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Social Support and Endocrine Function: A Randomized Trial with Breast Cancer Patients

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While there is clear evidence that psychological/behavioral interventions with cancer patients provide adjustment and coping benefits (Mark & Meyer, 1995) as well as positive immune and survival benefits (Fawzy et al., 1993, Speigel et al., 1989), the mechanisms for the benefits of such groups are not clearly understood. We propose that one of the mechanisms for the success of intervention groups may be through the provision of social support. Thus, by receiving needed support, patients may be "buffered" or protected from the more negative effects of the cancer stressor (e.g., depressive symptoms, Spiker, Trijsburg, & Duivenvoorden, 1997; and immune down-regulation, Andersen et al., 1998). We propose studying the impact of a psychological/behavioral intervention with breast cancer patients, using treatment (intervention) and control (no intervention) arms, on social support and endocrine responses. We also are interested in endocrine functioning as a biological marker of stress severity (Uchino, Cacioppo, & Kiecolt-Glaser, 1996). We propose studying the impact of a psychological/behavioral intervention with breast cancer patients, using treatment (intervention) and control (no intervention) arms, on social support and endocrine responses. We also are interested in endocrine functioning as a biological marker of stress severity (Uchino, Cacioppo, & Kiecolt-Glaser, 1996) in breast cancer patients. Data from this study will determine: (1) if an intervention is associated with significantly higher levels of social support among the intervention subjects, (2) if an intervention is associated with significantly lower endocrine stress responses among intervention subjects, and (3) test the stress buffering hypothesis of social support, that is test for an interaction between study arm (intervention vs. no intervention) and initial level of social support (high vs. low) across time (initial vs. post-treatment) on endocrine function.
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Introduction

Subject and Background of Previous Work

Social Support and Psychological Well-being. In the context of cancer, social support remains an “important domain of study” (p. 13, see Helgeson & Cohen, 1996, for a review). First, cancer is a severe stressor, having both life altering and threatening consequences (e.g., changes in employment, finances, relationships, dying, etc.). Social support is associated with psychological well-being in cancer patients (e.g., Bloom, Ross, & Burnell, 1978; Bloom & Speigel, 1984; Burman & Margolin, 1992; Helgeson & Cohen, 1996; Jamison, Wellisch, & Pasnau, 1978; Rodrique & Park, 1996). In particular, the positive aspects of social support include access to information, understanding, companionship, financial aid, and physical assistance (Cohen & Wills, 1985). Thus, it is not surprising that a responsive social network increases adjustment by connecting a person with a variety of resources (Auslander & Litwin, 1990; Clipp & George, 1990; Fiore Coppel, Becker, & Cox, 1986).

Second, although social support can be important, cancer patients may often find it unavailable, withdrawn, or insufficient (Bolger, Foster, Vinokur, & Ng, 1996; Dakof & Taylor, 1990; Dunkel-Schetter, 1984). For example, close friends and family members often feel it is best for the cancer patient to maintain optimism and to forgo discussing difficult issues such as the possibility of recurrence and/or death. A number of researchers have discussed the difficulties of cancer patients in obtaining and/or maintaining social support of others due to fear and stigma of the diagnosis, prolonged treatments, and family/friends may be overwhelmed by the physical and emotional demands of caregiving (Broadhead & Kaplan, 1991, Vernon & Jackson, 1989; Wortman, 1984). More recently, Bolger and colleagues (1996) in studying partner’s of breast cancer patients found that the partners were more likely to give support in response to patients’ physical needs but withdraw support when patients’ were emotionally distressed. Thus, with fewer or a lesser quality of social contacts, stressed individuals are left more isolated, more vulnerable to anxiety and depressive symptoms, and may have fewer ways to find resources to facilitate adjustment (Rook & Pietromonaco, 1987).

Impact of Psychological/Behavioral Interventions on Psychological Well-being. Psychological/behavioral interventions appear to provide an important social support function for persons whose social network is too small, unprepared, unresponsive, and/or overwhelmed. This has been the rationale for many peer support groups. In fact, data suggest that such groups are helpful in a variety of ways: providing support that patients cannot find elsewhere and/or sharing common experiences (e.g., diagnosis, treatment, threat of dying) that others do not understand (Helgeson & Cohen, 1996; Wortman & Lehman, 1985). However, over the past 15 years and with over 100 studies of psychosocial interventions with cancer patients conducted (Redd, 1995), it has been suggested that the effectiveness of peer support groups focused on discussion only may be less effective than those groups which have discussion and an educational component or even education alone (Helgeson & Cohen, 1996).
Other reviewers of the psychosocial oncology literature have also found benefits of psychological/behavioral interventions with cancer patients (Harman, 1991; Krupnick, Rowland, Goldberg, & Daniel, 1993; Meyer & Mark, 1995; Trisjburg, Knippenberg, & Rijpma, 1992). In particular, Mark and Meyer (1995) reviewed 45 randomized, controlled-outcome interventions with adult cancer patients and found using meta-analysis positive effect sizes of .24 for emotional adjustment measures (e.g., mood state, depression, locus of control, distress, personality traits), .19 for functional adjustment measures (e.g., social and work activity, control, distress, Karnofsky Status), and treatment- and disease-related symptoms (e.g., treatment related nausea, vomiting, pain, and nutritional status), and .28 for global measures (e.g., overall ratings across several of the above categories). They conclude that it would now be an “insufficient use of research resources to conduct more studies to simply answer the question - Do psychological/behavioral interventions have an impact on emotional adjustment, functional adjustment, and treatment- and disease-related symptoms of cancer patients? (p. 106, Mark & Meyer, 1995). There is clear evidence that such interventions are effective in enhancing adjustment.

Social Support as one Mechanism for the Effectiveness of Psychological/Behavioral Interventions on Psychological Well-being. The association between stress and psychological well-being has been linked causally to social support in some studies (Cohen, Teresi, & Holmes, 1987; Schaefer, Coyne, & Lazarus, 1981), suggesting that social support directly impacts adjustment. However, other studies have suggested that social support “buffers” people from stressful events (Cutrona, 1986; Eaton, 1978). This buffering hypothesis postulates that social bonds help protect or insulate people from stress and psychological distress, and possibly, physical illness. For example, a stressor is seen as less stressful because adequate social support is available to help boost coping and/or provide resources (Cohen & Wills, 1985). However, a person with lower levels of social support would not experience any protective effects when exposed to a stressor. One reason interventions may be effective is because they may provide resources to manage the stress of a cancer diagnosis and its treatment.

Social Support and Physical Well-being. There is growing evidence linking social support with ongoing physical health (Berkman & Syme, 1979; Blazer, 1982; Kiecolt-Glaser et al., 1987; Seeman & Syme, 1987; Thomas, Goodwin, & Goodwin, 1985). Increased morbidity and mortality rates have been associated with smaller social networks (Broadhead et al., 1983). House, Landis, and Umberson (1988) believe a variety of research results are suggestive of “an increased risk of death among persons with a low quantity and sometimes low quality of social contacts” (p. 540). These relationships hold even when baseline levels of support and health are controlled. Simply the presence of a spouse/partner is associated with better physical health (Verbrugge, 1989) and longer life (Goodwin, Hunt, Dey, & Samet, 1987; Neale, Tilley, & Vernon, 1986), while being without a partner is associated with increased mortality (Berkman & Syme, 1979; House, Robbins, & Metzner, 1982). In fact, being without a partner is considered a risk factor for cancer recurrence (Bloom & Kessler, 1994; Goodwin et al., 1987).

Stress, Social Support, and Immune and Endocrine Pathways. It appears that stress, whether chronic or acute sets into motion important biological effects involving the autonomic, endocrine, and immune systems. For instance, stress may be routed to the immune system by the central
nervous system via activation of the sympathetic nervous system or through neuroendocrine-immune pathways (de la Torre, 1994). In the latter case, a variety of hormones released under stress have been implicated in immune modulation (e.g., cortisol, catecholamines, and growth hormone; Baum, Grunberg, & Singer, 1982; Rabin, Cohen, Ganguli, Lysle, & Cunnick, 1989; Sabharwal et al., 1992). Acute or time limited stressors can produce immunological changes in relatively healthy individuals (Glaser et al., 1986; 1987; 1991) and chronic stressors are associated with down-regulation rather than adaption, with some of the largest immune effects found for lengthy stressors or ones with interpersonal components (Herbert & Cohen, 1993; Kiecolt-Glaser, Dura, Speicher, Trask, & Glaser, 1991). Many of the qualities of chronic stressors, such as continued emotional distress and disrupted life tasks (e.g., employment, relationships) occur with decreases in quality of life found in studies of cancer patients.

In an extensive review, Uchino, Cacioppo, and Kiecolt-Glaser (1996) state that social support is reliably related to beneficial effects of the cardiovascular, endocrine, and immune systems, and that these three systems interact. For breast cancer patients, not only is endocrine function important but its connection to the immune system is important as well. Hormone receptor status is specifically tested and determines not only treatment (e.g., whether or not to use tamoxifen) but survival time as well. Patients diagnosed with receptor negative tumors experience, on average, higher recurrence rates and shorter survival times.

In terms of the connections between endocrine and immune function, endocrine function, via hormones, influences immune function by increasing natural killer cell (NK) lysis in response to acute catecholamine release and decreasing NK lysis in response to mitogens, and glucocorticoids also play a role in regulating immune responses (e.g, decreasing NK lysis; for a review see Uchino et al., 1996). Endocrine function has been measured through a number of hormones: EPI, NEPI, CORT, ACTH, growth hormone (GH), and prolactin (PRL). Specifically, CORT facilitates vasoconstrictive effects and has been associated with cardiovascular disease (Kiecolt-Glaser et al., 1996), and both catecholamines (e.g., EPI, NEPI) and CORT are related to decreased immune responsiveness (Ader et al., 1991).

