Biobehavioral Intervention for Cancer Stress: Conceptualization, Components, and Intervention Strategies

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Trials testing the efficacy of psychological interventions for cancer patients had their beginnings in the 1970s. Since then, hundreds of trials have found interventions to be generally efficacious. In this article, we describe an intervention grounded in a conceptual model that includes psychological, behavioral, and biological components. It is from this biobehavioral view that an intervention was developed and tested among newly diagnosed cancer patients. It was found efficacious for biobehavioral outcomes, health, and disease endpoints. Here we provide investigators and clinicians with an elaborated description of the components and strategies to aid in replication and dissemination.

In 1994 we offered a conceptualization for understanding the relationship between the stress of cancer diagnosis and treatment and subsequent disease progression. A randomized clinical trial (RCT), called the Stress and Immunity Breast Cancer Project (SIBCP), was designed to test the hypothesis that patients receiving a psychological intervention designed to target stress and relevant behaviors would show improved survival compared to patients who received usual care. Consecutive cases of patients (N=227) newly diagnosed with regional (Stage II or II) breast cancer were accrued from a National Cancer Institute comprehensive cancer hospital. All had received surgical treatment and were accrued prior to beginning adjuvant therapy (radiation and/or chemotherapy) and randomized to intervention-plus-assessment or assessment-only study arms. The endpoints were reduction in risk for recurrence and breast cancer death. Previously reported, the intervention produced significant gains across secondary outcomes [distress, social adjustment, health behaviors (diet, smoking cessation), treatment adherence, health] and also enhanced T cell immunity (Andersen, Farrar et al., 2007; Andersen et al., 2004). After a mean of 11 years of follow-up, intervention patients had a reduced risk of disease progression, i.e., breast cancer recurrence [Hazard Ratio (HR)=0.55, P=.034] and death from breast cancer (HR=0.44, P=.016; Andersen et al., 2008).

To facilitate understanding, replication, and dissemination, we provide intervention detail. We begin with an overview of the conceptual model as originally described (Andersen, Kiecolt-Glaser, & Glaser, 1994) and subsequently empirically supported. This introduction outlines the constructs that informed the development of the intervention and specification of the intervention targets and outcomes.

Biobehavioral Model of Cancer Stress and Disease Course

Psychological Pathways

Our conceptualization begins, not surprisingly, with the view that severe, acute stress occurs at the time of cancer diagnosis (see Figure 1). The acute distress accompanying diagnosis can, in turn, contribute to a stable, lower quality of life for cancer patients, and trial data supported this hypothesis (Golden-Kreutz & Andersen, 2004; Golden-Kreutz et al., 2005). Moreover, patients who cope poorly at the time of diagnosis report lower meaning in life in the year following the end of cancer treatments (Jim et al., 2006).

After the initial shock, patients anxiously anticipate the beginning of difficult cancer therapies; for the majority, treatment is multimodal. Many studies have focused on

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alleviating the fears surrounding chemotherapy, including conditioned reactions (e.g., anticipatory nausea and vomiting; Redd, Montgomery, & DuHamel, 2001). Emotional distress may linger longer after treatment has ended. For example, midway through our trial taxane chemotherapies were introduced and added onto standard regimens (e.g., Adriamycin plus Cytoxan). As others had found (Fountzilas et al., 2005), patients receiving taxanes experienced significantly higher rates of selected toxicities, including arthralgia/myalgia (45% vs. 26%) and ataxia (20% vs. 5%). However, unexpected was the finding that those receiving the taxanes had significantly worse emotional distress and quality of life throughout treatment. Emotional recovery for taxane patients required 2 years, on average, versus 6 to 12 months for nontaxane patients. Thus, cancer treatments can confer risk for psychological distress of long duration (Thornton et al., 2008).

There are many other examples of psychological and behavioral changes in the months following diagnosis and into the early survivorship years. Cancer treatments have the potential to impact intimate relationships, as we (Yurek, Farrar, & Andersen, 2000) and others (Kornblith & Ligibel, 2003) have found. Cancer can bring financial strain (Arndt et al., 2004). Treatment or recovery can disrupt one’s employment, including job loss for some (Bradley et al., 2005). One fifth of cancer survivors report these difficulties (Hewitt, Breen, & Devesa, 1999). Residual poor mental health may also contribute to job strain, as we found that continuing cancer-specific stress covaried with employment absenteeism for a subset of patients from the trial who were subsequently found to have diagnosed or subsyndromal posttraumatic stress disorder (PTSD; Shelby et al., 2008).

**Biological Pathways**

Stress triggers important biological effects involving the autonomic, endocrine, and immune systems. Stress may be routed to the immune system by the central nervous system (CNS) via activation of the sympathetic nervous system or through neuroendocrine-immune pathways (i.e., the release of steroid hormones, glucocorticoids). Stress-related changes in neuroendocrine function have been documented in studies of the hypothalamic-pituitary-adrenal (HPA) axis. Cancer patients may exhibit dysregulation of the HPA axis similar to that observed in depressed patients without cancer (i.e., hypersecretion of ACTH and cortisol, adrenal and pituitary hypertrophy; Lundstrom & Furst, 2003; Raison & Miller, 2001) or show blunted ACTH and cortisol diurnal variation in response to acute stress (Bower, Ganz, & Aziz, 2005; Giese-Davis et al., 2004; Mazzoccoli et al., 2005). Also, hormones released under stress (e.g., catecholamines, cortisol, prolactin, and growth hormone) have been implicated in immune modulation (Bergmann & Sautner, 2002; Rontgen et al., 2004). Lymphocytes, monocytes/macrophages, and granulocytes possess receptors for neurotransmitters that are capable of immune regulation (Engler et al., 2004; Kohm & Sanders, 2001).

