured in the afternoon (Stetler & Miller),
whereas the current study utilized morning CORT. Finally, the longitudinal covariation
of marital distress and disease endpoints (e.g., survival) could be assessed for this patient
population.

A last future direction would be to build upon current study findings by utilizing
alternative methodological approaches to study the effects of marital distress in advanced
and recurrent breast cancer patients. For example, moderation/mediation analyses, such
as those described in Kiecolt-Glaser and Newton’s (2001) conceptual framework, could
be useful for assessing directionality in relations between marital distress and other
biobehavioral variables for this population.
Conclusion

A first look at the long-term relationship between marital distress and psychological distress, optimism, exercise frequency, endocrine/immune functioning, and physical health outcomes for advanced and recurrent breast cancer survivors was provided. The data implicate marital distress as a correlate of poorer psychological adjustment observed immediately following diagnosis and persisting across the next 12 months. Considering the relations between heightened psychological distress and poorer biobehavioral outcomes, the current study urges further attention to maritally-distressed patients.
References


New England Journal of Medicine, 327, 473-480.

Helgeson, V.S. (1991). The effects of masculinity and social support on recovery from 
myocardial infarction. Psychosomatic Medicine, 53, 621-633.

Reconciling descriptive, correlational, and intervention research. Health 
Psychology, 15, 135-148.

disease-free breast cancer survivors with healthy women. Psycho-Oncology, 14, 
307-314.

marital adjustment: An empirical comparison of three measures. Journal of 
Family Psychology, 8, 432-446.

morbidity and mortality. Social Science and Medicine, 36, 217-225.


Hilton, B.A. (1989). The relationship of uncertainty, control, commitment, and threat of 
recurrence to coping strategies used by women diagnosed with breast cancer. 
Journal of Behavioral Medicine, 12, 39-54.

satisfaction in women: A longitudinal case-control study about the role of breast 
cancer, personal assertiveness, and partners’ relationship-focused coping. British 
Journal of Health Psychology, 13, 737-754.

Marital dissatisfaction, psychological distress, and the coping of parents of 


Scholarly Inquiry for Nursing Practice, 10, 99-123.


Appendix A. Mixed-effects models fixed effects with marital distress across the four assessments as a time-varying, continuous variable.
Appendix A. Mixed-effects models fixed effects with marital distress across the four assessments as a time-varying, continuous variable.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Effects</th>
<th>Estimate</th>
<th>SE</th>
<th>t</th>
<th>Significant Covariates</th>
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<tbody>
<tr>
<td>Psychological Distress</td>
<td>IES</td>
<td>Time-varying Distress</td>
<td>-0.044</td>
<td>0.158</td>
<td>-0.281 B, D, E, H, B x Quadratic</td>
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<tr>
<td></td>
<td></td>
<td>Months</td>
<td>2.823</td>
<td>2.399</td>
<td>1.176 D x Quadratic</td>
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<tr>
<td></td>
<td></td>
<td>Quadratic Term</td>
<td>-0.331</td>
<td>0.209</td>
<td>-1.584 E x Quadratic</td>
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<tr>
<td></td>
<td></td>
<td>Time-varying Distress x Months</td>
<td>-0.105</td>
<td>0.062</td>
<td>-1.709</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Time-varying Distress x Quadratic</td>
<td>0.010</td>
<td>0.005</td>
<td>1.885 D x Quadratic</td>
</tr>
<tr>
<td></td>
<td>PSS-10</td>
<td>Time-varying Distress</td>
<td>-0.190</td>
<td>0.066</td>
<td>-2.877** A, B, D, G, H, A x Months, G x Months, H x Months</td>
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<tr>
<td></td>
<td></td>
<td>Months</td>
<td>-0.288</td>
<td>0.595</td>
<td>-0.484</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Time-varying Distress x Months</td>
<td>0.002</td>
<td>0.010</td>
<td>0.182</td>
</tr>
<tr>
<td></td>
<td>BHS</td>
<td>Time-varying Distress</td>
<td>0.025</td>
<td>0.034</td>
<td>0.741 C, E, F, H, C x Months, E x Months, H x Months</td>
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<td></td>
<td></td>
<td>Months</td>
<td>0.274</td>
<td>0.178</td>
<td>1.541</td>
</tr>
<tr>
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<td></td>
<td>Time-varying Distress x Months</td>
<td>-0.008</td>
<td>0.004</td>
<td>-1.819+</td>
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<td></td>
<td>POMS-TMD</td>
<td>Time-varying Distress</td>
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<td>0.217</td>
<td>-2.675** A, G, G x Months</td>
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<td>Months</td>
<td>0.302</td>
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<td></td>
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<td>Time-varying Distress x Months</td>
<td>0.033</td>
<td>0.030</td>
<td>1.105</td>
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<tr>
<td>Individual Differences</td>
<td>Optimism</td>
<td>Time-varying Distress</td>
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<td>0.069</td>
<td>-0.813 B, F, H, B x Months, F x Months, H x Months</td>
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<td></td>
<td></td>
<td>Months</td>
<td>-0.090</td>
<td>0.242</td>
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<td>Time-varying Distress x Months</td>
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<td>0.006</td>
<td>1.302</td>
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<tr>
<td>Health Behaviors</td>
<td>Exercise frequency</td>
<td>Time-varying Distress</td>
<td>-0.072</td>
<td>0.143</td>
<td>-0.505 C, F, G, H, C x Months, F x Months, H x Months</td>
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<tr>
<td></td>
<td></td>
<td>Months</td>
<td>-1.883</td>
<td>0.926</td>
<td>-2.033*</td>
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<td></td>
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<td>Time-varying Distress x Months</td>
<td>0.023</td>
<td>0.021</td>
<td>1.065</td>
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Appendix A. Continued.

<table>
<thead>
<tr>
<th>Endocrine</th>
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<th>Time-varying Distress x Months</th>
<th>months</th>
<th>months squared</th>
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<tbody>
<tr>
<td><strong>CORT</strong></td>
<td>-0.005</td>
<td>0.072</td>
<td>0.069</td>
<td>A, D, H</td>
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<td>Months</td>
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<td>0.417</td>
<td>-0.433</td>
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<td>Time-varying Distress x Months</td>
<td>0.008</td>
<td>0.011</td>
<td>0.717</td>
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<td><strong>ACTH</strong></td>
<td>-0.118</td>
<td>0.137</td>
<td>-0.867</td>
<td>A, B, G</td>
</tr>
<tr>
<td>Months</td>
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<td>0.960</td>
<td>1.659</td>
<td>A x Months, B x Months</td>
</tr>
<tr>
<td>Time-varying Distress x Months</td>
<td>0.006</td>
<td>0.022</td>
<td>-0.304</td>
<td></td>
</tr>
<tr>
<td><strong>NEPI</strong></td>
<td>-0.218</td>
<td>2.670</td>
<td>-0.082</td>
<td>A, C, D, E, G, H</td>
</tr>
<tr>
<td>Months</td>
<td>26.230</td>
<td>23.739</td>
<td>1.105</td>
<td>A x Months, G x Months, H x Months</td>
</tr>
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<td>Time-varying Distress x Months</td>
<td>-0.023</td>
<td>0.396</td>
<td>-0.059</td>
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<tr>
<td><strong>EPI</strong></td>
<td>0.674</td>
<td>1.132</td>
<td>0.595</td>
<td>A, C, D, E, G, H</td>
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<td>Months</td>
<td>12.683</td>
<td>9.289</td>
<td>1.365</td>
<td>A x Months, G x Months, H x Months</td>
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<td>Time-varying Distress x Months</td>
<td>0.000</td>
<td>0.206</td>
<td>0.002</td>
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<table>
<thead>
<tr>
<th>Immune</th>
<th>Time-varying Distress</th>
<th>Time-varying Distress x Months</th>
<th>months</th>
<th>months squared</th>
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<tr>
<td><strong>PHA</strong></td>
<td>-0.006</td>
<td>0.013</td>
<td>-0.524</td>
<td>A, F, H, I, I x Months</td>
</tr>
<tr>
<td>Months</td>
<td>-0.007</td>
<td>0.112</td>
<td>-0.063</td>
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<td>Time-varying Distress x Months</td>
<td>0.001</td>
<td>0.002</td>
<td>0.435</td>
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<tr>
<td><strong>Con A</strong></td>
<td>-0.023</td>
<td>0.013</td>
<td>-1.738+</td>
<td>D, H, I, D x Months, I x Months</td>
</tr>
<tr>
<td>Months</td>
<td>0.008</td>
<td>0.115</td>
<td>0.073</td>
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<tr>
<td>Time-varying Distress x Months</td>
<td>0.002</td>
<td>0.002</td>
<td>0.886</td>
<td></td>
</tr>
<tr>
<td><strong>NKCC</strong></td>
<td>0.001</td>
<td>0.013</td>
<td>0.073</td>
<td>B, C, J, C x Months, J x Months</td>
</tr>
<tr>
<td>Months</td>
<td>-0.036</td>
<td>0.081</td>
<td>-0.446</td>
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</tr>
<tr>
<td>Time-varying Distress x Months</td>
<td>0.003</td>
<td>0.002</td>
<td>1.349</td>
<td></td>
</tr>
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</table>
**Physical Health**