Unfortunately, only 10 studies (e.g., Arnetz, Edgren, Levi, & Otto, 1985; Cobb, 1974; Kirschbaum, Klauer, Filipp, & Hellhammer, 1995; Seeman, Berkman, Blazer, & Rowe, 1994) have examined the connections between social support and endocrine function and none have included cancer patients. In fact, the studies are primarily with healthy adults. It is, therefore, difficult to make firm conclusions regarding the specific mechanisms connecting social support and the endocrine system. Studies have varied in type of endocrine measure used (e.g., CORT, catecholamines), timing of sample collection (morning versus afternoon; hormones fluctuate diurnally), method of sample collection (e.g., blood, urine), and type of social support measure (e.g, perceived social support, amount of social participants, number of social contacts).

However, across the existing studies, those individuals with fewer social contacts/lower social support show greater endocrine reactivity under stress, and with stressors including group participation (e.g., giving a speech, engaging in mental arithmetic; Uchino et al., 1996). Uchino and colleagues urge that future research is needed on stressors, social support, and the endocrine system. Further, they note that there is insufficient research on chronic stressors - only 3 studies.
Thus, this study will address the current research need.

**Purpose and Scope of the Research**

**Context of the Research.** The research is being conducted within the ongoing Stress and Immunity Breast Cancer Project at The Ohio State University (supported by grants from the American Cancer Society, US Army initiative in breast cancer, and the NIMH, B. L. Andersen, P.I.). This larger study is currently in its fifth year of data collection and has received funding through the year 1999. This research is a randomized clinical trial of an intervention with psychological/behavioral intervention and no intervention (assessment only) arms (See Table 1). The intervention is based on a biobehavioral model of cancer stress and disease course (See Figure 1 for the conceptualization of the model and Andersen, Kiecolt-Glaser, and Glaser, 1994, for a discussion). Randomization is stratified by four factors: nodal status and bone marrow transplantation (BMT; 4 levels: negative nodes but tumor > 2 cm, 1-3 positive nodes, >4 positive nodes with BMT, and > 4 positive nodes without BMT), hormone receptor status (2 levels: positive vs. negative), menopausal status (2 levels: pre and perimenopausal vs. postmenopausal), and support status (2 levels: spouse/partner vs. none). Each subject completes a two hour assessment that includes an interview and questionnaires about psychological, interpersonal, behavioral, physical functioning/medical status and a blood draw to assess immune and endocrine function every 4 months during their first year of participation and every 6 months during years 2-4 (See Table 1 for diagram of the research design). Every subject receives a payment of $20.00 per assessment. Intervention subjects participate in a year long intervention with 4 months of weekly sessions (intensive phase) and 8 months of monthly sessions (maintenance phase). See Table 2 for an operalization of the model and Table 3 for description of the intervention (Note the support component, Intensive: Part 3).

**Preliminary Data.** At the time the study was proposed 90+ subjects had been randomized with approximately 40 subjects having completed the intensive phase of the intervention. Using GLM analysis for repeated measures, results indicated significant Group (intervention vs. no intervention) X Time (initial vs. 4 months) interactions across the stress, quality of life, and health behavior domains (compliance data had not been analyzed). For example, the significant Group X Time interaction for the SF-36 (quality of life measure) was F(1, 97) = 4.04, p < .05, and follow-up multiple comparisons indicated a significant increase in quality of life scores for the intervention group, yet no significant change for the control group. The same pattern of results had been found for the stress measures (e.g, Impact of Events), with significant reductions in stress for the intervention group (all p's < .05) yet no significant change for the no intervention arm (all p's > .10). We also have evidence of a stress/immune relationship, with significant negative correlations ranging from -.27 to -.24 (all p's < .05), n = 61) between stress (Impact of Events) and immunity (NK lysis at 100:1; 50:1, 25:1 ratios). Thus, the effectiveness of the intervention has been confirmed and it is possible to examine the effectiveness of stress reduction and endocrine enhancement.
Hypotheses. Three hypotheses are tested. (1) Intervention subjects will report more social support, across several measures, than the assessment only subjects. (2) Intervention subjects will show a more positive endocrine response than the assessment only subjects. (3) There will be an interaction effect (2X2X2 design) for social support (high vs. low) across time (initial assessment vs. post intervention) for the intervention subjects (intervention vs. no intervention) on endocrine function but no interaction for the no intervention subjects. In other words, those intervention subjects with low initial support will show the greatest stress reduction and increase in social support, and, in turn, lower levels of endocrine stress markers (e.g., EPI, NEPI, CORT). This will test the stress buffering hypothesis of social support on endocrine function.

Body

Experimental Methods

Subjects. The subjects are women with stage II or III breast cancer. To date 181 women have been accrued in the larger study (total n = 235). Accrual is expected to continue throughout 1999. For the present study, recruitment and accrual issues are not specific problems as the subjects are already participating in the larger study. However, the upfront refusal rate for the larger study is approximately 30%, consistent with data from other intervention studies. Additionally, the drop out rate from the study is extremely low (< 10%) for subjects at a mean of 18 months of participation.

Psychological Measures. Uchino and colleagues (1996) have noted that comparing results across studies of social support and endocrine function has been problematic due to varying methods of social support measurement. In the current study, multiple measures of social support are used to enhance convergent validity and reliability. Additionally, two measures of perceived stress are also used.

Presence of spouse/partner. Randomization is stratified by the presence/absence of a spouse/partner. This is an important methodologic feature of the design as the presence of a spouse/partner has been related to survival in individuals with chronic illness (Berkman & Syme, 1979) and stage of disease at diagnosis and survival in cancer patients (Goodwin et al., 1987).

Social Adjustment. Social and occupational activities are assessed with a modified version (Andersen, Anderson, & dePross, 1989) of the Katz Social Adjustment Scales (Katz & Lyerly, 1963). It is a 25-item inventory composed of five factors (73% of the variance): Child and home activities (5 items), social contact with friends (4 items), contacts with relatives (3 items), recreational items (7 items), and employment involvement (5 items). Internal consistencies range from .68 to .95 and the measure is sensitive to short (4 months) and long term (12 months) recovery from cancer in women (Andersen et al., 1989).
Social Network. The Social Network Index Interview (SNII, Cohen, 1991) assesses social integration and is potentially less subject to mood-related biases than perceptions of support (Seeman & Syme, 1987). This measure assesses the number of people with whom the individual had contact with on a regular basis and the number of important roles fulfilled by these supports (e.g., spouse, parent, child, employee, friend, neighbor). The number of roles and the number of relationships across roles are predictors of mortality in epidemiologic studies (e.g., Berkman & Syme, 1979; Blazer, 1982). Internal consistency is .60 with test-retest reliability over six months greater than .80 (S. Cohen, personal communication, March 1991).

Support Perceptions. The Interpersonal Support Evaluations List (ISEL; Cohen, Marmelstein, Kamarck, & Hoberman, 1985) contains 40 questions measuring the perceived availability of the following resources: someone to talk to about problems, material aid, someone to do things with, and someone to compare the self with for self-esteem. Cohen et al. (1985) report that the internal consistency of the ISEL subscales range from .60 to .92, and they are not overlapping (.24, ns). A four week test-retest reliability is .87 for the total scale.

Life Stress. The Perceived Stress Scale measures an individual's appraisal of their life, in general, as stressful (Cohen, Kamarck, & Marmelstein, 1983). Specifically, items assess the degree to which individual's perceive their life as unpredictable, uncontrollable, and overloading. This measure is a predictor of symptomatology beyond that due to depressive symptoms and norms are available on community dwelling adults (Cohen & Williamson, 1988).

Cancer Stress. The Impact of Events Scale (Horowitz, Wilner, & Alvarez, 1979) examines intrusive and avoidant thinking/behavior related to cancer diagnosis and treatment. The 15 item scale has two subscales, avoidance and intrusion (r = .42), and internal consistency is .82 and .78 with two-week test-retest of .79 and .89, respectively (Horowitz et al., 1979).

Endocrine Measures. Multiple endocrine measures are also included because stress related responses among hormones are frequently dissociated, and there is no single mechanism of endocrine change (Delahunt & Mellsop, 1987; Rose, 1984). The three hormones to be measured are EPI, NEPI, and CORT, often referred to as stress hormones (Kiecolt-Glaser et al., 1996). These three have been chosen because they are more stress responsive than other hormones such as PRL and GH (Delahunt & Mellsop, 1987; Rose, 1984). As previous researchers have used (e.g., Uchino, Cacioppo, Malarkey, & Glaser, 1995), plasma EPI and NEPI are assessed using high performance liquid chromatography and a Waters system with an electrochemical detector. The coefficient of variation for this assay is 15% for EPI and 9% for NEPI. Plasma CORT levels are assayed using a florescent polarization technique (Uchino et al., 1995). This technique has a coefficient of variation of less than 10%. Blood endocrine levels are tested on frozen plasma which has been and will continue to be kept on each subject. Thus, endocrine assays can be conducted with subjects' past blood draws as well as from subjects currently being accrued during the present study.
Statistical Analyses.