Data on psychological variables and immunity in cancer patients are accumulating. Correlational data have shown relationships between heightened distress, broadly defined [e.g., depressive symptoms (Sachs et al., 1995), low social support (Lutgendorf et al., 2000; Turner-Cobb et al., 2000)], and down regulated immunity. Data from this trial (Andersen et al., 1998) showed a robust relationship between patients’ stress and lower NK cell lysis and T-cell proliferative responses, replicated in multiple assays, as patients entered the trial. Longitudinal data showed that NK and T cells are sensitive to different aspects of the stress response. Specifically, T cell blastogenesis covaries with patients’ initial (peak) subjective stress, but NK cell lysis correlates with change (reduction) in stress across time (Thornton et al., 2007). Finally, the trial data showed

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**Figure 1.** The biobehavioral model of cancer stress and disease course (adapted from Figure 1 in Andersen, B.L., Kiecolt-Glaser, J.K., and Gaser, R. (1994). A biobehavioral model of cancer stress and disease course. *American Psychologist, 49,* 389-404). Used with permission.
that the intervention was associated with differential improvements in T cell blastogenesis for the intervention arm in comparison to declining levels for the assessment arm (Andersen, Farrar et al., 2007; Andersen et al., 2004).

Behavioral Pathways

There are important behavioral sequelae to stress (see Figure 1). Negative health behaviors may increase in frequency (Ng & Jeffery, 2003). Those anxious may use alcohol or drugs to self-medicate (Bing et al., 2001; Goeders, 2004; Johnstone, Garrity, & Strauss, 1997). Cigarette smoking and caffeine intake can increase during periods of stress (Ng & Jeffery, 2003). Distressed individuals can have appetite disturbances and/or dietary changes (Wardle et al., 2000). The taste of foods may change with stress (Bergdahl & Bergdahl, 2002). Disturbances of taste or eating habits (e.g., food restriction or taste aversions from chemotherapy) can occur (Ravasco et al., 2004). Disturbed sleep can occur (Steptoe, O'Donnell, Marmot, & Wardle, 2008).

The model suggests that health behaviors, in turn, may affect immunity. In general, negative health behaviors have an adverse, down-regulating effect on immunity, and some appear to increase stress hormones (e.g., cortisol) as well. Alcohol usage appears to blunt immune responses, e.g., impair natural killer (NK) cell and interleukin-2 (IL-2) activity (Diaz et al., 2002; Frank, Witte, Schrodli, & Schutt, 2004). Cigarette smoking is associated with NK cell suppression and production of pro- vs. anti-inflammatory cytokines (Zeidel et al., 2002). The release of corticotrophin-releasing hormone (CRH), a main component of the stress system, may suppress appetite (Tsigos & Chrousos, 2002). Insomnia is associated with nocturnal sympathetic arousal (i.e., increases in circulating norepinephrine) and declines in NK cell lysis (Savard et al., 2003). Difficulties may be compounded with multiple negative health behaviors. For example, depression and cigarette smoking are synergistic, and yield lower levels of NK cell lysis than either one alone (Jung & Irwin, 1999). In summary, studies indicate several linkages between negative health behaviors and elevations in stress-related hormones and/or lowered immune responses.

Alternatively, if negative health behaviors can be reduced and/or positive health behaviors increased, important sympathetic and adrenocortical changes and/or immunity changes may occur. Smoking abstinence, even for a day, has been found to reduce cortisol levels (Steptoe & Ussher, 2006) and increase NK cell cytotoxicity (Meliska et al., 1995). Nutritional improvements can enhance immune responses and reduce rates of infection (Galban et al., 2000). Physical activity (exercise) may have positive consequences for immune (Fairey et al., 2005) and endocrine systems (Mastorakos & Pavlatou, 2005; Na et al., 2000).

The second behavioral factor is treatment compliance (adherence). In general, depression is a risk factor for noncompliance with medical treatment (DiMatteo, Lepper, & Croghan, 2000). In cancer, emotional distress (McDonough et al., 1996) has been associated with low rates of continuing (Ayers et al., 1994) and completing chemotherapy (Levin, Mermelstein, & Rigberg, 1999). The base rate of dropout is generally low (e.g., <5-10%), except for maintenance therapies. Lengthy tamoxifen treatment trials (e.g., 5 years duration) have had discontinuation rates among breast cancer patients ranging from 23% to 40% (Fisher et al., 1998; Fisher et al., 1996; Powles et al., 1998). Unfortunately, compliance has been understudied in cancer, despite its importance.

Summary

The biobehavioral model is a useful heuristic for understanding the interaction of psychological, behavioral, and biologic factors relevant to the progression of cancer. Data support the importance of the variables identified in the model and their predicted relationships. Indeed, the cancer stressor brings a negative, biobehavioral cascade, but when the stressor is reduced via an intervention, biobehavioral responses improve.