<table>
<thead>
<tr>
<th></th>
<th>Physical Health KPS</th>
<th>SWOG</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Time-varying Distress</td>
<td>Time-varying Distress</td>
</tr>
<tr>
<td></td>
<td>-0.102 0.143 -0.714</td>
<td>0.001 0.001 0.826</td>
</tr>
<tr>
<td></td>
<td>-0.316 0.948 -0.334</td>
<td>0.013 0.008 1.570</td>
</tr>
<tr>
<td></td>
<td>0.016 0.016 0.989</td>
<td>0.000 0.000 -0.890</td>
</tr>
</tbody>
</table>

Significant covariates: 
- **A** = age (continuous);  
- **B** = cancer diagnosis (recurrent/Stage IV);  
- **C** = surgical treatment at baseline or during follow-up (yes/no);  
- **D** = receiving chemotherapy at baseline or during follow-up (yes/no);  
- **E** = receiving radiation at baseline or during follow-up (yes/no);  
- **F** = participation in intervention arm of RCT (yes/no);  
- **G** = died during follow-up (yes/no);  
- **H** = baseline CESD score (continuous);  
- **I** = % lymphocytes that are T-Cells;  
- **J** = absolute NK cell counts.

*p<.10*  
*p<.05*  
**p<.01**
Appendix B. Random effect covariance structures and residual variances for continuous, time-varying marital distress mixed-effects models.
Appendix B. Random effect covariance structures and residual variances for continuous, time-varying marital distress mixed-effects models.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Random Effect Covariance Structure</th>
<th>Residual Variance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Psychological Distress</td>
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<td></td>
</tr>
<tr>
<td>IES</td>
<td>(63.873)</td>
<td>87.624</td>
</tr>
<tr>
<td>PSS-10</td>
<td>(7.194)</td>
<td>18.619</td>
</tr>
<tr>
<td>BHS</td>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td>POMS-TMD</td>
<td>(173.874)</td>
<td>169.133</td>
</tr>
<tr>
<td>Individual Differences</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Optimism</td>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td>Health Behaviors</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exercise frequency</td>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td>Endocrine Responses</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CORT</td>
<td>(6.560)</td>
<td>18.611</td>
</tr>
<tr>
<td>ACTH</td>
<td>(23.998)</td>
<td>59.453</td>
</tr>
<tr>
<td>EPI</td>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td>NEPI</td>
<td>(14762.660)</td>
<td>25482.415</td>
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<tr>
<td>Immune Responses</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Con A</td>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td>PHA</td>
<td>(0.122)</td>
<td>0.712</td>
</tr>
<tr>
<td>NKCC</td>
<td>(0.139)</td>
<td>0.530</td>
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<tr>
<td>Physical Health</td>
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<tr>
<td>KPS</td>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td>SWOG</td>
<td>(0.004)</td>
<td>0.005</td>
</tr>
</tbody>
</table>
Appendix C: Outcome measures
Impact of Events Scale (IES): cancer-specific stress
**Impact of Events Scale**

**Instructions:** Indicate how frequently these comments have been true in describing your feelings about having cancer **DURING THE PAST SEVEN DAYS.** If they did not occur during that time, please indicate "not at all.”

- I thought about how my life had been before I was diagnosed.
  - Not at all
  - Rarely
  - Sometimes
  - Often

- I thought about how my life might have been different if I had not developed cancer and not had to undergo medical treatment (such as surgery, radiation, and/or chemotherapy) for it.
  - Not at all
  - Rarely
  - Sometimes
  - Often

- I felt the need to discuss my illness or my feelings about having cancer.
  - Not at all
  - Rarely
  - Sometimes
  - Often

- I talked with someone about my thoughts, feelings, or experiences during the time of my diagnosis and/or treatment.
  - Not at all
  - Rarely
  - Sometimes
  - Often

- I thought about having cancer when I didn't mean to.
  - Not at all
  - Rarely
  - Sometimes
  - Often

- I avoided letting myself get upset when I thought about it or was reminded of having cancer.
  - Not at all
  - Rarely
  - Sometimes
  - Often

- I tried to remove cancer from my memory.
  - Not at all
  - Rarely
  - Sometimes
  - Often

- I had trouble falling asleep or staying asleep because pictures or thoughts about cancer or having cancer treatment came into my mind.
  - Not at all
  - Rarely
  - Sometimes
  - Often

- I had waves of strong feelings about this disease.
  - Not at all
  - Rarely
  - Sometimes
  - Often

- I had dreams about being a cancer patient.
  - Not at all
  - Rarely
  - Sometimes
  - Often
Assessment

Impact of Events Scale

Page Two

I stayed away from reminders of cancer.
- Not at all
- Rarely
- Sometimes
- Often

I felt as if my diagnosis/treatments hadn't happened or weren't real.
- Not at all
- Rarely
- Sometimes
- Often

I tried not to talk about it.
- Not at all
- Rarely
- Sometimes
- Often

Pictures about having cancer or undergoing cancer treatment popped into my mind.
- Not at all
- Rarely
- Sometimes
- Often

Other things kept making me think about cancer.
- Not at all
- Rarely
- Sometimes
- Often

I was aware that I still had a lot of feelings about cancer, but I didn’t want to deal with them.
- Not at all
- Rarely
- Sometimes
- Often

I tried not to think about it.
- Not at all
- Rarely
- Sometimes
- Often

Any reminder brought back feelings about having cancer.
- Not at all
- Rarely
- Sometimes
- Often

My feelings about it were kind of numb.
- Not at all
- Rarely
- Sometimes
- Often

Compared to before you had cancer, how do you feel your life is now?
- Worse
- About the same
- Better

Subject ID
Perceived Stress Scale-10 Item Version (PSS-10): global stress
**Feelings of Stress**  
**PSS-10**

We are interested in your feelings and thoughts for the **LAST MONTH**. Indicate how often you felt or thought a certain way by choosing the appropriate response.