Group Differences/Intervention Effects. Major hypotheses involve the expectation of significant group differences by time (intervention vs. no intervention). Investigation of such effects will be accomplished primarily via the use of repeated-measures multivariate analysis of covariance (2X2 MANCOVA). The primary design is a group by time points design, with dependent variables being the psychological measures of social support and stress and endocrine measures. Dependent variables will be grouped by content areas so as to take into account their intercorrelations, as well as to reduce the number of separate significance tests that are conducted. Of particular interest will be the Group X Time interaction, indicating any differential change between groups due to the intervention. Analyses will also be conducted using the stratification variables (tumor size/nodal status, ER/PR status, menopausal status, presence of a spouse/partner) as additional independent variables. We will examine Group X Time X Status interaction effect for each of these stratification status indicators, so as to assess whether the intervention works differentially for different kinds of patients, but particularly for those with or without a spouse/partner.

Relationships Among Variables-Test of the Stress Buffering Model. To test the associations among variables specified in the stress-buffering model, bivariate relationships will first be evaluated using simple correlations and contingency tables. More complex relationships will be investigated using multiple regression methods. For example, hierarchical regression with sets of independent variables will be used in which endocrine outcomes are regressed on measures of social support and stress. Analyses will focus on the amount of variance explained in the dependent variables as well as the unique contribution of each of the independent variables in accounting for that variance, as measured by squared semi-partial correlations. These analyses will be conducted within and across groups of subjects, as well as within and across time points.

Individual Differences. We expect that individuals will vary with respect to their patterns of change over time on relevant variables, such as social support, stress, and endocrine function. Therefore, we will examine individual differences in patterns of change over time using hierarchical linear models (HLM; Bryk and Raudenbush, 1993). For example, each individual will exhibit a unique pattern of change over time in stress and/or social support. For subjects in the intervention we hope to see an improvement in these measures (e.g., a reduction in stress and/or improvement in social support), followed by stabilization. Finally, we also plan to investigate social support as a key individual difference variable, given its well-documented role as a predictor of mortality in epidemiological studies (House, Umberson, & Landis, 1988; with parallel data linking marital status to stage and survival among cancer patients (Goodwin et al., 1987).

Results and Discussion of the Statement of Work

The army funding, beginning in August 1997 (DAMD17-97-1-7062), has enabled the principal investigator to accomplish both research and professional goals as will be discussed below: Task 1 and 2 (Endocrine Panel Selection and Management), Task 3 (Management of Data), Task 4 (Professional Development), and Task 5 (Intervention Therapist).
Task 1 and Task 2: Endocrine Panel Selection and Management. I have met regularly (every 2 months) with Drs. Andersen and Malarky over the past year regarding endocrine data (collection, management, and analysis). These meetings have also included laboratory personnel as needed (e.g., proper collection of salivary CORT). The final endocrine panel of the larger study (all data is available for the present study) includes CORT, PRL, GH (results from frozen plasma), EPI, NEPI, and ACTH (results from fresh plasma), and we are also collecting salivary CORT. The decision to include salivary CORT was made to increase data collection (CORT is one of the primary stress hormones), as some of the subjects are unable to give blood due to effects of treatment. Therefore, we are able to collect salivary CORT. In addition, we are also able to examine the relationship between two measures of CORT in breast cancer patients (to date, $r = .55$, $p < .01$, $n = 40$).

During the last year, the past frozen samples have been analyzed ($n = 112$ at the initial assessment). All endocrine assays are currently up-to-date. We have not experienced any significant problems with “unusual” values within or across assays.

Currently, we (DiLillo, Golden-Kreutz, Courtney, Malarky, & Andersen) are writing a paper for publication emphasizing stress responses to cancer and psychological and serum CORT outcomes in breast cancer patients. Please see abstract of paper in appendix and Table 4 for preliminary results. *This abstract and accompanying data are unpublished and are not for public distribution.

Task 3: Management of Data. We have continued to maintain checks on the collection, accuracy, and management of the social support data gathered through the larger study using regularly scheduled contacts (weekly staff meeting with research personnel). Again, we have not encountered any significant problems in data collection or management. To date, we have collected initial data on 181 subjects (goal of 235 through 1999 for the larger study) and have data on 98 subjects through 12 months of participation. At this time, we plan to begin analyses of the stress buffering hypothesis over the next 3 months and then to begin preparation/submission of results to academic journals.

We (Golden-Kreutz, Courtney, DiLillo, & Andersen) are also nearing the submission stage of another paper emphasizing stress and depressive symptoms in breast cancer patients. The paper, included in the appendix, is unpublished and is not for public distribution.

We are emphasizing stress and psychological and/or endocrine outcomes in our first analyses and presentations/publications in order to establish the stress effects of breast cancer. These papers are to be followed by analyses and publications regarding the stress buffering effects of social support.

Task 4: Professional Development. During the past year, for behavioral medicine training I have been involved with the following: (1) An extensive reading of the PNI literature with additional focus on endocrine research (under the direction of Drs. Malarky and Andersen). This reading has been vitally important in the development of studies and preparation of manuscripts. (2) Attending monthly meetings of the Health Psychology Graduate Colloquium Series in the
Department of Psychology. This Health Psychology Series emphasizes current research and professional issues in the field and is regularly attended by faculty, postdocs, and graduate students in psychology. Additionally, I presented a talk (November, 1997) titled “The role of health psychologists in the assessment and management of organ recipients: A case study of liver transplantation” based on my clinical experience with medical patients. (3) Attending monthly/bimonthly meetings of the PNI Journal Club for PNI faculty (e.g., Andersen, Malarky, Kiecolt-Glaser, Glaser), graduate students, and medical residents across university departments (including medicine, immunology, endocrinology, psychology, oral biology). I also presented to the Journal Club (February, 1998) recently published data from the larger study, a publication in which I was involved. The reference is below. (4) For further behavior medicine training, also attended the following conferences/invited presentations: Barbara Rimer, DR.P.H, invited address (“Cancer Risk and the Impact of Genetic Testing”) at the James Cancer Hospital and Research Institute, Columbus, Ohio (February, 1998), and Psychosocial Interventions and Cancer Conference at the University of Pittsburgh Cancer Institute, Pittsburgh, PA (October, 1998).

I was also active in additional professional development activities (e.g., improving writing skills, expanding collegial contacts, and presenting research findings at national/international meetings. The following are references of presentations and papers in which I was involved with the larger study:

Publications.

Presentations.


Book Chapters.
**Task 5: Intervention Therapist.** I continue to be the lead co-therapist for the larger project. To date, I have co-lead 8 intervention groups (7 through the entire one year intervention). I receive supervision from Dr. Andersen regarding group processes, as needed. I have also spent the last year training advanced level clinical psychology graduate students in conducting the group intervention. In the training of students, we have weekly supervision meetings regarding group process, therapeutic techniques, and teaching cognitive/behavioral stress management skills to women with breast cancer. I am a licensed psychologist in the State of Ohio (license #5055). By continuing as the group therapist, I am gaining skills as a psychotherapist, group therapist, and have the opportunity to engage in teaching/supervision.

**Conclusions**

The proposed research is relevant to understanding how the diagnosis and treatment of breast cancer affects a women’s psychological and physical well-being. The above is important as psychological/behavioral research has documented that the psychosocial burdens of a cancer diagnosis and treatment are significant in number, severity, and scope (see Andersen, 1994 for a review), and that psychological distress and stressors (e.g., negative life events) are reliably associated with negative changes in immunity (See Herbert & Cohen, 1993; Kiecolt-Glaser, 1988 for reviews). Psychological/behavioral interventions for cancer patients are effective in preventing decreases in psychological well-being and improving coping (see Mark & Meyer, 1995 for a review). Further, these interventions may also be associated with immunity enhancement (e.g., Fawzy et al., 1993) and even improved survival (Speigel, Bloom, Karemer, & Gottheil, 1989). We are studying the impact of a psychological/behavioral intervention with breast cancer patients on social support, stress, and endocrine function. Thus, this present study tests social support as a potential psychological mechanism of the endocrine response to the cancer stressor.

The present study is providing the principal investigator an opportunity to develop into an independent researcher in the areas of cancer, stress, and psychoneuroendocrinology. To date, Tasks 1-5 are all on schedule. As the second year begins, the data, both psychological and endocrine, are ready for analyses of the stress buffering hypothesis of social support. Additionally, professional development goals have been met with success and provide evidence of developing professional independence.
References


Addenda

Acronym and symbol definition: None

Figure and tables

Figure 1: Theoretical model. A biobehavioral model of the psychological (Stress and QoL), behavioral (compliance and health behaviors), and biologic pathways from cancer stressors to disease course. (CNS = Central Nervous System). From Andersen, Kiecolt-Glaser, & Glaser (1994).

Table 1: Research design. Schematic of the research design for subjects across the 5 years of study participation.

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<th>YEAR 1</th>
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<th>YEARS 2-5</th>
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<tr>
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<td>Dx./Ca. Trt</td>
<td>Follow up (months)</td>
</tr>
<tr>
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<td>4</td>
</tr>
<tr>
<td>1</td>
<td>x--Inten--x--Maintenance--x--Maintenance--x</td>
<td>x</td>
</tr>
<tr>
<td>2</td>
<td>x--None--x--None--x--None--x--None--x--None--x</td>
<td>x</td>
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</table>

Note: Dx. = Cancer diagnosis and Ca.Trt. = Beginning of initial cancer treatment; Inten(sive) = Weekly (x18) intervention sessions with reliability/validity checks on intervention integrity; Maintenance = Monthly (x8) intervention sessions with reliability/validity checks; x = Psychological, health behavior, compliance, and immune, endocrine, and cardiovascular assessments and disease endpoints.
Table 2: Operationalization of the theoretical model. Constructs, measured variables, and intervention components.