Overview of the Biobehavioral Intervention (BBI) Format

The intervention was provided in groups (8 to 12 patients) led by two clinical psychologists. Therapists followed a session-by-session manual and patients received a companion treatment handbook. Sessions were 1.5 hours, with an intensive phase of 18 weekly sessions during the first 4 months and then a maintenance phase of 8 monthly sessions, for a total of 26 sessions (39 therapy hours) over 12 months. This number of sessions was the same as that for some survival trials (23 sessions; Kissane et al., 2007; Kissane et al., 2004), half that of others (Goodwin, Leszcz, & Ennis, 2001; Spiegel et al., 2007) and longer than one (Boesen et al., 2007).

SIBCP significantly departed from other trials in the spacing of sessions. We reasoned that the maintenance of gains would be critical to achieve any survival effect. The established efficacy of psychosocial interventions for cancer patients comes primarily from analyses of post-treatment outcomes. There are few data on the durability of treatment effects and, to our knowledge, no discussions of ways to maintain treatment gains. This circumstance is not unique. Karoly and Anderson (2000) reviewed the psychotherapy literature and found that less than 10% of the papers addressed maintenance and/or relapse.
prevention. Longer-lasting effects can be achieved by simply offering more treatment, as has been shown in psychotherapy studies (Hansen, Lamber, & Forman, 2002). This is also the case in cancer. Rehse and Pukrop’s (2003) meta-analysis discovered that the number of sessions was the most important moderator of outcome, more powerful than characteristics of the patients or intervention methods used. Thus, we increased the number of sessions beyond the typical 8 to 10, but more importantly, extended the intervention period across months. Our study of the mechanisms of the intervention effectiveness found that, indeed, gains achieved during the intensive phase were at least maintained, if not increased, during maintenance (Andersen, Shelby, et al., 2002). This is also the case in cancer. Rehse and Pukrop’s (2003) meta-analysis discovered that the number of sessions was the most important moderator of outcome, more powerful than characteristics of the patients or intervention methods used. Thus, we increased the number of sessions beyond the typical 8 to 10, but more importantly, extended the intervention period across months. Our study of the mechanisms of the intervention effectiveness found that, indeed, gains achieved during the intensive phase were at least maintained, if not increased, during maintenance (Andersen, Shelby, et al., 2002). This was particularly true for reductions in symptoms and signs of illness. Continued use of relaxation training, communicating assertively to health care providers (oncologists), and exercising more were important for continued improvements in health.

Procedures to Maximize Adherence

Treatment dropout was of particular concern as high dropout or low attendance would threaten the validity of the test of the survival hypothesis. We anticipated high rates of fatigue and other symptomatology from ongoing adjuvant cancer therapies. Also, some patients might have fragile health from other chronic illnesses or aging (20% of the sample was over 60). For reasons such as these a procedure was devised to reduce the likelihood of dropout, reduce attendance variability among patients who remained, and achieve the prescribed treatment dose for all. Secondarily, we also wanted to eliminate (or at least minimize) disruption in the groups due to absenteeism.

The first group session provided an orientation to the intervention, and patients were asked to notify the therapist in advance if they were to be absent. Patients were also told that, with their permission, the group members would be informed about the reason for their absence to reduce worries/concerns about the missing participant. Within 3 days of any absence, the lead therapist conducted a telephone session with the absent participant. The therapist discussed the week’s topic, assigned any homework, and provided an update on the group members; handouts were mailed or faxed to the participant. This effort was also facilitated by the patient having a treatment handbook.

This was a successful procedure. Patients appreciated the personal attention, expression of concern, and opportunity to stay connected. When the participant returned to the group, no “catch up” was necessary. There were no differences between cohorts in attendance, there was high intervention arm retention (93%), and patients received an average of 92% of the intervention sessions. Patients also reported very high satisfaction with the telephone sessions.

Post hoc analyses suggest that therapy attendance (treatment dose) was important for a further lowering of risk of disease progression (Andersen et al., 2008). The survival analyses were intent to treat and thus conducted with all participants (N=227). However, clinical trial analysts may commonly exclude patients who received little or none of the treatment being studied, with the perspective that a more accurate view of the specific efficacy of the treatment is then provided. Excluding 16 of 114 (14%) of the intervention arm patients who attended less than 20% of the intervention sessions (i.e., 5 or fewer of 26 sessions), the data were reanalyzed using an N of 211. Using the same analytic procedures, the results were replicated. For comparison, however, the follow-up analyses showed a 68% reduced risk of breast cancer death for patients in the intervention arm when the low attendance patients were removed, and a 56% risk reduction when they were not (i.e., intent-to-treat analyses).

BBI Components and Strategies: Intensive Phase

As specified by the model, the intervention was designed to reduce stress, enhance quality of life (operationalized as emotional adjustment, social adjustment and support, and breast-specific concerns), increase positive health behaviors, decrease negative health behaviors, and improve compliance. With these as targets, therapy components were designed anew or selected from previously published, effective treatments for anxiety reduction or symptom management. Table 1 summarizes the intervention targets, treatment components and strategies, and their sequencing. See Andersen et al. (2004) for the relevant outcomes for each intervention component.