**IN THE LAST MONTH, HOW OFTEN HAVE YOU...**

<table>
<thead>
<tr>
<th>Feelings of Stress</th>
</tr>
</thead>
<tbody>
<tr>
<td>been upset because of something that happened unexpectedly?</td>
</tr>
<tr>
<td>o Never</td>
</tr>
<tr>
<td>o Almost never</td>
</tr>
<tr>
<td>o Sometimes</td>
</tr>
<tr>
<td>o Fairly often</td>
</tr>
<tr>
<td>o Very often</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>felt you were unable to control the important things in your life?</th>
</tr>
</thead>
<tbody>
<tr>
<td>o Never</td>
</tr>
<tr>
<td>o Almost never</td>
</tr>
<tr>
<td>o Sometimes</td>
</tr>
<tr>
<td>o Fairly often</td>
</tr>
<tr>
<td>o Very often</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>felt you were nervous and &quot;stressed?&quot;</th>
</tr>
</thead>
<tbody>
<tr>
<td>o Never</td>
</tr>
<tr>
<td>o Almost never</td>
</tr>
<tr>
<td>o Sometimes</td>
</tr>
<tr>
<td>o Fairly often</td>
</tr>
<tr>
<td>o Very often</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>felt confident about your ability to handle your personal problems?</th>
</tr>
</thead>
<tbody>
<tr>
<td>o Never</td>
</tr>
<tr>
<td>o Almost never</td>
</tr>
<tr>
<td>o Sometimes</td>
</tr>
<tr>
<td>o Fairly often</td>
</tr>
<tr>
<td>o Very often</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>felt things were going your way?</th>
</tr>
</thead>
<tbody>
<tr>
<td>o Never</td>
</tr>
<tr>
<td>o Almost never</td>
</tr>
<tr>
<td>o Sometimes</td>
</tr>
<tr>
<td>o Fairly often</td>
</tr>
<tr>
<td>o Very often</td>
</tr>
</tbody>
</table>
Feelings of Stress

We are interested in your feelings and thoughts for the LAST MONTH. Indicate how often you felt or thought a certain way by choosing the appropriate response.

IN THE LAST MONTH, HOW OFTEN HAVE YOU...

felt that you could not cope with all the things that you had to do?
- Never
- Almost never
- Sometimes
- Fairly often
- Very often

been able to control the irritations in your life?
- Never
- Almost never
- Sometimes
- Fairly often
- Very often

felt that you were on top of things?
- Never
- Almost never
- Sometimes
- Fairly often
- Very often

been angered because of things that happened that were outside of your control?
- Never
- Almost never
- Sometimes
- Fairly often
- Very often

felt difficulties piling up so high that you could not overcome them?
- Never
- Almost never
- Sometimes
- Fairly often
- Very often
Beck Hopelessness Scale (BHS): hopelessness
This questionnaire consists of a list of twenty statements. Please read each statement carefully one by one. If the statement describes your attitude for the past week, including today, fill in TRUE. If it does not describe your attitude, fill in FALSE.

<table>
<thead>
<tr>
<th>Assessment</th>
<th>Subject ID</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>H. S.</td>
</tr>
</tbody>
</table>

- **True** I look forward to the future with hope and enthusiasm.
- **False**

- **True** I might as well give up because there's nothing I can do about making things better for myself.
- **False**

- **True** When things are going badly, I am helped by knowing that they can't stay that way forever.
- **False**

- **True** I can't imagine what my life would be like in ten years.
- **False**

- **True** I have enough time to accomplish the things I most want to do.
- **False**

- **True** In the future I expect to succeed in what concerns me most.
- **False**

- **True** My future seems dark to me.
- **False**

- **True** I happen to be particularly lucky and I expect to get more of the good things in life than the average person.
- **False**

- **True** I just can't get the breaks, and there's no reason to believe I will in the future.
- **False**

- **True** My past experiences have prepared me well for the future.
- **False**

- **True** All I can see ahead of me is unpleasantness rather than pleasantness.
- **False**

- **True** I don't expect to get what I really want.
- **False**

- **True** When I look ahead to the future, I expect that I will be happier than I am now.
- **False**
Assessment

○ True  Things just won't work out the way I want them to.
○ False

○ True  I have great faith in the future.
○ False

○ True  I never get what I want, so it's foolish to want anything.
○ False

○ True  It is very unlikely that I will get any real satisfaction in the future.
○ False

○ True  The future seems vague and uncertain to me.
○ False

○ True  I can look forward to more good times than bad times.
○ False

○ True  There's no use in really trying to get something I want because I probably won't get it.
○ False

Subject ID
Life Orientation Test (LOT): optimism
Instructions: Please indicate the extent to which you agree with each of the following statements in general.

1. In uncertain times, I usually expect the best.
   ○ Strongly Agree ○ Agree ○ Neutral ○ Disagree ○ Strongly Disagree

2. It's easy for me to relax.
   ○ Strongly Agree ○ Agree ○ Neutral ○ Disagree ○ Strongly Disagree

3. If something can go wrong for me, it will.
   ○ Strongly Agree ○ Agree ○ Neutral ○ Disagree ○ Strongly Disagree

4. I always look on the bright side of things.
   ○ Strongly Agree ○ Agree ○ Neutral ○ Disagree ○ Strongly Disagree

5. I'm always optimistic about my future.
   ○ Strongly Agree ○ Agree ○ Neutral ○ Disagree ○ Strongly Disagree

6. I enjoy my friends a lot.
   ○ Strongly Agree ○ Agree ○ Neutral ○ Disagree ○ Strongly Disagree

7. It's important for me to keep busy.
   ○ Strongly Agree ○ Agree ○ Neutral ○ Disagree ○ Strongly Disagree

8. I hardly ever expect things to go my way.
   ○ Strongly Agree ○ Agree ○ Neutral ○ Disagree ○ Strongly Disagree
<table>
<thead>
<tr>
<th>Subject ID</th>
<th>Assessment</th>
</tr>
</thead>
</table>

9. Things never work out the way I want them to.

<table>
<thead>
<tr>
<th>Strongly Agree</th>
<th>Agree</th>
<th>Neutral</th>
<th>Disagree</th>
<th>Strongly Disagree</th>
</tr>
</thead>
</table>

10. I don't get upset too easily.

<table>
<thead>
<tr>
<th>Strongly Agree</th>
<th>Agree</th>
<th>Neutral</th>
<th>Disagree</th>
<th>Strongly Disagree</th>
</tr>
</thead>
</table>

11. I'm a believer in the idea that "every cloud has a silver lining".

<table>
<thead>
<tr>
<th>Strongly Agree</th>
<th>Agree</th>
<th>Neutral</th>
<th>Disagree</th>
<th>Strongly Disagree</th>
</tr>
</thead>
</table>

12. I rarely count on good things happening to me.

<table>
<thead>
<tr>
<th>Strongly Agree</th>
<th>Agree</th>
<th>Neutral</th>
<th>Disagree</th>
<th>Strongly Disagree</th>
</tr>
</thead>
</table>
Profile of Mood States (POMS-TMD): total mood disturbance
### MOODS (POMS)

**Instructions:** Indicate how you have been feeling in **THE LAST WEEK, INCLUDING TODAY.**

<table>
<thead>
<tr>
<th>Mood</th>
<th>Not at all</th>
<th>A little</th>
<th>Moderately</th>
<th>Quite a bit</th>
<th>Extremely</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tense</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Angry</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Worn out</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unhappy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lively</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Confused</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peeved</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sad</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Active</td>
<td></td>
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</tr>
<tr>
<td>On edge</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Grouchy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blue</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Energetic</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hopeless</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uneasy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Restless</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unable to concentrate</td>
<td>Not at all</td>
<td>A little</td>
<td>Moderately</td>
<td>Quite a bit</td>
<td>Extremely</td>
</tr>
<tr>
<td>Fatigued</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Annoyed</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Discouraged</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Indicate how you have been feeling in **THE LAST WEEK, INCLUDING TODAY.**

<table>
<thead>
<tr>
<th>MOODS</th>
<th>Not at all</th>
<th>A little</th>
<th>Moderately</th>
<th>Quite a bit</th>
<th>Extremely</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resentful</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nervous</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Miserable</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cheerful</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bitter</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exhausted</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anxious</td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Helpless</td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weary</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bewildered</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Furious</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Full of Pep</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Worthless</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Forgetful</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vigorous</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uncertain about things</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bushed</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
</tbody>
</table>
Karnofsky Performance Status Scale (KPS): functional status
Please indicate which of the following statements best represents the amount of sleep you have had in the last three days.