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<tr>
<th>Construct</th>
<th>Measured Variables</th>
<th>Intervention Components</th>
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<tr>
<td><strong>Stress</strong></td>
<td>Perceived Stress Scale</td>
<td>Rationale (Gatchel, Baum &amp; Krantz's stress model)</td>
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<td></td>
<td>Impact of Events Scale</td>
<td>Progressive Muscle Relaxation training</td>
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<td><strong>Quality of Life:</strong></td>
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<td>Emotional adjustment</td>
<td>Distress: POMS</td>
<td>Cognitive restructuring (A-B-C model)</td>
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<td>Mental health: BDI</td>
<td>Problem Solving</td>
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<tr>
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<td>COPE</td>
<td>Positive Coping</td>
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<tr>
<td>Social adjustment</td>
<td>Social and occupational activities</td>
<td>Social network identification (circle model)</td>
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<td>Social network interview</td>
<td>Increasing contacts and/or assistance with network</td>
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<td></td>
<td>Interpersonal Support Evaluations List</td>
<td>Assertive communication skills training</td>
</tr>
<tr>
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<td>Group support</td>
</tr>
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<td>Breast component:</td>
<td>Sexual Experience Scale</td>
<td>Sexuality and menopausal change information</td>
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<td>Body Satisfaction</td>
<td>Body acceptance and sexuality exercises</td>
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<td>Role play of partner communication re: sexuality</td>
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<td>Health Behaviors</td>
<td>Positive: Diet, exercise</td>
<td>Diet: Low fat/high fiber information</td>
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<td>Dietary assessment and feedback</td>
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<td>Dietary monitoring and meal planning</td>
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<td>Exercise: Exercise and stress management;</td>
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<td>Walking program</td>
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<td>Negative: Alcohol consumption, smoking</td>
<td>Referral info. for cessation and/or self help groups</td>
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<td>Reports of drug dose; Dose intensity</td>
<td>Disease and treatment information</td>
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<td>Interactions with health care providers</td>
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<td>No. and Site(s) of Disease;</td>
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<tr>
<td></td>
<td>Disease free interval</td>
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</tbody>
</table>

Table 3: Intervention. Description of the Intervention Components: Intensive and Maintenance

**Intensive: Part 1: Stress reduction and enhancing QoL (emotional adjustment)** (Sessions 1, 4-7). There are four components. (a) A simplified version of Gatchel, Baum, and Krantz's (1989) model of stress as a psychophysiological process will be offered as a way to conceptualize the cancer stressor. Adaptive coping strategies (e.g. seeking information, positive appraisal) will be introduced as skills that can be learned and applied
Intensive: Part 2: Compliance (Sessions 2-3, Portions of Session 10). Of the very few studies focused on compliance, the data suggest information about the disease and treatment (Richardson et al., 1987; Robinson, 1990), and enlistment of help of significant others, i.e. social support (Richardson et al., 1987). There will be three components. (a) Disease and treatment information will be offered to reduce uncertainty and aid in medical decision making and compliance. Existing educational materials (e.g. the NCI's Breast Cancer Digest and American Cancer Society materials) will be used. (b) The use of relaxation and distraction in coping with treatments (e.g. chemotherapy side effects) and anxiety vis-a-vis follow up medical examinations will be discussed. (c) Assertive communication exercises will be conducted to enhance communication with physicians and other health care professionals (see below under Part 3).

Intensive: Part 3: Improving QoL (social support and breast specific component) (Sessions 8-13). There are four components. (a) The supportive context of the group intervention will be used to direct social comparisons among the group members; as women learn that many of their reactions to the cancer "crisis" are normal and shared by others, problem solving strategies and ways of adaptive coping will be fostered (e.g. Taylor's conceptualization of adjustment to threatening events; Taylor, Lichtman, & Wood, 1984). (b) Women's social network will be identified using a concentric circle model (with the patient at the center). We will systematically cover five levels of social relationships (e.g. coworkers and friends; physicians; parents/in laws and siblings; children of all ages; and spouse/spouse equivalent) and identify sources of satisfaction and clarify areas of difficulty (Cohen & Wills, 1985). (c) Assertive communication skills, modeled after the work of Jakubowski and Lange (1978) will be taught to assist women in expressing their thoughts, feelings, and needs in a manner which facilitates support from and communication with members of their social networks. Four techniques are used: specificity and clarity of one's message; direct communication; "owning" one's message (use of "I," "my" etc. in statements); and, asking for feedback. These skills will be practiced across the five levels of social relationships identified in (b) above. (d) Specific breast cancer sequelae of body changes, menopausal changes, hormonal changes with Tomoxifan therapy, and impact on sexual self schema (esteem) will be discussed as well as coping with sexual changes as discussed in Andersen and Elliot (1993). This session will be prefaced by a session focused on social support from the partner.

Intensive: Part 4: Health behaviors, (Sessions 14-17). There are three components: diet, exercise, and negative health behaviors. (a) Information on a low fat eating plan will be offered to achieve dietary change (dietary fat ≤ 25% of energy intake and dietary fiber of 20-30 grams/day from fruits, vegetables, and grains; these are NCI fat and fiber guideline levels). The intervention will provide participants with the skills and knowledge to gradually lower their fat and increase their fiber intake, and was adapted from the procedures from the WINS study. The guidelines emphasize the influence of discriminative stimuli for eating, the substitution of low-fat food items for high fat foods, and the setting of step-wise goals for lowering fat intake. The guiding conceptualization will be that of health behavior change rather than dieting. We will begin and end the dietary intervention with individualized, stage matched reports for dietary change (i.e. fat reduction and specific fiber recommendations based on current eating pattern). Such reports are generated by incorporating the data from the stages of change (Prochaska et al., 1994), Decisional Balance (Janis & Mann, 1977), and the Food Frequency Questionnaire (Kristal, Sellett, Henry, & Fowler, 1990; see below). Recent data demonstrate that messages individually tailored to an individual's stage of change generated a significantly greater reduction in dietary fat intake than non-tailored messages based on NCI Dietary Guidelines (Campbell, DeVellis, Strehler, Zimmerman, DeVellis, & Sandler, in press; Greene, Rossi, Geed, Willey, & Prochaska, in prep). Consultant Geoffrey Greene has developed these procedures and will provide the computer software for generating the reports. Finally, we note that if the dietary
data indicate deficiencies in RDA nutrients based on 2/3 of the 1989 RDAs (Food and Nutrition Board, 1989), women in either group (intervention or control) will be provided with appropriate educational materials to increase intake of the deficient nutrient(s). Study subjects will be monitored by project dietary research assistant supervised by co-PI Bossetti. We will monitor women with significant weight loss, a low albumin, or other indicators of compromised nutritional status to ensure that there is appropriate medical and dietary care, and to ensure that the dietary intervention is complimentary to any other dietary care which is needed.

(b) According to the American College of Sports Medicine's (1991) Guidelines for Exercise Testing and Prescription, "exercise therapy is becoming an accepted aspect of rehabilitation in patients with cancer. Regular exercise counteracts the detrimental effects of bed rest and provides psychological benefits" (pg. 178). Available data suggest that resuming or maintaining regular exercise would provide positive health benefits, as recent controlled trials suggest that even moderate levels of aerobic exercise performed 3-5 times per week for 20-30 minute intervals improve aerobic fitness in middle aged women (King, Haskell, Taylor, Kraemer, & DeBusk, 1991). In the only study that assessed the effect of aerobic activity in breast cancer patients, MacVicar et al (1989) reported that exercising on a stationary bicycle three times per week was associated with a 40% increase in aerobic efficiency and fewer reports of nausea than in non-exercise controls. The exercise intervention is modeled on the home walking protocol of King (1991) et al. which was found effective for older women. An exercise program of this magnitude (producing 50-60% of maximum heart rate) is sufficient to produce positive psychological benefits (King, Taylor, & Haskell, 1993), and low-intensity exercise appears to be beneficial for the immune system in terms of increasing the numbers of natural killer cells and the number of circulating lymphocytes (Newsholme & Parry-Billings, 1994). Didactic information will include how to set realistic goals, schedules for rest, techniques for increasing energy expenditure during activities of daily living, and coping strategies for setbacks. Women who are unable to perform the walking protocol due to treatment complications will be provided with alternative activity/rest goals. Co-PI Emery will provide guidance on the specific procedures for implementing and monitoring the exercise program.

Prior to participation in the exercise component, subjects will complete the Physical Activity Readiness Questionnaire (British Columbia Department of Health, 1975). This instrument was developed as a screening instrument and tested with over 1 million Canadians for the Canadian Home Fitness Test. It is 100% sensitive for the detection of medical contraindications to exercise and approximately 80% specific. In addition, co-PI Farrar will provide medical clearance for all subject's, and will provide medical consultation during the course of the study for any questions or concerns regarding exercise participation of subjects.

(c) Information on controlling negative health behaviors (i.e. alcohol consumption and smoking) will be provided along with specific referral to community/self help group resources. Disturbed sleep patterns will be addressed with recommendations regarding activity programming, relaxation training, and sleep pattern monitoring.