Following the first session, intensive sessions had a similar, structured sequence of events. The group environment was, by design, informal, welcoming, and supportive. The group therapy room was simply furnished with recliner chairs. The room was open 30 minutes prior to the sessions so that patients could meet, greet one another, and chat; coffee, juice, and snacks (e.g., crackers) were available. With the therapist’s arrival the reason (if known) for any member’s absence was noted. Relaxation training was done, providing a starting point for individuals to unwind from the hurried of the day and come together as a group. Afterwards, patients were asked to open their notebooks to the day’s topic and the lead therapist (D.M.G-K.) usually began a content-laden introduction. During and following this, group discussion was prompted with the therapists’ comments, redirections, or summaries as appropriate and any in-session
<table>
<thead>
<tr>
<th>Intervention Target</th>
<th>Intervention Component</th>
<th>Session Number</th>
<th>Utilization Measure*</th>
<th>Minimum Recommended Usage</th>
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| Stress              | • Conceptual model: Relationship of stress and immunity; Understanding stress and responses to it.  
• Problem solving.                                                                                                                                             | 1, 19          | Using info. on stressors to modify behaviors                                         | As needed                                                                                 |
|                     | 10-12, 20-21                                                                                     |                | Problem solving                                                                      |                                                                                           |
|                     |                                                                                                  | 20-21          |                                                                                       |                                                                                           |
| Quality of Life:    |                                                                                                  |                |                                                                                       |                                                                                           |
| Emotional distress  |                                                                                                  |                |                                                                                       |                                                                                           |
| Social adjustment   | • Relaxation training. Also: Problem solving, positive coping.                                                                                                 | 1-26           | Relaxation training                                                                   | 1/day for 20 min. ea.                                                                      |
|                     | • Social support: Identify social network, support needs, and contacts.                           | 4-9, 21, 22, 23| Identification and selection of support resources                                     |                                                                                           |
|                     | • Assertive communication skills training.                                                       | 5-7, 22        | Assertive communication                                                              |                                                                                           |
| Compliance          | • Assertive communication skills with physician. Also: Disease/treatment information, planning appointments, goal setting.                                     | 2-3, 5, 10-12, 20| Med. provider communication                                                          | 1) Identify 1 question prior to next MD visit and get it answered.                      |
|                     | 26                                                                                               |                | Relaxation training                                                                   | 2) Adhere to cancer treatment regimen.                                                    |
|                     |                                                                                                  |                | Exercise                                                                             | 3) Keep all appointments (appear on specified day/time).                                 |
| Health Behaviors    |                                                                                                  |                |                                                                                       |                                                                                           |
| Diet                | • Strategies for low fat/high fiber food consumption. Also: Food intake diary (2 x 3 days), energy balance information.                                         | 14-16, 24      | Eating less fat, eating more fiber                                                   | 1) Reduce daily fat intake to a maintenance level of 47 grams.                          |
|                     |                                                                                                  |                |                                                                                       | 2) Eat a maintenance level of 20-35 grams of fiber per day.                             |
| Exercise            | • Walking protocol and strategies to increase daily activity level.                              | 13, 25         | Use of strategies for increasing activity                                             | 3) Walk briskly (or equivalent) to 70-85% of maximal heart rate, 3/week for 20 min. ea.|
|                     | • Negative health behaviors.                                                                    | 14, 17         |                                                                                       | 4) Increase x (specific behavior) by y (identify method).                               |
| Physical functioning | • Strategies for symptom management (e.g., nausea, fatigue, hot flashes, disturbed sleep) and increasing daily activity level.                              | 1-26           | Relaxation training                                                                   | 1) Relaxation as recommended.                                                          |
|                     |                                                                                                  |                | Medical provider communication                                                        | 2) Increase activity level as recommended.                                               |

* See Andersen, Shelby, & Golden-Kreutz, 2007 for additional detail.
activities were accomplished. Sessions closed with assignments (if any) and good-byes, with therapists and patients often lingering to chat.

Stress Reduction and Enhancing Quality of Life (Emotional Adjustment; Sessions 1-26)

There were three components. The first group meeting provided to patients an explanation of Selye's General Adaptation Syndrome (Selye, 1956), a conceptual model for understanding their stress responses and adaptation to cancer. Cancer stressors (e.g., diagnosis, surgery, selection of adjuvant therapies) were discussed. We noted that people did not have unlimited reserves for coping with repeated stressful events: without resources, a state of physical exhaustion would result. Thus, the goal was to offer adaptive coping strategies that could be learned and applied generically to stressors. Then, using a list we helped each patient to identify her own warning signs of stress: emotional (e.g., low mood, irritability), behavioral (e.g., low energy/fatigue, memory difficulties), and body signs (e.g., pounding heart, abnormal breathing, headaches). Then, the A (Activity/Event)—B (Beliefs/Automatic thoughts)—C (Consequences/Feelings and Behaviors) model was offered to explain common responses to cancer stressors.