- I have had less sleep than I feel I need in the last three days.
- I have had as much sleep as I feel I need.
- I have had more sleep than I feel I need.
Southwest Oncology Group criteria (SWOG): symptoms/signs of illness and treatment Toxicities
**HEMATOLOGIC**

<table>
<thead>
<tr>
<th>WBC</th>
<th>PLT</th>
<th>Hgb</th>
<th>Grans/Bands</th>
<th>Lymphs</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;= 4.0</td>
<td>WNL</td>
<td>WNL</td>
<td>&gt;2.0</td>
<td>&gt;2.0</td>
<td>none</td>
</tr>
<tr>
<td>3.0 - 3.9</td>
<td>7.5 - normal</td>
<td>10.0-normal</td>
<td>1.5-1.9</td>
<td>1.5-1.9</td>
<td>mild</td>
</tr>
<tr>
<td>2.0 - 2.0</td>
<td>50.0-74.9</td>
<td>8.0-10.0</td>
<td>1.0-1.4</td>
<td>1.0-1.4</td>
<td>moderate</td>
</tr>
<tr>
<td>1.0 - 1.9</td>
<td>25.0-49.9</td>
<td>6.5-7.9</td>
<td>0.5-0.9</td>
<td>0.5-0.9</td>
<td>severe</td>
</tr>
<tr>
<td>&lt; 1.0</td>
<td>&lt; 1.0</td>
<td>&lt; 6.5</td>
<td>&lt; 0.5</td>
<td>&lt; 0.5</td>
<td>life threatening</td>
</tr>
</tbody>
</table>

**HEMORRHAGE**

**Hemorrhage (clinical)**
- none
- mild, no transfusion
- gross, 1-2 units transfusion per episode
- gross, 3-4 units transfusion per episode
- massive, >4 units transfusion per episode

**Rectal Bleeding**
- none
- intermittent, no steroids
- requires steroids
- requires transfusion (code also hemorrhage)
INFECTION

- Wound
- Respiratory
- Urinary Tract
- Abcess
- Other

- none
- no active treatment (e.g., viral)
- requires outpatient PO antibiotic
- requires IV antibiotic, antifungal, or hospitalization
- life threatening

CLOTTING

Fibrinogen
- WNL
- 0.99 - 0.75 x N
- 0.74 - 0.50 x N
- 0.49 - 0.25 x N
- <= 0.24 x N

Prothrombin Time
- WNL
- 1.01 - 1.25 x N
- 1.25 - 1.50 x N
- 1.51 - 2.00 x N
- > 2.00 x N

Partial Thromboplastin Time
- WNL
- 1.01 - 1.66 x N
- 1.67 - 2.33 x N
- 2.34 - 3.00 x N
- > 3.00 x N

Clotting Other
- none
- mild
- moderate
- severe
- life-threatening

SWOG 2 / SID: _________
CIRCULATORY

Hypertension
- none
- asymptomatic; increase >20mm, or >150/100 if previous WNL; No tx
- recurrent; or increase >20mm, or >150/100 if previous WNL; No tx
- requires tx
- hypertensive crisis

Edema
- none
- 1+ or dependent (eve. only)
- 2+ or independent (all day)
- 3+
- 4+ ; generalized anasarca

Hypotension
- none, or no change
- changes, but no tx required (includes transient orthostatic hypotension)
- requires fluid replacement or other tx; no hospitalization
- requires tx and hospitalization; resolves w/in 48hrs of stopping agent
- requires tx and hospitalization for >48hrs after stopping agent; or shock

Phlebitis / Thrombosis / Embolus
- none
- superficial (non-local)
- deep vein thrombosis
- major event (CVA or other infarct); pulmonary

Veno-Occlusive Disease
- none
- yes

Circulatory Other
- none
- mild
- moderate
- severe
- life-threatening

SWOG 3 / SID: __________
**CARDIAC**

**Dysrhythmia**
- none
- asymptomatic, transient; no tx
- recurrent/persistent; no tx
- requires tx
- requires monitoring

**EF / CHF**
- none
- asymptomatic, EF decline ≤ 20% of baseline
- asymptomatic, EF decline > 20% of baseline
- mild CHF; responsive to tx
- severe or refractory CHF

**Ischemia**
- none
- non-specific T-wave flattening
- asymptomatic, ST & T-wave changes
- angina w/o evidence of infarct
- acute MI

**Pericardial**
- none
- asymptomatic effusion; no tx
- pericarditis
- symptomatic effusion; tx required
- tamponade; tx urgent

**Cardiac Other**
- none
- mild
- moderate
- severe
- life-threatening

**LIVER**

**Billirubin**
- WNL
- <1.5 x N
- 1.5-3.0 x N
- >3.0 x N

**Transaminase**
- WNL
- ≤ 2.5 x N
- 2.6-5.0 x N
- 5.1-20.0 x N
- >20.0 x N

**Alk Phos. / 5' Nucleo.**
- WNL
- ≤ 2.5 x N
- 2.6-5.0 x N
- 5.1-20.0 x N
- >20.0 x N

**Liver Clinical**
- no change from baseline
- pre-coma
- hepatic coma

**Liver Other**
- none
- mild
- moderate
- severe
- life-threatening

**SWOG 4 / SID:** __________
LUNG

CO Diffusion
- >90% of pretx
- decrease to 76-90% pretx
- decrease to 51-75% pretx
- decrease to 26-50% pretx
- decrease to <= 25% pretx

Pulmonary Fibrosis
- normal
- x-ray changes; no sxs
- changes w/sxs (code)

Pulmonary Edema
- none
- x-ray changes; diuretic required
- requires intubation

Pneumonitis
- normal
- x-ray changes, sxs; no tx
- steroids required
- oxygen required
- assisted ventilation required

Cough
- no change
- mild, relieved by OTC meds.
- requires narcotic antitussive
- uncontrolled coughing spasms

Lung Other
- none
- mild
- moderate
- severe
- life-threatening

RENAL / BLADDER

Incontinence
- normal
- with cough, sneeze, etc.
- spontaneous, some control
- no control

Dysuria
- none
- mild pain
- pain, burning; controlled by pyridium
- not controlled by pyridium

Bladder Cramps
- none
- yes (code pain if applicable)

SWOG 5 / SID: _________
## GASTROINTESTINAL

### Nausea
- none
- able to eat (reasonable intake)
- able to eat (intake significantly decreased)
- no significant intake

### Diarrhea
- none
- increase of 2-3 stools per day
- increase of 4-6 stools per day; nocturnal stools; moderate cramping
- increase of 7-9 stools per day; incontinence; severe cramping
- increase of ≥ 10 stools per day, grossly bloody diarrhea; need for parenteral support