**Maintenance: Part 1: Preparation for maintenance (Session 18, Intensive).** To implement the maintenance plan, immediately prior to the final session of the intensive intervention, each woman will complete two measures:

1) **Stages of Change:** Following the procedures of Prochaska et al. (1994), a 4- or 5- item algorithm for determining the stage of change for the seven target areas which have been the main foci of the intensive intervention: relaxation training, adherence to medical therapy, social support, sexuality/body image, diet, exercise, and control of a negative/problematic health behaviors. For example, the first item on the algorithm will ask a woman if she has engaged in the desired positive behavior (e.g. practicing relaxation three times per week for 20 minutes; exercising 20 minutes three times per week; having one-two face to face interactions with a confidant per week). If a woman reports the undesired status or does not intend to change in the next 8 months (the length of the maintenance period), then she will be in the precontemplation stage. If she intends to change in the next 8 months, she will be in the contemplation stage. Women in the action stage will have reached a particular criterion (e.g. practicing relaxation three times per week) within the past 4 months (the length of the intensive intervention, or the relevant interval since the intervention was conducted during the intensive period). At this first assessment it is unlikely that any women will be in the maintenance phase (usually defined by maintaining the criterion behavior for six months).

2) **Decisional Balance:** Women will complete decisional balance measures (Janis & Mann, 1977) for each of seven specific target areas: relaxation training, adherence to medical therapy, social contact with an identified target, sexuality/body image, diet, exercise, and control of a negative/problematic health behavior. These measures will be brief (e.g. 8 item) measures which will tap the eight categories of decision making in the Janis
and Mann model: gains or losses for self, gains or losses for significant others, self-approval or self-disapproval, and approval or disapproval of others. For each measure the item content will be specific to the target area.

Following the method of Prochaska et al. (1994) a 5 point Likert scale will be used that ranges from not important (1) to extremely important (5) or strongly disagree (1) to strongly agree (5).

During the first portion of the last intensive therapy session the measures will be scored by research assistants. A brief, individualize report will be prepared for each woman which will summarize the level of the stage of change (i.e. precontemplation, contemplation, action, etc.) for each of the target areas. The report will be further individualized by providing stage-specific and target-specific intervention information for each woman, modeled after the work on individualized self-help interventions of Prochaska et al (1993). The session will begin by delivery of the reports to the women, with discussion of the stages of change model and its applicability to the intervention targets. The session will end by establishing target goals in each area for each woman.

**Maintenance: Part II: (Sessions 19-26).** The same general format will be used for the eight maintenance sessions. Six primary components will be included. (a) We will review the goals for the month, with each woman rating goal attainment and updating her current progress, vis-a-vis stage of change (e.g. determine whether she has moved from contemplation to action). (b) We will emphasize problem solving, social support seeking, and increasing awareness of cues (including self talk) as these general strategies, along with duration of therapist contact in a maintenance program (e.g. Perri et al., 1988), have been important in the maintenance of change (e.g. Urban, White, et al., 1992). (c) Each session we will revisit intervention strategies for one of the seven target areas: relaxation training, adherence to medical therapy, social support, sexuality/body image, diet, exercise, and control of a negative/problematic health behavior. However, this additional coverage of target areas will be broken down into stage specific interventions, i.e. brief modules on relaxation for precontemplators, relaxation for contemplators; relaxation for maintainers, etc. During the session the women will divide into small groups based on their respective stage of change for the target behavior and the interventions will be delivered within the small groups and stage appropriate exercises and written material will be provided. Given the previous intensive intervention period, it is likely that the women will fall into only 2 or 3 groups--contemplation, action or maintenance. With two therapists it will be possible to assist all the subgroups during this segment. (d) The session will close with goal setting for the next month. e) We will prompt the group members to maintain contact with one another between the monthly sessions. For example, women have been comfortable with sharing telephone numbers or some members pair up as "buddies" for bi-weekly contacts. These contacts are for social support and to facilitate maintenance of the behavior change goals. f) Crisis management will be needed for particular difficult situations which arise (e.g. local recurrence, death of a family member). The group will need to process such experiences and provide support to one another as is appropriate.
ABSTRACT

Avoidance and Intrusion: Distinct, Additive, and Interactive Patterns of Stress Response Following Surgical Treatment for Breast Cancer

DiLillo, V., Golden-Kreutz, D., Courtney, M., Malarky, W., & Andersen, B. (In preparation)

It has been well-documented that the diagnosis and surgical treatment of cancer is a stressful event with multiple negative consequences across a number of factors (e.g., mood, quality of life, physical functioning, endocrine/immune functioning). However, individuals have differing responses to cancer stress. We are proposing the use of a bivariate model of cancer stress based on two types of stress reactions, avoidance and intrusion. Avoidance is defined as the avoidance or denial of cancer-related memories and emotions, and intrusion is the cognitive and affective reexperiencing of the cancer-related event. The bivariate model includes four categories of stress responding: low stress (low avoidance and low intrusion), avoiders (high avoidance and low intrusion), intruders (low avoidance and high intrusion), and high stress (high avoidance and high intrusion). These categories provide clear profiles across psychological functioning (mood, perceived stress, quality of life, coping), physical functioning (side-effects of cancer surgery, medication use), and endocrine functioning (cortisol). Medical variables (e.g., stage of disease) were not important variables in differentiating the stress categories. Cancer patients using intrusion have significantly higher levels of psychological distress while those using avoidance have significantly increased cortisol levels. Thus, distress is expressed psychologically by intruders and biologically by avoiders. Furthermore, the categories differentiate among coping strategies employed and the types of physical symptoms reported. Therefore, the identification of patients experiencing distress related to their cancer diagnosis and treatment is associated with the type of stress they exhibit. This model can aid in the identification of those women at highest risk for long-term psychological and adjustment difficulties (including PTSD) and/or those with shorter disease free intervals.
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**Table 4:** Means from ANOVA's Comparing Selected Psychological and Physical Outcomes for Four Stress Groups Based on a 2X2 Factorial Design of Avoidance and Inhibition Symptomology.

*Not published data and not for public distribution.*
Objective stressors vs. subjective stress: Their utility in predicting depressive symptoms in women with breast cancer

Deanna M. Golden-Kreutz, Mary Elizabeth Courtney, Vicki DiLillo, and Barbara L. Andersen

Key words: Stress, depressive symptoms, breast cancer
Stress, whether measured objectively or subjectively, is associated with poor psychological and physical outcomes across a variety of groups (e.g., college students and adults in community smoking cessation program: Cohen, Kamarck, & Mermelstein, 1983; adult psychiatric patients: Hewitt, Flett, & Mosher, 1992; highway patrol officers: Hills & Norvell, 1991). While studies may include both objective and subjective measures of stress, few studies have examined their relative contribution in predicting outcomes (Cohen et al., 1983; Cohen & Williamson, 1986; Hills & Norvell, 1991; Pbert, Doerfler, & DeCosimo, 1992). Such comparisons would be important because an examination of the "predictive validities of objective and subjective stress measures" would clarify the role of perceptions in the relationship between stress and outcomes (e.g., psychological functioning; p. 386, Cohen et al., 1983). Interestingly, such an examination of variables has not been conducted with a cancer population.

The present study is an examination of the relative explanatory power of three different types of stress measures in predicting depressive symptomatology, the most common affective problem experienced by people diagnosed with cancer (Derogatis et al., 1983; See Spiker, Trijsburg, & Duivenvoorden, 1997 and Tope, Ahles, & Silverfarb, 1996, for reviews), in a sample of women who have had recent surgical treatment for breast cancer.

Conceptualization and measurement of stress

The conceptualization and methodology in research on self-reported stress has evolved over the last 20 years (See Table 1 for an overview of the type of stress measures available). For instance, early research on the psychological effects of
stress arose from the notion that difficult life events (unemployment, death of a relative, etc.) are stressors (Cobb & Kasl, 1977; Stroebe, Stroebe, Gergen, & Gergen, 1982). Thus, these studies focused on the objective assessment of stress (the type and/or number of life events or stressors). Objective measures inquire only about the presence/absence, total number, or type of events experienced during a specified period of time (e.g., during the last year) and do not involve evaluations, feelings, or cognitions associated with the events. Number and/or type of life events have been linked to the development of psychopathology such as depression, anxiety, and schizophrenia (Brown & Burley, 1968; Paykel & Dowlutshahni, 1988). Additionally, it has been asserted that a greater number of events is related to poorer psychological and health outcomes (Baum, Gatchel, & Schaffer, 1983; Dohrenwend & Dohrenwend, 1974; 1978; Holmes & Rahe, 1967). Objective stressors have also been hypothesized to be important in the development of specific physical illnesses such as myocardial infarction (Neilson, Brown, & Marmot, 1989), rheumatoid arthritis (Simon & Laasko, 1985), appendicitis (Creed, 1981) and cancer (Geyer, 1991; Ginsberg, Price, Ingram, & Nottage, 1996).

Subjective measures of stress were developed in response to criticisms that the objective measurement of stressors do not account for individual differences in response to those stressors. That is, a person's response to stressors is not based completely on the type or number of events, but also involves cognitive appraisal processes as well (Cohen, Kamarck, & Meruelstein, 1983; Lazarus & Folkman, 1984). Subjective measures instead assess perceptions of stress during a specific time period.
Specific subjective measures inquire about the extent to which a given situation (e.g., occupation) or event (e.g., bereavement, cancer diagnosis) is perceived to have affected an individual. Additionally, specific subjective measures can be: 1) a one-item measure of how stressful a single event/situation is perceived to be, 2) a total score across items (stressors), or 3) a measure with several items assessing different aspects of a single event/situation. Alternatively, global subjective measures do not reference specific events/situations, but instead ask individuals if they perceive their lives as stressful.