Secondly, progressive muscle relaxation (PMR) training (Bernstein & Borkovec, 1973) was presented as a primary strategy for coping with cancer stressors, lowering tension on a daily basis, reducing the wear and tear on the body from stress, and for reducing or controlling cancer therapy symptoms (e.g., nausea, fatigue; Sessions 1-26). Instruction began in the first session with a 45-minute, 16-muscle-group procedure. Patients were provided with cassette tapes for home use and urged to practice at least times per week, 20 minutes each. Thereafter, each session began with PMR. Across sessions, PMR was modified as proscribed (Bernstein & Borkovec, 1973) through to Session 18. By then, patients could become deeply relaxed when using a 2-minute, relaxation-by-recall procedure.

Third, problem-solving training (Sessions 10–12), following the principles of Goldfried and Davison (1976) and Hawton and Kirk (1989), consisted of the following stages: overview, defining and formulating target problems, generating solutions, making decisions, implementing solutions, and verifying selected solutions. To learn the principles, the group members worked collaboratively on solutions for two common problems: fatigue and time management. To enhance generalization, patients targeted one or two other areas for problem-solving as homework.

Considering these three procedures, follow-up analyses (Andersen, Shelby, et al., 2007) indicated that more frequent use of PMR was associated with the lowering of emotional distress, more so than the other strategies. Also, the combination of the conceptualization for understanding daily stressors and relaxation was associated with improved health (i.e., reduction in symptoms, signs, and cancer treatment toxicities).

Improving Quality of Life (Social Adjustment; Sessions 4-7, 21, 22)

For some interventions, social support among group members is a central element of treatment (Spiegel et al., 1989). The SIBCP intervention was not conceptualized as a “support group,” per se. However, we learned that as patients share their reactions to the cancer crisis, their problem-solving and adaptive coping is fostered. For example, the first SIBCP strategy aimed at improving social adjustment was prompting patients to accept the spontaneous offers of help from friends and family. The majority of patients were extremely reluctant to do so, but they were encouraged by other group members who had accepted assistance and found it beneficial. There are other examples that could be cited, but what is important to note is that patients’ feelings of involvement in the group and receiving support from the group (i.e., cohesion) were important for treatment outcome. Specifically, patients reporting greater cohesion from the intensive, weekly sessions also achieved greater improvement (e.g., lower distress) and higher functional performance during the maintenance phase (Andersen, Shelby, et al., 2007).

Three strategies for achieving improved social adjustment were used. First, assertive communication skills, modeled after the work of Jakubowski and Lange (1978), assisted women in expressing their thoughts, feelings, and needs to facilitate support from friends and family. The same procedures were used to enhance patients’ communication with health care providers and get their medical needs met. Four techniques were taught: specificity and clarity of one’s message; direct communication; “owning” one’s message (e.g., use of “I” and “my” in statements); and asking for feedback. Skills were practiced across the social relationship categories identified below.

Second, we helped patients identify their social network: individuals with whom they had regular contact, either in person, by telephone, or through letters/email, as well as those with whom they felt extremely close but did not have regular contact. We encouraged patients to identify at least 10 individuals. Next, patients used a simple diagram to identify how close they felt to each person and then evaluated each individual’s capability for providing emotional support, task support (e.g., helping with household tasks, child care, etc.), both, or neither to the patient. Patients then made a listing of their current needs for emotional or task support and tried to “match” their needs to capable members of their network. This exercise led patients to (a) appreciate that they were not alone and (b) be
realistic (and strategic) about who could (or could not) meet their specific needs. We reasoned that with an objective appraisal, patients would be more successful in receiving the type and amount of support when it was needed. Following the introduction of this strategy, patients were to make one request of emotional support and one request for task support per week.

Third, during consecutive sessions, three levels of social relationships (i.e., coworkers, friends, and physicians; family members and children of all ages; and spouse/spouse equivalent) were examined. Therapists provided didactic information regarding common psychosocial reactions of these individuals to a person with cancer. Patients discussed the joys and disappointments in the responses of these individuals to their diagnosis, identifying sources of satisfaction and areas of difficulty. As described above, patients identified target individuals for assertive communication and/or requests for specific support.

Improving Quality of Life (Breast Specific; Sessions 8-9, 23)

This session followed that on social support from the partner. The sequelae of breast cancer [e.g., body changes, menopausal changes, symptoms with hormonal therapy (e.g., vaginal discharge), hair loss with chemotherapy] and impact on sexual self-schema (esteem) were discussed. Information on normal sexual responding and the role of hormonal responses in female sexuality was provided. Coping with body and sexual changes as discussed in Andersen and Elliot (1993) was also included. Educational materials were provided [e.g., American Cancer Society (ACS) publication on sexuality and cancer] and strategies for coping with loss of sexual desire, a common problem, were emphasized, as was initiating communication with the partner about sexuality. If intercourse (or an equivalent) activity was currently not possible, difficult, or not desired (loss of desire is common during cancer treatment), we emphasized maintaining emotional intimacy (or other forms of physical intimacy) with the partner. Oftentimes couples refrain from holding, touching, etc., when intercourse is not occurring.