## Vomiting
- none
- 1 episode per 24hrs
- 2-5 episodes per 24hrs
- 6-10 episodes per 24hrs
- >10 episodes per 24hrs; requires tx

## Constipation
- none
- stool softener required
- laxatives required
- obstruction w/ enema; evac. required

## Gastritis / Ulcer
- none
- antacid required
- requires vigorous med mgmt; no surg.
- requires surgery for ulcer
- perforation; bleeding

### Small Bowel Obstruction
- none
- intermittent; no tx
- requires tx
- requires surgery

### Ileus
- none
- yes, ≤ 96 hrs
- yes, > 96 hrs

### Intestinal Fistula
- none
- yes

### GI Other
- none
- mild
- moderate
- severe
- life-threatening

---

**SWOG 7 / SID:** __________
NEUROLOGIC / NEUROCENTRAL

Disorientation
- normal; no change
- disorientation; easily re-oriented
- disorientation; requires supervision
- disorientation or hallucinations; institutionalization

Somnolence / Agitation
- normal
- somnolence or agitation; non-disabling
- somnolence or agitation; needs care giver
- somnolence or agitation; institutionalization
- coma

Cerebral Necrosis
- absent
- present

Convulsions
- normal
- focal seizure; no altered consciousness
- focal seizure; altered consciousness
- generalized seizure; tonic / clonic; absence attack
- seizure w/LOC >10 mins

Malaise / Fatigue / Lethargy
- normal
- mild, able to continue normal activity
- change in normal activity
- in bed or chair >50% waking hrs.

Neurocortical Other
- none
- mild
- moderate
- severe
- life-threatening

Anxiety / Depression
- none
- mild, able to continue normal activity
- change in normal activity
- unable to function
- suicidal

Personality Change
- none
- change, non-disruptive to patient or family
- disruptive to patient or family
- harmful to self / others
- psychosis

CNS Other
- none
- mild
- moderate
- severe
- life-threatening

SWOG 8 / SID: _________
PAIN

Bone Pain
- normal
- non-narcotics
- oral narcotics
- parenteral narcotics
- uncontrollable

Tumor Flare
- none
- non-narcotic; redness; increased tumor size
- oral narcotics
- parenteral narcotics
- uncontrollable

Abdominal Pain
- normal
- non-narcotics
- oral narcotics
- parenteral narcotics
- uncontrollable

Other Pain
- normal
- non-narcotics
- oral narcotics
- parenteral narcotics
- uncontrollable

NEUROMOTOR

Weakness
- none; no change
- subjective only
- mild objective; no significant impairment
- objective; impairment
- paralysus

Incoordination / Ataxia
- normal
- slight; dysdiadochokinesia
- intention tremor; dysmetria; nystagmus
- locomotor ataxia

Cerebellar Necrosis
- absent
- present

Speech Impairment
- none
- slurred speech
- expressive aphasia or severe difficulty
- mute

Neurocerebellar Other
- none
- mild
- moderate
- severe
- life-threatening

Neuromotor Other
- none
- mild
- moderate
- severe
- life-threatening

SWOG 9 / SID: ________
NEUROSENSORY

Parasthesia
- normal
- mild
- moderate; non-disabling
- disabling (interferes w/function)

Numbness / Other PNS
- normal
- non-disabling; objective sensory loss
- disabling; objective sensory loss

Reflexes
- normal
- diminished
- loss of deep tendon reflexes

Hearing
- normal; no change
- asymptomatic; loss on audiometry only
- tinnitus
- loss interferes w/function; hearing aid
- deaf; non-correctable

Vision
- normal; no change
- symptomatic; sub-total loss; blurred
- blindness

Taste
- normal; no change
- slightly altered; metallic taste
- markedly altered

Neurosensory Other
- none
- mild
- moderate
- severe
- life-threatening
NEUROLOGIC OTHER

Dizziness / Vertigo
- none
- non-disabling
- disabling

Restlessness
- normal
- requires sedation

Insomnia
- normal
- occasional; may require meds
- difficulty despite meds

Headache
- none
- mild
- moderate or severe, transient
- unrelenting, severe

Neurologic Other
- none
- mild
- moderate
- severe
- life-threatening

DERMATOLOGIC

Local Reaction
- none
- pain
- pain, swelling, inflammation; phlebitis
- ulceration; necrosis
- plastic surgery indicated

Rash (code also ulcer / necrosis)
- none
- asymptomatic; scattered; macular or papular
- scattered eruption w/ puritis or other sx
- generalized symptomatic eruption
- exfoliative dermatitis

Blistering
- none
- asymptomatic eruption
- limited eruption; symptomatic
- generalized, symptomatic eruption

SWOG 11 / SID: _________
Table 1. Proportion of patients assessed having received each type of cancer treatment since the previous assessment, by time point.