Research indicates that individuals vary in their ratings of events as desirable or undesirable, and that events perceived as undesirable are more strongly related to negative psychological outcomes (Sarason, Johnson, & Siegel, 1978; Vinokur & Selzer, 1975; Zautra & Reich, 1983). Subjective stress measures of both types (specific, global) have consistently been better predictors of psychological and physical outcomes than objective measures (Cohen et al., 1983; Martin, Kazarian, & Breiter, 1995; Pbert et al., 1992; Sarason et al., 1978; Vinokur & Selzer, 1975).

Fifteen years ago, Cohen and colleagues (1983) offered a global measure of perceived stress, the Perceived Stress Scale (PSS), contending that such a measure provides a greater explanation of the stress response than do objective stressors and specific subjective measures. They raised three basic concerns with concurrent methods. First, while specific subjective measures have greater predictability of psychological and physical outcomes over objective measures, this advantage is
relatively small due to the use of single-item specific subjective measures. Second, people may misattribute stress levels to a specific event. In other words, it is common to associate stress with a current, identifiable event (e.g., recent death of relative, divorce) than with less discrete or more chronic circumstances (e.g., financial problems, stressful job). Finally, responses to an event are better reflected by global stress measures than stress associated with specific events or situations. For instance, a person's response to an event does not occur in isolation but in the context of other factors (socioeconomic status, personality, etc.) and, of course, all of these factors may contribute to stress perceptions. Research using the PSS has found that global stress is, in fact, more strongly associated with psychological outcomes than either objective or specific subjective measures (Cohen et al., 1983; Kuiper, Olinger, & Lyons, 1986; Martin et al., 1995; Pbert et al. 1992).

Stress measurement in cancer populations

The majority of studies that have examined the relationships among objective stressors and cancer have explored life events as predictors of disease. While a number of these studies suggest that number and/or type of life events are positively related to the subsequent diagnosis (Ginsberg, Price, Ingram, & Nottage, 1996; Cooper and Faragher, 1993; Geyer, 1991), progression (Funch & Marshall, 1983), or recurrence (Ramirez et al., 1989) of cancer, other studies have found no relationship between the occurrence of life events and disease (Roberts, Newcomb, Trentham-Diets, & Storer, 1996; Edwards et al., 1990). In contrast to the numerous studies that have investigated the prediction of disease outcomes from number and/or type of life
events experienced, fewer studies have examined the relationship between life events and psychological outcomes in cancer populations. In general, these studies suggest that increased number of life events are positively related to psychological distress in cancer patients (Burberg, Penman, & Holland, 1984; Grassi, Malacarne, Maestri, & Ramelli, 1997; & VanServellen, Sarna, Padilla, & Brecht, 1996).

In recent years, the methodology has shifted to the use of specific subjective measures of stress, with cancer as the identified event. While early studies have documented the acute stress experienced at diagnosis (e.g., Andersen, Anderson, & deProsse, 1989; Weisman & Worden, 1976), contemporary studies suggest that cancer diagnosis and treatment may, in fact, constitute a "traumatic event" (4th ed; DSM-IV: American Psychiatric Association, 1994; Cordova et al., 1995; Andrykowski, Cordova, Studts, & Miller, 1998). As a result, existing measures of traumatic stress such as the Impact of Events Scale (IES; Horowitz, Wilner, & Alvarez, 1979) have been modified for cancer populations (changing the word "event" on the original scale to "disease" or "cancer"). Much of the research examining cancer stress has, in fact, used the IES to examine the frequency or severity of trauma-related cognitions and behaviors, and their relationships to psychological outcomes (Baider & Kaplan De-Nour, 1997; Cordova et al., 1995; Schwartz et al., 1995). Research has found consistent positive relationships between intrusive thoughts and severity of psychological distress, and weaker or no relationship between avoidant cognitions and psychological distress (Baider & Kaplan De-Nour, 1997; Cordova et al., 1995; Hall & Baum, 1995; Schwartz et al., 1995).

Fewer cancer studies have included globally perceived stress measures, and
these have often been with pediatric patients (Bull & Drotar, 1991; Varni et al., 1994) or those with recurrent disease (Schulz et al., 1995). Varni and colleagues (1994) found, for example, that higher perceived global stress predicted increased psychological distress (e.g., depression and anxiety) in adolescent survivors of pediatric cancer. Thus, the research focus has been on objective stressors and cancer specific stress, with few studies examining global stress in a cancer population.

Cancer and depressive symptoms

The diagnosis and treatment of cancer are well-documented stressors and their negative impact on psychological well-being and quality of life have been thoroughly discussed elsewhere (e.g., Andersen, 1992; Andersen, Kiecolt-Glaser, & Glaser, 1994). Weisman and Worden (1976), for example, noted that the diagnosis of cancer produces an “existential plight,” meaning that the news brings shock, disbelief, and emotional turmoil. As such, sadness, fear, and confusion often characterize the diagnostic period. Not surprisingly, depressive symptoms/depression are the most common affective problem found in cancer populations (Derogatis et al., 1983; Spiker et al, 1997; Tope et al., 1996). It has been estimated that the majority of people diagnosed with cancer will experience some degree of depressive symptomatology and that approximately 50% of them will meet the American Psychiatric Association’s criteria for a formal psychiatric disorder, although the clear majority of these diagnoses represent adjustment disorders (Derogatis et al., 1983). While the emotional crisis which characterizes the diagnostic period lessens as time passes (Andersen, Anderson, & deProesse, 1986; Bloom, 1987; Edgar, Rosberger, & Nowlis, 1992), rates
of diagnosable depression in women post-surgery (6 months or less) for breast cancer have ranged from 6% (Watson et al., 1991) to 29% (Rijken, deKruif, Komproe, & Roussell, 1995). With over 180 thousand new breast cancer diagnoses made annually in the United States (American Cancer Society, 1994), a significant number of women with breast cancer will experience clinically significant depressive symptoms post surgery. However, exactly what types of stress (non-cancer related versus cancer related) and the manner in which stress is experienced (objective stressor versus perceived stress) are contributing to this depressive symptomatology remain to be clarified.

In addition to stress, there may be other important contributors to depressive symptoms in women with breast cancer. A variety of sociodemographic variables are correlated with the incidence of and/or mortality resulting from breast cancer. While incidence of breast cancer is associated with age (age increases risk), race (whites and hispanics have higher rates of diagnosis than african americans), and SES measured as income, education, and/or occupation ( ). However, much less is known about how these variables relate to depressive symptoms. Inconsistent findings exist regarding age and depressive symptoms in women with breast cancer. Some studies suggest that younger women are more depressed (Hughson et al., 1988; Lee et al. 1992), other studies suggest that older women have greater symptoms (Carver et al., 1994; Levy et al., 1993) and still other research suggests no relationship (Pinder et al., 1993). While there is evidence to suggest that women of lower SES report more depressive symptoms (Pinder et al., 1993) and have poorer outcomes when diagnosed
with depression (Dean, 1987) than women of higher SES, other studies have found no relationship between SES and depressive symptoms (Hughson, Cooper, McArdle, & Smith, 1988; Stanton & Snider, 1993). Furthermore, the same inconsistent pattern of findings is found with respect to depressive symptoms and having a partner, although there appears to be little support for such a relationship (Pistrang & Barker, 1995) and more support for no relationship (Hughson et al., 1988; Pinder et al., 1993; Stanton & Snider, 1993). Clearly, further research is needed to clarify the role of sociodemographics in depressive symptoms of women with breast cancer.

Stage of disease at diagnosis, type of surgical treatment (lumpectomy and mastectomy) and time since treatment are disease variables that have been frequently researched in regards to psychological outcomes in women with breast cancer. While it is widely believed that women with more advanced disease have greater depressive symptoms, again the research provides mixed results (Glanz & Lerman, 1992; Pinder et al., 1993; Stanton & Snider, 1993). However, the research appears to be more consistent in that type of surgery has little impact on level of depressive symptoms (e.g., Edgar et al., 1992; Lee et al., 1992), and that over time (time since diagnosis and/or treatment) depressive symptoms tend to remit (Edgar et al., 1992; Lee et al., 1992).

Interestingly, personality variables have also been examined in the context of cancer. The most commonly studied personality variable is neuroticism (defined as negative affectivity; e.g., Watson & Pennebaker, 1989). While neuroticism is questionable in terms of predicting cancer occurrence and progression (Amelang,
Schmidt-Rathjens, & Matthews, 19??; Dattore, Shontz, & Coyne, 1990), it appears that neuroticism is related to psychological outcomes. In fact, neuroticism has been described as a risk factor for psychological distress in the general population (Watson & Pennebaker, 1989). Positive associations between neuroticism and negative affective states (e.g., depressive symptoms) have been found in cancer populations (Jenkins, May, & Hughes, 1991; VanderZee, Buunk, & Sanderman, 1996). However, the research on neuroticism and cancer psychological outcomes has been lacking in empirical strength. There is the need to clarify what relationship neuroticism has with depressive symptoms in a cancer population.

Aim of the research

The present study tests the relative explanatory power of measures of objective stressors and subjective stress in predicting depressive symptoms in women who had recent surgical treatment for breast cancer. The predictive value of the above measures is examined while controlling for variables known to be associated with depressive symptomatology in women with breast cancer. Specifically, we controlled for the influence of sociodemographics, disease characteristics, and the personality variable, neuroticism.