Compliance (Sessions 2-3, 5, 10-12, 20)

The few available data suggested that information about the disease and treatment and enlistment of help of significant others (i.e., social support; Richardson et al., 1987) would be important strategies. Three were used. First, disease and treatment information was offered (and patients were urged to seek information as homework if they wished) to reduce uncertainty, aid in medical decision-making, and enhance compliance. Educational materials were developed for incorporation into intervention sessions and/or patients’ independent use. Today, similar materials are readily available from the National Cancer Institute or the ACS. Secondly, patients were encouraged to use relaxation and distraction to reduce anxiety and cope prior to and during radiotherapy and/or chemotherapy treatments and to control symptomatology afterwards (Redd et al., 2001). These strategies were also recommended to cope with anxieties with follow-up oncology appointments. Third, assertive communication (see description above) was recommended to enable patients’ direct communication with their health care professions. Patients were also taught to prepare for appointments (e.g., write down questions), use aids for remembering physician recommendations (e.g., note taking, tape recording), and reminded that they were entitled to adequate time with their providers. Fourth, the problem-solving component for managing fatigue (see above) was very important as fatigue was moderate to severe through the first 4 to 6 months of the intervention for all patients as they received radiation and/or chemotherapy. While it improved thereafter, fatigue did not fully resolve until 18 to 24 months (Thornton et al., 2008) following diagnosis.

Health Behaviors (Sessions 13-17, 24, 25)

Increasing activity level. Exercise provides positive health benefits (Courneya, 2003), mood improvements (Valenti et al., 2008), and symptom reduction (Winningham, 2001). In Session 13, patients completed a questionnaire (British Columbia Department of Health, 1975) to gauge their readiness for exercise. Patients were taught how to monitor their heart rate and determine an estimated training heart rate range. They were then encouraged to increase their daily activity level, aiming for at least 20 minutes of walking, three times per week, according to the Winningham protocol (Winningham, 2001). (Patients with pre-cancer exercise routines were encouraged to resume their preferred activity on the same schedule.) Didactic information included how to set realistic activity goals, schedule activity and rest cycles, increase energy expenditure during activities of daily living, and cope with exercise frequency setbacks. Women unable to perform the walking protocol due to treatment complications were provided with alternative activity/rest goals.

Patients were also provided ACS information on exercises for arm mobility, exercises were practiced in session, and patients were urged to incorporate them into their activity regimen. (Note: In conducting health behavior change interventions, it is important that physicians provide medical clearance for patients. Also, medical consultation should be readily available for any concerns regarding health behavior interventions or the participation of patients in them.)
**Diet.** The dietary component was preceded by patients completing two 24-hour food diaries (unannounced) during Sessions 11 and 13. These were analyzed and summarized by a dietician in Session 14. This provided individualized information on fat and fiber intake to each patient. It was used to illustrate the ease of avoiding (e.g., processed meats, fast foods) or substituting foods (e.g., skim for whole milk) to significantly reduce fat intake. Also, the dietician emphasized the importance of protein intake to increase energy and aid in recovery from surgery and the adjuvant therapies. The intervention target was to lower fat intake from the American norm of 60 grams/day to 40 and increase fiber, fruit, and vegetable consumption to the ACS-recommended 5 to 9 servings per day (Subar et al., 1992).

In conjunction with the dietary intervention, therapists helped patients identify their emotional, behavioral, or situational cues for eating (e.g., “I often find myself eating when…”). From this a patient distinguished if she needed to change the cue (e.g., watch less TV), change the behavior (e.g., eat healthy snacks rather than cookies), or plan ahead (e.g., buy healthy snacks rather than chips) for healthier choices. Effective procedures from weight management programs (e.g., controlling portion size, only eating at the kitchen table) were also reviewed and a copy of the ACS Eating Healthy cookbook was provided. Finally, during the course of the intervention we had provided juice and inexpensive, low-fat snacks during the sessions to introduce patients to alternatives to high-fat snacking. In summary, the guiding conceptualization of the dietary component was that of health behavior change rather than dieting. (Note: Patients with significant weight loss, a low albumin, or other indicators of compromised nutritional status were monitored to ensure that the dietary intervention was complimentary to any other needed dietary care.)

**Negative health behaviors.** Only limited, focused efforts could be used to help patients change negative or problematic health behaviors (e.g., Manley et al., 1991). Disturbed sleep patterns were addressed with information on sleep hygiene (Savard et al., 1999), recommendations for activity programming (exercise) during the day, and relaxation was recommended for difficulty falling or staying asleep. Regarding smoking, all patients were queried as to their smoking status in Session 14. Usually smokers will acknowledge a desire to reduce, if not stop, smoking, and all were provided referral to cessation experts in the community. Also, therapists framed smoking cessation as an example of an important, health behavior choice, emphasizing that the choice for cessation was the patient’s, and that cessation would yield immediate benefits toward a post-cancer, healthy lifestyle. Group members provided ready support and encouragement for reduction efforts. Patients’ cessation efforts were reassessed in Session 17 and monthly during maintenance. Despite the few numbers of smokers enrolled in the trial, significantly more patients in the intervention arm reduced or stopped smoking (Andersen et al., 2004).

**Preparation for Maintenance (Sessions 17, 18)**

The Transtheoretical Model of Behavior Change (Prochaska & DiClemente, 1983) provided a framework and method. Not widely used in cancer control, this conceptualization is more common to prevention research (e.g., smoking cessation, fruit and vegetable consumption, mammography screening; Greene et al., 1999; Prochaska et al., 1994). It is suggested that people pass through five stages of change: precontemplation (no intention to change), contemplation (seriously considering change), preparation (taking steps to change), action (actively involved in meaningful change), and maintenance (maintaining meaningful change). As change through the stages occurs, there is to be a change in the decisional balance. Thus, the model integrates constructs from Bandura’s self-efficacy theory (Bandura, 1982) and Janis and Mann’s (1977) decisional balance model.