<table>
<thead>
<tr>
<th>Time Point</th>
<th>Surgery</th>
<th>Radiation Therapy</th>
<th>Chemotherapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>27.6%</td>
<td>20.4%</td>
<td>54.1%</td>
</tr>
<tr>
<td>4 months</td>
<td>3.1%</td>
<td>4.1%</td>
<td>51.0%</td>
</tr>
<tr>
<td>8 months</td>
<td>5.1%</td>
<td>8.2%</td>
<td>35.7%</td>
</tr>
<tr>
<td>12 months</td>
<td>1.0%</td>
<td>6.1%</td>
<td>27.6%</td>
</tr>
</tbody>
</table>
Table 2. Equivalence of groups (relationship Non-Distressed versus Distressed) at the baseline assessment on sociodemographic, disease/prognostic, and cancer treatment variables.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Non-Distressed (n=73)</th>
<th>Distressed (n=25)</th>
<th>Total (N=98)</th>
<th>Group comparisons</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sociodemographic</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (Years)</td>
<td>52.83 (11.28)</td>
<td>53.21 (10.62)</td>
<td>52.93 (11.07)</td>
<td>0.93</td>
</tr>
<tr>
<td>Race (% Caucasian)</td>
<td>98.6%</td>
<td>92.0%</td>
<td>96.9%</td>
<td>0.16</td>
</tr>
<tr>
<td>Education (Years)</td>
<td>14.74 (3.00)</td>
<td>14.75 (2.59)</td>
<td>14.74 (2.88)</td>
<td>0.98</td>
</tr>
<tr>
<td>Marital Status (% Married)</td>
<td>98.6%</td>
<td>92.0%</td>
<td>96.9%</td>
<td>0.16</td>
</tr>
<tr>
<td>Family Income ($1,000/Year)</td>
<td>80.82 (65.16)</td>
<td>77.68 (40.09)</td>
<td>79.99 (59.34)</td>
<td>0.63</td>
</tr>
<tr>
<td>Disease/Prognostic</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recurrent vs. Stage IV disease, % recurrent</td>
<td>90.4%</td>
<td>76.0%</td>
<td>86.7%</td>
<td>0.07</td>
</tr>
<tr>
<td>For recurrent, duration of disease-free interval (in months)</td>
<td>47.55 (40.14)</td>
<td>54.76 (61.54)</td>
<td>49.16 (45.46)</td>
<td>0.55</td>
</tr>
<tr>
<td>Cancer Treatment at Baseline</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Post-Surgery (% Yes)</td>
<td>30.1%</td>
<td>20.0%</td>
<td>27.6%</td>
<td>0.24</td>
</tr>
<tr>
<td>Radiation Therapy (% Yes)</td>
<td>23.3%</td>
<td>12.0%</td>
<td>20.4%</td>
<td>0.18</td>
</tr>
<tr>
<td>Chemotherapy (% Yes)</td>
<td>50.7%</td>
<td>64.0%</td>
<td>54.1%</td>
<td>0.18</td>
</tr>
<tr>
<td>Hormonal Therapy (% Yes)</td>
<td>28.8%</td>
<td>20.0%</td>
<td>26.5%</td>
<td>0.28</td>
</tr>
<tr>
<td>RCT Participation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RCT participation (% Yes)</td>
<td>23.0%</td>
<td>24.0%</td>
<td>29.6%</td>
<td>0.33</td>
</tr>
<tr>
<td>Of RCT participants, group assignment (Intervention vs. Assessment-only, % Intervention)</td>
<td>56.5%</td>
<td>83.3%</td>
<td>62.1%</td>
<td>0.24</td>
</tr>
</tbody>
</table>
Table 3. Descriptive statistics for the measure of depressive symptoms, stress, health behavior, endocrine responses, immune responses, and health outcomes at baseline and 12 months for the Non-Distressed and Distressed groups.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Non-Distressed (n=73)</th>
<th>Distressed (n=25)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>12 Months</td>
</tr>
<tr>
<td>Depressive Symptoms</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(not an outcome)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CES-D (20-item) ≥16 cutoff %</td>
<td>11.14 (8.09)*</td>
<td>15.46 (8.67)*</td>
</tr>
<tr>
<td>Psychological Distress</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IES &gt;19 cutoff %</td>
<td>22.87 (14.76)</td>
<td>17.18 (14.64)</td>
</tr>
<tr>
<td>PSS-10</td>
<td>15.11 (5.48)**</td>
<td>12.33 (6.40)</td>
</tr>
<tr>
<td>BHS mild, moderate, or severe %</td>
<td>2.55 (2.89)</td>
<td>3.20 (3.48)</td>
</tr>
<tr>
<td>Total Mood Disturbance</td>
<td>14.26 (17.40)**</td>
<td>11.46 (20.23)</td>
</tr>
<tr>
<td>Individual Differences</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Optimism</td>
<td>24.21 (4.86)</td>
<td>24.12 (4.85)</td>
</tr>
<tr>
<td>Health Behaviors</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physical activity</td>
<td>16.07 (9.74)</td>
<td>17.64 (11.47)</td>
</tr>
<tr>
<td>Endocrine responses</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CORT</td>
<td>9.75 (5.53)</td>
<td>10.72 (4.52)</td>
</tr>
<tr>
<td>ACTH</td>
<td>15.10 (7.73)</td>
<td>20.55 (15.14)</td>
</tr>
<tr>
<td>EPI</td>
<td>65.97 (92.93)</td>
<td>55.55 (88.37)</td>
</tr>
<tr>
<td>NEPI</td>
<td>473.71 (246.88)</td>
<td>479.18 (203.87)</td>
</tr>
<tr>
<td>Immune responses</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Con A (mean Z score)</td>
<td>-0.11 (0.72)*</td>
<td>0.39 (1.01)</td>
</tr>
<tr>
<td>PHA (mean Z score)</td>
<td>-0.08 (0.93)</td>
<td>0.30 (0.96)</td>
</tr>
<tr>
<td>NKCC (mean Z score)</td>
<td>-0.10 (0.98)</td>
<td>0.22 (0.91)</td>
</tr>
<tr>
<td>Health</td>
<td></td>
<td></td>
</tr>
<tr>
<td>KPS</td>
<td>76.85 (12.00)</td>
<td>81.48 (12.19)</td>
</tr>
<tr>
<td>Symptoms/Signs</td>
<td>0.26 (0.11)</td>
<td>0.23 (0.10)</td>
</tr>
</tbody>
</table>

*Significant group difference, p < .05.

**Significant group difference, p < .01.
<table>
<thead>
<tr>
<th></th>
<th>(1)IES</th>
<th>(2)PSS-10</th>
<th>(3)BHS</th>
<th>(4)POMS-TMD</th>
<th>(5)LOT</th>
<th>(6) KPS</th>
<th>(7)CES-D</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1)</td>
<td>1.000</td>
<td>.</td>
<td>.</td>
<td>.</td>
<td>.</td>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td>(2)</td>
<td>.488**</td>
<td>1.000</td>
<td>.</td>
<td>.</td>
<td>.</td>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td>(3)</td>
<td>.165</td>
<td>.310**</td>
<td>1.000</td>
<td>.</td>
<td>.</td>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td>(4)</td>
<td>.320**</td>
<td>.714**</td>
<td>.465**</td>
<td>1.000</td>
<td>.</td>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td>(5)</td>
<td>-.180</td>
<td>-.290**</td>
<td>-.509**</td>
<td>-.335**</td>
<td>1.000</td>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td>(6)</td>
<td>-.192</td>
<td>-.437**</td>
<td>-.294**</td>
<td>-.561**</td>
<td>.364**</td>
<td>1.000</td>
<td>.</td>
</tr>
<tr>
<td>(7)</td>
<td>.401**</td>
<td>.636**</td>
<td>.548**</td>
<td>.785**</td>
<td>-.400**</td>
<td>-.589**</td>
<td>1.000</td>
</tr>
</tbody>
</table>

*Significant, p < .05.

**Significant, p < .01.
Table 5. Baseline correlation estimates for biologic variables.

<table>
<thead>
<tr>
<th></th>
<th>(1)CORT</th>
<th>(2)ACTH</th>
<th>(3)EPI</th>
<th>(4)NOREPI</th>
<th>(5)PHA</th>
<th>(6)Con A</th>
<th>(7)NKCC</th>
<th>(8)CES-D</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1)</td>
<td>1.000</td>
<td>.</td>
<td>.</td>
<td>.</td>
<td>.</td>
<td>.</td>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td>(2)</td>
<td>.206</td>
<td>1.000</td>
<td>.</td>
<td>.</td>
<td>.</td>
<td>.</td>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td>(3)</td>
<td>.224</td>
<td>.288*</td>
<td>1.000</td>
<td>.</td>
<td>.</td>
<td>.</td>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td>(4)</td>
<td>.071</td>
<td>.035</td>
<td>.257*</td>
<td>1.000</td>
<td>.</td>
<td>.</td>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td>(5)</td>
<td>.063</td>
<td>-.015</td>
<td>-.094</td>
<td>-.005</td>
<td>1.000</td>
<td>.</td>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td>(6)</td>
<td>.063</td>
<td>-.160</td>
<td>.017</td>
<td>.180</td>
<td>.684*</td>
<td>1.000</td>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td>(7)</td>
<td>.107</td>
<td>.224</td>
<td>.045</td>
<td>.085</td>
<td>.076</td>
<td>-.011</td>
<td>1.000</td>
<td>.</td>
</tr>
<tr>
<td>(8)</td>
<td>.325**</td>
<td>-.009</td>
<td>.261*</td>
<td>-.121</td>
<td>.094</td>
<td>-.008</td>
<td>.003</td>
<td>1.000</td>
</tr>
</tbody>
</table>

*Significant, p < .05.

**Significant, p < .01.
Table 6. Baseline correlation estimates for physical health and health behaviors variables.

<table>
<thead>
<tr>
<th></th>
<th>(1)KPS</th>
<th>(2)SWOG</th>
<th>(3)Exercise</th>
<th>(4)CES-D</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1)</td>
<td>1.000</td>
<td>.</td>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td>(2)</td>
<td>-.460**</td>
<td>1.000</td>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td>(3)</td>
<td>.034</td>
<td>-.050</td>
<td>1.000</td>
<td>.</td>
</tr>
<tr>
<td>(4)</td>
<td>-.589**</td>
<td>.303**</td>
<td>.035</td>
<td>1.000</td>
</tr>
</tbody>
</table>

*Significant, \( p < .05 \).