Considering the prior research in the assessment of "stress", we predicted the following: First, subjective measures of stress are stronger predictors of depressive symptoms than objective measures. Second, globally measured stress is a stronger predictor of depressive symptoms than the stress associated with specific events (life event stress and cancer stress). Additionally, this study allows for the exploration of
specific types of objective stressors (e.g., financial difficulty, significant family conflict) that may be related to depressive symptoms in women with breast cancer.

Method

Participants

The study sample consisted of 166 women who ranged in age from 30 to 84 years ($M = 50.4; SD = 10.9$). Ninety percent of the women were White ($n = 150$) and 10% were minorities (African American, 9%, $n = 14$; Hispanic, 1%, $n = 2$). The majority of the women were living with a romantic partner (72%, $n = 119$). Education, measured by years of school attendance, was as follows: $<12$ years (2%, $n = 4$); 12 years (22%; $n = 37$); 13-15 years (29%, $n = 48$); 16 years (18%, $n = 30$); and $>16$ years (28%, $n = 47$). Annual family income included: $<$15,000 (9%, $n = 14$); $15,000-29,000$ (18%, $n = 28$); $30,000-49,000$ (22%, $n = 35$); $50,000-79,000$ (22%, $n = 35$); and $>80,000$ (28%, $n = 44$).

All women had regional disease, eighty-six percent ($n = 142$) had been diagnosed with Stage II breast cancer and the remaining 14% ($n = 24$) with Stage III disease (American Joint Committee on Cancer and the International Union Against Cancer staging systems). Regarding type of surgery, 39% ($n = 65$) of the women had had lumpectomies and 61% ($n = 101$) had had mastectomies (modified radical mastectomy, 57%, $n = 95$; radical mastectomy, 1%, $n = 1$; and elective bilateral mastectomy, 3%, $n = 5$). Days since surgery (DSS) were calculated as the number of days between surgery and assessment dates. The average participant was assessed 36 days following
surgery ($SD = 16.6$, range 5-101). Disease and surgery information were verified using information from the women's medical charts and surgical reports.

Procedures

Participants were women from a larger prospective, longitudinal study testing a biobehavioral model of cancer stress (Andersen, Kiecolt-Glaser, & Glaser, 1994) with women newly diagnosed and treated for breast cancer. The women were recruited into the larger study from mid-1994 to early 1998 using a variety of strategies including referrals of eligible women from physicians' offices as well as newspaper advertisements, press releases, and project flyers. Eighty-four percent ($n = 139$) were being treated at a National Cancer Institute-designated university-affiliated Comprehensive Cancer Center. The remaining 16 percent ($n = 27$) were receiving treatment at local community hospitals. At the time of assessment, all participants had been surgically treated (lumpectomy or mastectomy) within the preceding four months but had not yet begun adjuvant treatment (e.g., chemotherapy, radiation).

Psychological, behavioral, and medical information was collected through an extensive interview conducted at the University's General Clinical Research Center, or the Breast Cancer Center of the cancer hospital. All of the women were paid $20.00 for their participation.

Measures

The measures described below were part of the assessment battery used in the
larger longitudinal study.

Control variables

Nine variables that could account for significant variance in predicting depressive symptoms were tested. These included five sociodemographic variables: age, race (White or minority status), partner status (yes or no), years of education, and annual family income. Three disease variables were also examined: stage of disease (stage II or stage III), extent of surgery (lumpectomy or mastectomy), and the number of days since surgery.

The neuroticism factor from Goldberg's Big-Five Factor Structure (1992) was used. Items from this factor were extracted from a factor analysis with the present sample as suggested by Goldberg (personal communication, 1996). Essentially confirming the items as originally proposed, the factor included 16 trait adjectives, X positive (e.g., calm) and X negative (e.g., angry, emotional). Each woman rated the extent to which these trait adjectives described her, as compared to others of the same sex and age, on a nine-point Likert scale from “extremely inaccurate” to “extremely accurate.” Seven items are reverse scored. Total scores range from -63.0 to 81.0, with a mean 4.3 (SD = 17). Higher scores indicate stronger trait neuroticism. The coefficient alpha reliability for the present sample was .91.

Predictors

Objective stressors and associated perceived stress. An event scale was used, adapted from a similar measure in the Women's Health Initiative study (Matthews et al., 1997). Participants were asked to indicate if they had experienced any of five stressful
life events during the previous 12 months. See Table 2 for a listing of the life events assessed as well as the other type of stress measures used in the present study. If the event was endorsed as having occurred, the women were then asked to rate emotional upset for the event (3=very much, 2=moderately, or 1=not much). Total scores range from 0 to 15 with higher scores indicating more distress about the event/s. Three scales were calculated: presence versus absence of each event, the total number of events reported, and the sum of the distress ratings with a score of zero for participants who did not endorse any items.

**Subjective cancer stress.** The IES (Horowitz et al., 1979) is a standardized self-report measure used to examine cognitions involving the re-experiencing of a traumatic event (intrusion), and denial of thoughts related to the trauma and avoidant behaviors (avoidance; Miller, 1996). Fifteen items are used, seven for the intrusive subscale (e.g., "I had trouble falling or staying asleep because pictures or thoughts about cancer or having cancer treatment came into my mind") and eight items for the avoidant subscale (e.g., "I tried not to think about it"). Women rated each cancer-related event or feeling, experienced in the previous week, using a 4-point Likert scale (not at all, rarely, sometimes, and often) weighted 0, 1, 3, and 5. Three scores are obtained from the IES, a total score (IES-T) and intrusion (IES-I) and avoidance (IES-A) subscale scores. Total scores range from 0 to 75 with higher scores indicating increased severity of cancer-related stress. Similar to previous research, in the present study the word "event" was changed to "cancer." In the present sample the coefficient alpha reliability was .87, consistent with other studies reporting reliabilities of .78-.83.
(Cordova et al. 1995, Horowitz et al., 1979; Schwartz, Lerman, Miller, Daly, & Masny, 1995).

Global stress. The PSS (Cohen et al., 1983), a non-specific measure of perceived stress, is a standardized self-report questionnaire used to determine the extent to which a person judges the events in her life to be unpredictable, uncontrollable, and overloading (Cohen et al., 1983). Based on Cohen and Williamson's (1986) recommendation, the PSS-10 was used, a ten-item version of the PSS, due to its improved internal reliability and factor structure over other versions of the PSS (PSS-14 and PSS-4). Examples of the questions 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 each item in terms of the frequency of occurrence on a 5-point Likert scale (never, almost never, sometimes, fairly often, very often) in the past month. Total scores range from 0 - 40. Higher scores indicate greater overall stress. Coefficient alpha reliability for the PSS scales ranges from .75 to .86 (Cohen et al., 1983; Hewitt et al., 1992; Martin et al., 1995; & Pbert et al., 1992) and in the present sample was .86.

Outcome

Depressive symptoms. The short form (Kohout, Berkamn, Evans, & Cornoni-Huntley, 1993) of the Center for Epidemiological Studies Depression scale (CES-D; Comstrock & Helsing, 1976; Radloff, 1977) is a standardized self-report questionnaire used to identify current symptoms of depression, with emphasis on depressed affect. The CES-D short form consists of 11 items (e.g., "I felt everything I did was an effort"
and "I felt sad") rated on a 3-point Likert scale from "hardly ever or never" to "much or most of the time." Participants were asked to respond based on their feelings during the previous week. Total scores range from 0 to 22 with higher scores reflecting greater depressive symptoms. Unlike other measures of depressive symptoms (e.g., Beck Depression Inventory, Hamilton Rating Scale for Depression), the CES-D is relatively unaffected by physical symptoms and is, therefore, commonly used in research with medical patients (Devins et al., 1988). Consistent with other research, coefficient alpha reliability in the present sample was .74 (Himmelfarb & Murrell, 1983; Kohout et al., 1993).

Results

Preliminary Data

Correlations between control variables and depressive symptoms. Of the nine variables tested (age, race, partner status, education, income, stage of disease, type of surgery, DSS, and neuroticism), only two were significantly correlated with depressive symptoms, race ($r = -0.19$, $p < .01$) and neuroticism ($r = 0.38$, $p < .0001$). Thus, both being of minority status (African American or Hispanic) and having higher levels of neuroticism were related to higher CES-D scores. The average neuroticism score of the participants was 4.3 ($SD = 17$; range -32 to 46). Based on these results, only race and neuroticism were examined in the primary analyses.

Descriptive data. The median number of life events reported by the participants was one. The distribution of reported life events was as follows: no events (26%, $n = 44$); one event (42%, $n = 70$); two events (16%, $n = 26$); three events (11%, $n = 18$);
four events (4\%, n = 7); and five events (1\%, n = 1). The most-to-least frequently reported life events were 1) death or serious illness of close friend or relative (n = 79); 2) major financial difficulty (n = 45); 3) major conflict with children or grandchildren (n = 30); 4) divorce or breakup involving family members or close friends (n = 29); and 5) muggings, robberies, accidents, or similar events (n = 25). The median subjective stress associated with the life events was 3.0 (m = 4.4, sd = 2.9, range 1 -13). Thus, most participants reported experiencing at least one life event which they rated as 'very much' distressing.

The mean of the IES-T was 25.3 (SD = 14.2, range 0 - 65). While no published norms are available for the IES-T and its subscales, the mean in the present study is somewhat higher than those reported in other breast cancer samples (M = 16.4, Cordova et al., 1995; M = 11.5, Baider, Peretz, & De-Nour, 1992). These mean differences may be due to the retrospective design of the previous studies. Nonetheless, total scores above 19 are considered clinically significant in that feelings/behaviors are occurring at a problematic level for an individual (Horowitz, 1982). Avoidance and Intrusion subscale means were 12.3 (SD = 7.9, range 0-36) and 12.9 (SD = 8.4, range 0-35), respectively. Therefore, the average woman in the present study was experiencing a significant degree of stress associated with her recent breast cancer diagnosis and surgery.