During Session 18, patients used a 5-item algorithm to determine their stage of change for six target areas: relaxation training, adherence to medical therapy, social support, diet, exercise, and control of a negative/problematic health behavior. For each target a minimum criterion was specified (see Table 1). If a patient reported no activity or did not intend to change in the next month (the duration between maintenance sessions), she would categorize herself as being in the precontemplation stage. If there was intention to change, the contemplation stage would be indicated. Patients in the action stage would have reached the criterion (e.g., practicing relaxation three times per week) within the past month. The criterion for the maintenance stage was meeting the criterion behavior for 6 months. The session ended with patients specifying goals for each target area during the upcoming month.

**BBI: Maintenance Phase**

The same general format was used for Sessions 19–26. A therapist led the group in relaxation. Patients reviewed their goals for the previous month and rated their attainment and change stage. Patients were generally in the contemplation, action, or maintenance phases. Therapists emphasized problem solving, social support seeking, and increasing awareness of patients’ personal cues of distress. All of these strategies had been identified previously (e.g., Urban et al., 1992) as central to maintaining change. Therapists reviewed all of the intervention strategies, covering a different topic each session (see Table 1 for topics by session numbers). Each session closed with goal-setting for the coming month.
In addition, therapists prompted two extra-group activities. Each patient was asked to set aside 1 hour per week, scheduled at the same time as the group meeting (e.g., 4:00 p.m. on Tuesdays) for her own “session.” We encouraged patients to reflect on their progress and use the time as a specific reminder to “take care of myself.” Also, group members were prompted to maintain contact with one another between sessions. All patients were comfortable in sharing telephone or email contacts and were paired as “phone buddies” for biweekly contacts. The latter two activities were included to facilitate maintenance of the behavior change goals and to ease transition to the end of the intervention.

Provisos

In comparison to other therapy literatures, intervention research in cancer is still in development despite the passage of almost 30 years (e.g., Gordon et al., 1980). Unlike the cognitive behavior therapy research literature which has compared components of a “package” (Borkovec et al., 2002), RCTs with cancer patients have included varied interventions with few replications (Goodwin et al., 2001; Spiegel et al., 1989; Spiegel et al., 2007). The biobehavioral intervention described here was designed for a specific goal: to reduce risk of breast cancer recurrence and death. As such, it included some components that other trials did not (i.e., health behaviors, compliance) as previous investigators hypothesized that they might account, in part, for survival findings (Fawzy et al., 1993; Spiegel et al., 1989).

The health behavior component could be removed for those not having the time or expertise to conduct these specialized sessions. However, we should also note that the patients enjoyed the dietary component as it represented a change effort they could make on a daily basis to improve their health. Our very brief exercise instruction (i.e., one session plus monitoring) did not achieve group differences in physical activity levels (Andersen et al., 2004), but the process data suggest exercise was relevant to outcomes. In the intervention arm, there was a significant impact on compliance (chemotherapy dose intensity) and health improvements for those who exercised frequently compared to those who did not (Andersen, Shelby, et al., 2007). The health behavior sessions occurred consecutively, but the compliance content was interspersed throughout the sessions. We believe this component had something important to offer. Clinically, patients appeared to be empowered by the message that they should take charge of their medical care and have the health care system work for them.

This intervention, like most in cancer, was offered in a group format. We have since conducted it with individuals and found it easy to do. In fact, individual treatment might lead to greater gains, as has been shown when individual and group treatment of mood and anxiety disorders have been compared. Meta-analyses show effect sizes for individual treatment to be substantially larger than those for group treatment (Osborn, Demoncoda, & Feuerstein, 2006).

The Biobehavioral Intervention in Context

For those unfamiliar with interventions for cancer patients, it might be informative to compare this intervention with the most efficacious psychological treatments currently available for anxiety and depressive disorders: cognitive behavioral treatments (CBT). In Table 2 we attempt to do so, with the reference point being the BBI treatment. We specify content unique and essential to each treatment and content essential but not unique. As indicated, the unique components of each treatment are very different. Essentially, BBI offers detailed analysis and change in adherence, health behaviors, and social relationships. BBI is conceptualized to address the cancer crisis. In contrast, CBT is conceptualized to address the “crisis” (and chronicity) of troublesome anxious or depressive emotions. It has exhaustive coverage of cognitive change and systematic monitoring and change of day-to-day activities and troublesome emotions, thoughts, and behaviors. While the BBI may change cognitions and/or increase activity level, it does so only in the service of other goals (e.g., reducing cancer-specific stressors, increasing activity through exercise) and, thus, not in a systematic manner. While CBT may prompt patients to seek more information about cancer or talk to one’s physician, for example, it does so in the service of goals, such as reducing worry or increasing assertive skills.