**Significant, \( p < .01 \).
Table 7. Mixed-effects models comparing fixed effects trajectories of dichotomous Non-Distressed versus Distressed marital groups.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Effects</th>
<th>Estimate</th>
<th>SE</th>
<th>t</th>
<th>Significant Covariates</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Psychological Distress</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Time</td>
<td>2.534</td>
<td>1.411</td>
<td>1.796</td>
<td>H x Quadratic</td>
</tr>
<tr>
<td></td>
<td>Quadratic Term</td>
<td>-0.150</td>
<td>0.095</td>
<td>-1.587</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Group x Time</td>
<td>-1.620</td>
<td>0.876</td>
<td>-1.850+</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Group x Quadratic</td>
<td>0.132</td>
<td>0.071</td>
<td>1.850</td>
<td></td>
</tr>
<tr>
<td>PSS-10</td>
<td>Group</td>
<td>-1.952</td>
<td>1.158</td>
<td>-1.685+</td>
<td>A, B, D, F, G, H, A x Time,</td>
</tr>
<tr>
<td></td>
<td>Time</td>
<td>-0.260</td>
<td>0.468</td>
<td>-0.556</td>
<td>G x Time, H x Time</td>
</tr>
<tr>
<td></td>
<td>Group x Time</td>
<td>0.099</td>
<td>0.128</td>
<td>0.770</td>
<td></td>
</tr>
<tr>
<td>BHS</td>
<td>Group</td>
<td>0.430</td>
<td>0.636</td>
<td>0.675</td>
<td>C, E, F, H</td>
</tr>
<tr>
<td></td>
<td>Time</td>
<td>-0.081</td>
<td>0.080</td>
<td>-1.018</td>
<td>C x Time, E x Time</td>
</tr>
<tr>
<td></td>
<td>Group x Time</td>
<td>-0.011</td>
<td>0.064</td>
<td>-0.168</td>
<td></td>
</tr>
<tr>
<td>POMS-TMD</td>
<td>Group</td>
<td>-15.120</td>
<td>4.101</td>
<td>-3.687**</td>
<td>A, G,</td>
</tr>
<tr>
<td></td>
<td>Time</td>
<td>0.973</td>
<td>1.149</td>
<td>0.846</td>
<td>G x Time</td>
</tr>
<tr>
<td></td>
<td>Group x Time</td>
<td>0.952</td>
<td>0.395</td>
<td>2.413*</td>
<td></td>
</tr>
<tr>
<td><strong>Individual Differences</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Optimism</td>
<td>Group</td>
<td>-0.768</td>
<td>1.182</td>
<td>-0.650</td>
<td>E, F, H</td>
</tr>
<tr>
<td></td>
<td>Time</td>
<td>0.216</td>
<td>0.154</td>
<td>1.405</td>
<td>E x Time, F x Time</td>
</tr>
<tr>
<td></td>
<td>Group x Time</td>
<td>0.027</td>
<td>0.088</td>
<td>0.304</td>
<td></td>
</tr>
<tr>
<td><strong>Health Behaviors</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exercise frequency</td>
<td>Group</td>
<td>-0.885</td>
<td>2.503</td>
<td>-0.354</td>
<td>C, F, G, H</td>
</tr>
<tr>
<td></td>
<td>Time</td>
<td>-1.190</td>
<td>0.475</td>
<td>-2.504*</td>
<td>C x Time, F x Time, H x Time</td>
</tr>
<tr>
<td></td>
<td>Group x Time</td>
<td>0.252</td>
<td>0.285</td>
<td>0.884</td>
<td></td>
</tr>
</tbody>
</table>
Table 7. Continued.

### Endocrine

<table>
<thead>
<tr>
<th>Substance</th>
<th>Group</th>
<th>Time</th>
<th>Group x Time</th>
<th>Group x Quadratic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cortisol</td>
<td>1.909</td>
<td>0.240</td>
<td>-0.140</td>
<td>1.673+</td>
</tr>
<tr>
<td></td>
<td>1.220</td>
<td>0.143</td>
<td>0.161</td>
<td></td>
</tr>
<tr>
<td>ACTH</td>
<td>-1.529</td>
<td>1.812</td>
<td>1.033</td>
<td>2.802**</td>
</tr>
<tr>
<td></td>
<td>-0.620</td>
<td>2.803</td>
<td>0.683</td>
<td>2.721</td>
</tr>
<tr>
<td>Norepinephrine</td>
<td>14.267</td>
<td>42.517</td>
<td>-4.584</td>
<td>0.292</td>
</tr>
<tr>
<td></td>
<td>48.838</td>
<td>20.116</td>
<td>5.223</td>
<td>2.113*</td>
</tr>
<tr>
<td>Epinephrine</td>
<td>-3.758</td>
<td>12.728</td>
<td>-1.614</td>
<td>-0.195</td>
</tr>
<tr>
<td></td>
<td>19.230</td>
<td>6.118</td>
<td>2.821</td>
<td>-0.572</td>
</tr>
</tbody>
</table>

### Immune

<table>
<thead>
<tr>
<th>Substance</th>
<th>Group</th>
<th>Time</th>
<th>Group x Time</th>
<th>Group x Quadratic</th>
</tr>
</thead>
<tbody>
<tr>
<td>PHA</td>
<td>-0.174</td>
<td>-0.005</td>
<td>0.050</td>
<td>-0.780</td>
</tr>
<tr>
<td></td>
<td>0.223</td>
<td>0.072</td>
<td>0.031</td>
<td>-0.066</td>
</tr>
<tr>
<td>Con A</td>
<td>-0.461</td>
<td>-0.709</td>
<td>0.064</td>
<td>-1.954*</td>
</tr>
<tr>
<td></td>
<td>0.236</td>
<td>0.278</td>
<td>0.022</td>
<td>-2.545</td>
</tr>
<tr>
<td>NKCC</td>
<td>-0.090</td>
<td>0.037</td>
<td>0.016</td>
<td>-0.411</td>
</tr>
<tr>
<td></td>
<td>0.219</td>
<td>0.039</td>
<td>0.031</td>
<td>0.540</td>
</tr>
</tbody>
</table>

**Note:** The table entries include statistical values such as group means, time points, and interaction terms. The significance levels are indicated with symbols such as *, **, and +.
Table 7. Continued.