The average PSS-10 score was 18.6 (SD = 6.8, range 1-36), a value higher than that reported by Cohen and Williamson (1986) for a national probability sample of adults (M = 13.02). Other mean comparisons are difficult since much of the research
has used the PSS-14 with mean scores of 19.62 for the national probability sample (Cohen and Williamson, 1986), 23.18 and 23.67 for two college samples and 25.0 for adults in a smoking cessation program (Cohen et al., 1983), 29.07 for adult psychiatric outpatients (Hewitt et al., 1992), and 33.80 for adolescent psychiatric inpatients (Martin et al., 1995).

Finally, CES-D scores ranged from 0 to 14 ($M = 6.1; SD = 3.5$). The CES-D was designed to identify depressive symptomatology in epidemiological studies of community populations and was not intended to be used for diagnostic purposes (Sheehan, Fifield, Reisine, & Tennen, 1995). However, a cut-off score of 16, based on the full scale CES-D (range 0 to 60), is widely accepted as indicating clinical depression (Comstock & Helsing, 1976; Kohout et al., 1993). There are no published norms or accepted cut-off scores suggestive of clinical depression for the IOWA version of the short form of the CES-D. Therefore, using the full scale cut-off as a guide, we consider 5.87 (i.e., $16/20 \times 22$) to be a reasonable cut-off score for the short form used in the present study. This would indicate that the average woman in the present study had depressive symptoms of clinical significance.

**Correlations among stress measures.** Correlations between objective stressors and subjective stress measures are presented in Table 3. Overall, the pattern of no-to-moderate correlations between differing measures indicated that they represent relatively separate stress constructs but also share some degree of covariation. This pattern is consistent with the findings of other research examining the correlations between objective stressors and subjective stress measures (e.g., Cohen et al., 1983;
Pbert et al., 1992). For instance, while there were many significant correlations among reported life events, number of events and the subjective stress associated with the life events (17 of 21 correlations were significant ranging from .13 to .91), there were no or weaker correlations between these variables and the IES-T and its subscales (6 of 21 correlations were significant ranging from .13 to .19). Thus, these measures appear to be assessing differing aspects of stress: life event stress and cancer stress. Additionally, the correlation between the IES subscales (r = .54) was consistent with previous research reporting correlations of .51 (Epping-Jordan, Compas, & Howell, 1994) and .68 (Cordova et al., 1995). The above correlations suggest that while the subscales are related they also are measuring different aspects of cancer-related stress, avoidance and intrusive thoughts.

In addition, the PSS-10 was significantly correlated with virtually all other stress measures (8 of 10 correlations were significant ranging from .14 to .51). This suggests that globally perceived stress is a product of objective stressors, life event stress and cancer stress. Further, as expected, the magnitude of the correlations among subjective stress measures was greater than those with objective stressors.

Correlations between stress measures and depressive symptoms. Correlations among objective stressors, subjective stress measures and depressive symptoms are presented in Table 4. Of the objective measures, major financial difficulty, major conflict with grand/children, and total number of life events were significantly correlated with CES-D scores (p < .05). Additionally, all of the subjective measures (life event stress, IES-T and its subscales, and PSS-10) were significantly correlated with CES-D
scores ($p < .01$). The fact that the CES-D is based on subjective self-ratings likely accounts for the larger correlations between the subjective stress measures and depressive symptoms. Only those variables significantly correlated with CES-D scores were used in the primary analyses. However, the high correlation between number of life events and life event stress ($r = .91$) suggests that these variables are measuring the same construct. Therefore, to avoid multicollinearity, only life event stress was included in the primary analyses.

Primary Analyses

**Stress measures as predictors of depressive symptoms.** Hierarchical regression analyses were used to examine the relative power of objective stressors, specific stress measures, and global stress measures in predicting depressive symptoms after controlling for the effects of race and neuroticism. Two regression analyses were conducted, one using the IES-T and the second using the subscales, IES-A and IES-I. The second regression was conducted to test the relative contribution of avoidance and intrusive thoughts related to cancer in explaining CES-D scores. Variables were entered into the regressions based on both theoretical considerations and the pattern of correlations found between the stress measures and depressive symptoms. The order of entry was as follows: race, neuroticism, major conflict with children or grandchildren, major financial difficulty, life event stress, IES, and PSS-10. Table 5 provides the results of the hierarchical regression analyses. For each step, the increment of variance accounted for is reported along with the final beta coefficients representing the unique effect of each predictor. Major conflict with children or
grandchildren and life event stress were not significant predictors of depressive symptoms and were not included in the final model.

At Step 1 in the first regression (testing IES-T scores), race was entered into the analysis and accounted for significant variance in depressive symptoms (final model $F(1, 164) = 5.89, p < .01$). Approximately four percent percent of the total variance in depressive symptoms could be attributed to being of minority status. In Step 2, neuroticism was entered into the equation, producing a significant increment (14%) in the variance accounted for in depressive symptoms, (final model $F(2, 163) = 17.46, p < .0001$). In Step 3, major financial difficulty was entered, producing a relatively small, but statistically significant increment (2%) in predicting depressive symptoms, (final model $F(3, 162) = 13.10, p < .0001$). In Step 4, the IES-T was entered and produced an additional significant increment (22%; final model, $F(4, 161) = 28.23, p < .0001$). Increased cancer-related stress was predictive of greater depressive symptoms. At Step 5, globally perceived stress was added, contributing a significant increment (10%) of prediction for depressive symptoms, (final model $F(5, 160) = 33.83, p < .0001$). Thus, the higher the global stress the higher the level of depressive symptoms. Interestingly, neuroticism was a significant predictor of depressive symptoms until globally perceived stress was entered. This indicates that globally perceived stress mediates the function of neuroticism.

In the second regression (testing IES-A and IES-I) the first three steps were identical to those of the first regression. At Step 4, IES-A was entered and accounted for a significant increment (10%) of variance in depressive symptoms, (final model $F(4,$
With the entry of IES-I in Step 5, IES-A was no longer significant. The IES-I added another significant 13% increment in depressive symptoms and remained a significant increment in the final model, $F(5, 160) = 24.37, p < .0001$). Thus, intrusive thoughts related to breast cancer were more strongly predictive of depressive symptoms than was avoidance. In Step 6, PSS was entered and added a significant increment (9%) of variance in depressive symptoms, (final model, $F(6, 159) = 28.81, p < .0001$).
Table 1

Types of Stress Measures

<table>
<thead>
<tr>
<th>Objective (Stressors)</th>
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<tbody>
<tr>
<td>- Type of Life Event (e.g., financial loss, bereavement, job loss)</td>
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<tr>
<td>- Total Number of Life Events</td>
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<table>
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<tr>
<th>Subjective (Perceived Stress)</th>
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<tbody>
<tr>
<td>- Specific (stress associated with identified event)</td>
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<tr>
<td>- Global (stress associated with life in general)</td>
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Table 2

**Stress Measures**

**Objective (Stressors)**

- Type of Life Events
  1) Death or serious illness of a close friend or relative
  2) Major financial difficulty
  3) Divorce or breakup involving family members or close friends
  4) Major conflict with children or grandchildren
  5) Muggings, robberies, accidents, or similar events

- Total Number of Life Events

**Subjective (Perceived Stress)**

- Specific
  1) Life Event Stress (Stress associated with life events)
  2) Cancer Stress (Impact of Events Scale-IES)

- Global
  1) Perceived Stress Scale (PSS-10)
Table 3. Pearson bivariate correlations among the objective stressors and the subjective stress measures.

<table>
<thead>
<tr>
<th>Measure</th>
<th>1</th>
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<td>1. Death</td>
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<td>2. Finances</td>
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<tr>
<td>3. Conflict w/kids</td>
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<td>.21**</td>
<td>1.00</td>
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<td>.13*</td>
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**** p < .0001; *** p < .001; ** p < .01; * p < .05.
Table 4

Correlations among Objective Stressors, Subjective Stress, and Depressive Symptoms

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<tr>
<th>CES-D</th>
<th>Stress Measure</th>
<th>r</th>
<th>p</th>
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Table 5

Results of Hierarchical Regression Analyses for Predicting Depressive Symptoms

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<th>Variable</th>
<th>( R^2 )</th>
<th>F</th>
<th>beta</th>
<th>t</th>
<th>( R^2 ) total</th>
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Note. \( N = 166 \).

* \( p < .05 \).  ** \( p < .025 \).  *** \( p < .0001 \).
MEMORANDUM FOR Administrator, Defense Technical Information Center (DTIC-OCA), 8725 John J. Kingman Road, Fort Belvoir, VA 22060-6218

SUBJECT: Request Change in Distribution Statement

1. The U.S. Army Medical Research and Materiel Command has reexamined the need for the limitation assigned to technical reports. Request the limited distribution statement for reports on the enclosed list be changed to "Approved for public release; distribution unlimited." These reports should be released to the National Technical Information Service.

2. Point of contact for this request is Ms. Judy Pawlus at DSN 343-7322 or by e-mail at judy.pawlus@det.amedd.army.mil.

FOR THE COMMANDER:

PHYLLIS M. KINEHART
Deputy Chief of Staff for Information Management