The essential but nonunique elements are ones that are specifically included in BBI and ones often used in CBT as necessitated by a patient’s unique difficulties. For example, Beck and colleagues (Beck, Rush, Shaw, & Emery, 1979) discuss assertive training and role playing (e.g., Chapter 7—“Application of Behavioral Techniques”) and alternative solutions (problem solving; e.g., Chapter 8—“Cognitive Techniques”). It is also the case that while relaxation is often a component of CBT treatment of anxiety disorders, it is not a routine component for CBT for depression.

What is “missing” from this intervention compared to the typical CBT “package” for anxiety or depression? The most obvious difference is the absence of focus on changing cognitions. While some strategies did address specific negative cognitions and behaviors (e.g., stress cues, eating cues), we did not focus on cognitions, per se, or use thought records. Like behavioral activation, however, we made efforts to increase patients’ engagement in activities and contexts that might allow them to experience pleasure, relaxation, or a sense of control,
though it was not done or monitored systematically, excepting that for PMR. Because stamina was limited, patients were urged to make choices for enjoyable activities with family/friends rather than the mundane (e.g., dusting, vacuuming). Also, group treatment provided no venue for identifying or changing a patient’s core beliefs or schema about the self. However, we emphasized that the cancer diagnosis and the months of treatment that followed offered an opportunity to take perspective on one’s life and to choose which aspects of life (or relationships) to be continued or reduced in frequency or eliminated.

The intervention was designed to alleviate stress and anxiety, though post hoc analyses show that it also alleviated depressive symptoms (Thornton et al., in press). This is not entirely surprising in view of the comorbidity of anxiety and depressive symptomatology. We found that patients entering the trial with significant depressive symptomatology and receiving the intervention improved across outcomes whereas depressed patients in the assessment arm showed no improvements. A stable distress trajectory for the assessment patients suggests that significant depressive symptoms among cancer patients may not remit without treatment. Thus, the BBI might be worth considering in a second generation of trials focused on the cancer patient with major depression, who is typically undiagnosed and untreated (Dausch et al., 2004; Schwartz & Drotar, 2006).

### Summary and Conclusions

A biobehavioral model of cancer stress and disease course provided the foundation for a clinical trial testing the efficacy of an intervention including both intensive and maintenance phases. Some have queried and suggested to us that the diverse content and multiple components of the BBI would be overwhelming for patients. We do not believe this to be the case as, for example, patients provided high satisfaction ratings for each of the components (Andersen, Shelby, et al., 2007). Also, a guiding principle offered to the patients was that “good things go together.” That is, practicing relaxation, complying with treatment recommendations, exercising, changing one’s diet, etc., were complimentary strategies to reduce stress, speed recovery, and improve quality of life.

As clinical research progresses, focus needs to shift to patients in greatest need. This is important, as cancer patients with significant symptoms of depression and anxiety are underserved. We would view BBI as best suited to the 50% to 60% of patients responding to cancer diagnosis and treatment with moderate to severe distress. We have learned from this trial and our ongoing studies that many, upwards of 50%, of the individuals with moderate/severe distress had pre-cancer psychopathology symptoms (e.g., major depressive disorder, generalized anxiety disorder) such that the significant

<table>
<thead>
<tr>
<th>Comparison of the Biobehavioral Intervention (BBI) and Cognitive Behavioral Therapy (CBT) components</th>
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<td><strong>Biobehavioral Intervention (BBI)</strong></td>
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<tr>
<td><strong>Components UNIQUE and essential</strong></td>
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<tr>
<td>1) Concept: Cancer stress is a psychological, physiological, and behavioral phenomenon.</td>
</tr>
<tr>
<td>2) Adherence</td>
</tr>
<tr>
<td>a) Education re: Cancer disease/treatment</td>
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<tr>
<td>b) Coping with physical symptoms (e.g., nausea)</td>
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<tr>
<td>3) Health behavior change</td>
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<tr>
<td>a) Exercise and diet</td>
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<tr>
<td>b) Negative behaviors, e.g., smoking</td>
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<td>4) Social adjustment change</td>
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<tr>
<td>a) Social network identification</td>
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<tr>
<td>b) Identify emotional and task support needs</td>
</tr>
<tr>
<td>c) Education re: Responses of others to cancer</td>
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<td>5) Maintenance: Stages of change conceptualization</td>
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</table>

**Components essential but NOT UNIQUE**

- 1) Progressive muscle relaxation
- 2) Seeking information to cope
- 3) Assertive communication
- 4) Problem solving

* Any of these strategies may be employed with CBT.
distress occurring with the cancer diagnosis represents recurrent psychopathology. Our data suggest that this type of distress does not resolve on its own. As noted above, depressive symptoms for patients in the assessment arm continued through the 12 months following diagnosis, unlike those for patients who received the BBI intervention.

To date, the majority of trials accrue patients and offer psychological treatments in the earliest days of the cancer crisis. A variety of data would attest that this strategy should continue, as it not only alleviates initial stress, but, having done so, reduces the likelihood of subsequent distress, and meaning in life can be enhanced. Interventions should, however, be designed to optimize late outcomes. Without planning and programming, maintenance does not occur. Achieving durable intervention effects is, however, possible and an important step to transition patients to stable functioning. We offer this intervention as one strategy for doing so.

References


Kissane, D. W., et al. Supportive-expressive group therapy for women with metastatic breast cancer: survival and psychosocial outcome from a randomized controlled trial. Psycho-Oncology, 16 (4), 277.