<table>
<thead>
<tr>
<th>Physical Health</th>
<th>Group</th>
<th>Time</th>
<th>Group x Time</th>
<th>A, B, C, D, F, H, B x Time, C x Time, G x Time</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>KPS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Group</td>
<td>-0.992</td>
<td>2.176</td>
<td>-0.456</td>
</tr>
<tr>
<td></td>
<td>Time</td>
<td>-0.115</td>
<td>0.783</td>
<td>-0.147</td>
</tr>
<tr>
<td></td>
<td>Group x Time</td>
<td>0.420</td>
<td>0.244</td>
<td>1.724+</td>
</tr>
<tr>
<td></td>
<td>SWOG</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Group</td>
<td>-0.010</td>
<td>0.022</td>
<td>-0.463</td>
</tr>
<tr>
<td></td>
<td>Time</td>
<td>0.010</td>
<td>0.006</td>
<td>1.670+</td>
</tr>
<tr>
<td></td>
<td>Group x Time</td>
<td>-0.002</td>
<td>0.002</td>
<td>-0.981</td>
</tr>
</tbody>
</table>

+p<.10

* p<.05

** p<.01

Significant covariates: 
- A=age (continuous); 
- B=cancer diagnosis (recurrent/Stage IV); 
- C=surgical treatment at baseline or during follow-up (yes/no); 
- D=receiving chemotherapy at baseline or during follow-up (yes/no); 
- E=receiving radiation at baseline or during follow-up (yes/no); 
- F=participation in intervention arm of RCT (yes/no); 
- G=died during follow-up (yes/no); 
- H=baseline CESD score (continuous), I= % lymphocytes that are T-Cells; 
- J= absolute NK cell counts.
Table 8. Random effect covariance structures and residual variances for dichotomous marital distress groups mixed-effects models.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Random Effect Covariance Structure</th>
<th>Residual Variance</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Psychological Distress</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IES</td>
<td>( 65.810 )</td>
<td>81.476</td>
</tr>
<tr>
<td>PSS-10</td>
<td>( 9.171 )</td>
<td>17.680</td>
</tr>
<tr>
<td>BHS</td>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td>POMS-TMD</td>
<td>( 175.646 )</td>
<td>160.221</td>
</tr>
<tr>
<td><strong>Individual Differences</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Optimism</td>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td><strong>Health Behaviors</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exercise frequency</td>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td><strong>Endocrine Responses</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CORT</td>
<td>( 6.225 )</td>
<td>18.618</td>
</tr>
<tr>
<td>ACTH</td>
<td>( 24.330 )</td>
<td>60.841</td>
</tr>
<tr>
<td>EPI</td>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td>NEPI</td>
<td>( 15670.408 )</td>
<td>24279.886</td>
</tr>
<tr>
<td><strong>Immune Responses</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Con A</td>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td>PHA</td>
<td>( 0.135 )</td>
<td>0.705</td>
</tr>
<tr>
<td>NKCC</td>
<td>( 0.112 )</td>
<td>0.555</td>
</tr>
<tr>
<td><strong>Physical Health</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>KPS</td>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td>SWOG</td>
<td>( 0.003 )</td>
<td>0.006</td>
</tr>
</tbody>
</table>
Table 9. Post-hoc power, effect sizes, and required N to detect a significant effect when power achieved < .80 for Group and Group x Time effects (N=98).

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Effect Size</th>
<th>Power</th>
<th>N Required to Detect Significant Effect when Power Achieved &lt; .80</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Effect</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Group</td>
<td>Group x Time</td>
<td>Group</td>
</tr>
<tr>
<td>Psychological Distress</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IES</td>
<td>0.08</td>
<td>-0.11</td>
<td>0.55</td>
</tr>
<tr>
<td>PSS-10</td>
<td>-0.12</td>
<td>0.05</td>
<td>0.79</td>
</tr>
<tr>
<td>BHS</td>
<td>0.06</td>
<td>-0.02</td>
<td>0.26</td>
</tr>
<tr>
<td>POMS-TMD</td>
<td>-0.29</td>
<td>0.16</td>
<td>0.99</td>
</tr>
<tr>
<td>Individual Differences</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Optimism</td>
<td>-0.06</td>
<td>0.04</td>
<td>0.22</td>
</tr>
<tr>
<td>Health Behaviors</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exercise</td>
<td>-0.03</td>
<td>0.12</td>
<td>0.34</td>
</tr>
<tr>
<td>Endocrine Responses</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cortisol</td>
<td>0.11</td>
<td>-0.06</td>
<td>0.56</td>
</tr>
<tr>
<td>ACTH</td>
<td>-0.06</td>
<td>0.05</td>
<td>0.20</td>
</tr>
<tr>
<td>NEPI</td>
<td>0.02</td>
<td>-0.05</td>
<td>0.06</td>
</tr>
<tr>
<td>EPI</td>
<td>-0.01</td>
<td>-0.04</td>
<td>0.05</td>
</tr>
<tr>
<td>Immune Responses</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PHA</td>
<td>-0.09</td>
<td>0.14</td>
<td>0.34</td>
</tr>
<tr>
<td>Con A</td>
<td>-0.13</td>
<td>0.04</td>
<td>0.63</td>
</tr>
<tr>
<td>NKCC</td>
<td>-0.04</td>
<td>0.05</td>
<td>0.10</td>
</tr>
<tr>
<td>Physical Health</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>KPS</td>
<td>-0.03</td>
<td>0.11</td>
<td>0.09</td>
</tr>
<tr>
<td>SWOG</td>
<td>-0.04</td>
<td>-0.06</td>
<td>0.15</td>
</tr>
</tbody>
</table>
Figure 1. Current study sample eligibility.
Figure 2. Participant assessment status at each study time point.
Figure 3. Distressed and Non-Distressed group marital distress (DASS) by time point.
**Figure 4.** Distressed and Non-Distressed group cancer-specific stress (IES) by time point.

Group effect: non-significant
Time effect: non-significant
Group x Time effect: non-significant
**Figure 5.** Distressed and Non-Distressed group global stress (PSS-10) by time point.

Group effect: non-significant
Time effect: non-significant
Group x Time effect: non-significant
Figure 6. Distressed and Non-Distressed group hopelessness (BHS) by time point.

Group effect: non-significant
Time effect: non-significant
Group x Time effect: non-significant
Figure 7. Distressed and Non-Distressed group total mood disturbance (POMS-TMD) by time point.

- Group effect: significant ($p<.001$)
- Time effect: non-significant
- Group x Time effect: significant ($p=.013$)
Figure 8. Distressed and Non-Distressed group optimism (LOT) by time point.

Group effect: non-significant
Time effect: non-significant
Group x Time effect: non-significant
Figure 9. For women who exercised, total number of times exercised per month for Distressed and Non-Distressed groups by time point.

Group effect: non-significant
Time effect: significant (p=.006)
Group x Time effect: non-significant
Figure 10. Distressed and Non-Distressed group plasma cortisol (CORT) by time point.

Group effect: non-significant
Time effect: non-significant
Group x Time effect: non-significant
Figure 11. Distressed and Non-Distressed group plasma adrenocorticotropic hormone (ACTH) by time point.

Group effect: non-significant
Time effect: significant \((p=.005)\)
Group x Time effect: non-significant
Figure 1. Distressed and Non-Distressed group plasma epinephrine (EPI) by time point.

Group effect: non-significant
Time effect: significant ($p=.045$)
Group x Time effect: non-significant
Figure 13. Distressed and Non-Distressed group plasma norepinephrine (NEPI) by time point.

Group effect: non-significant
Time effect: significant \((p=.037)\)
Group x Time effect: non-significant
Figure 14. Distressed and Non-Distressed group mean blastogenic response to concanavalin A (Con A) Z score by time point.

Group effect: significant ($p=.052$)
Time effect: significant ($p=.003$)
Group x Time effect: non-significant
Figure 15. Distressed and Non-Distressed group mean blastogenic response to phytohemagglutinin (PHA) Z score by time point.

Group effect: non-significant
Time effect: non-significant
Group x Time effect: non-significant
Figure 16. Distressed and Non-Distressed group mean natural killer cell cytotoxicity (NKCC) Z score by time point.

Group effect: non-significant
Time effect: non-significant
Group x Time effect: non-significant
Figure 17. Distressed and Non-Distressed group mean Karnofsky Performance Status Scale (KPS) by time point.

Group effect: non-significant
Time effect: non-significant
Group x Time effect: non-significant
Figure 18. Distressed and Non-Distressed group mean Symptoms/Signs of Illness and Treatment Toxicities (SWOG) by time point.

Group effect: non-significant
Time effect: non-significant
Group x Time effect: non-significant