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Trajectories of Depressive Symptoms in Women Prior to and for Six Months After Breast Cancer Surgery

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Abstract

Depressive symptoms are common in women with breast cancer. This study evaluated how ratings of depressive symptoms changed from the time of the preoperative assessment to 6 months after surgery and investigated whether specific demographic, clinical, and symptom characteristics predicted preoperative levels of and/or characteristics of the trajectories of depressive symptoms. Characteristics that predicted higher preoperative levels of depressive symptoms included being married/partnered; receipt of adjuvant chemotherapy; more fear of metastasis; higher levels of trait anxiety, state anxiety, sleep disturbance, problems with changes in appetite; more hours per day in pain; and lower levels of attentional function. Future studies need to evaluate associations between anxiety, fears of recurrence, and uncertainty, as well as personality characteristics and depressive symptoms.

Keywords

depressive symptoms; breast cancer; anxiety

Introduction

Depression is a common problem in patients with breast cancer (Aapro & Cull, 1999; Berard, 2001; Massie, 2004). The diagnosis of a potentially life-threatening disease, the preparation for surgery, and the higher rates of depression in women in the general population (Miaskowski, 2004; Sevick, Rolih, & Pahor, 2000), put many patients with breast cancer at risk for depressive symptoms. In fact, across studies that used established cutoffs

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Conflict of interest
The authors declare that they have no conflicts of interest.

and symptom specific scales to evaluate patients prior to breast cancer surgery, 18% to 26% of these women were categorized as having clinically meaningful levels of depressive symptoms (Ozalp, Sarioglu, Tuncel, Aslan, & Kadiogullari, 2003; Parker, et al., 2007; Vahdaninia, Omidvari, & Montazeri, 2010). Depressive symptoms are associated with decreases in quality of life (QOL), poorer adherence to treatment, longer hospital stays, and higher mortality (Groenvold, et al., 2007; Massie, 2004; van't Spijker, Trijsburg, & Duivenvoorden, 1997; Wells, et al., 1989).

Women with breast cancer experience moderate to high levels of depressive symptoms before surgery (Aragona, Muscatello, & Mesiti, 1997; Goldberg, et al., 1992; Hegel, et al., 2006; Hughes, 1982; Maguire, et al., 1978; J. Morris & Royle, 1987; T. Morris, Greer, & White, 1977; Ozalp, et al., 2003; Stanton & Snider, 1993; Vahdaninia, et al., 2010), that progressively decline over the first year after surgery (Epping-Jordan, et al., 1999; Fallowfield, Hall, Maguire, & Baum, 1990; Gallagher, Parle, & Cairns, 2002; Henselmans, Helgeson, et al., 2010; Hinnen, et al., 2008; Lam, Bonanno, et al., 2010; Lam, Chan, Ka, & Fielding, 2007; Medeiros, et al., 2010; Millar, Purushotham, McLatchie, George, & Murray, 2005; Northouse, Templin, & Mood, 2001; Nosarti, Roberts, Crayford, McKenzie, & David, 2002; Parker, et al., 2007; Vahdaninia, et al., 2010). Unfortunately, direct comparisons of severity scores across studies are not meaningful due to differences in the methods used to assess depressive symptoms (e.g., clinical interviews, self-report measures); differences in inclusion and exclusion criteria; and differences in the number and timing of the assessments. In addition, some studies used psychological distress or psychological morbidity as proxy terms for depressive symptoms (Goldberg, et al., 1992; Groenvold, et al., 2007; Hegel, et al., 2006; Hughes, 1982; Ozalp, et al., 2003).

Studies of the risk factors for depressive symptoms in women, prior to and following breast cancer surgery, have evaluated a number of demographic and clinical characteristics, as well as psychosocial attributes and symptom characteristics. Across these studies, being younger (Avis, et al., 2013; Dean, 1987; Epping-Jordan, et al., 1999; Hartl, et al., 2010; Lam, et al., 2007; Parker, et al., 2007; Schlegel, Manning, Molix, Talley, & Bettencourt, 2012) and caring for children (Dean, 1987; Deshields, Tibbs, Fan, & Taylor, 2006; Lindviksmoen, Hofso, Paul, Miaskowski, & Rustoen, 2012; Schlegel, et al., 2012) increased a woman’s risk for psychological morbidity in the first year after breast cancer surgery. Findings regarding marital status are inconsistent with two studies reporting that women who were married or partnered were less likely to experience distress than women who were single, divorced, or widowed (Lam, et al., 2007; Schlegel, et al., 2012), one study finding the opposite association (Dean, 1987), and two finding no differences (Lam, Fielding, & Ho, 2005; Maunsell, Brisson, & Deschenes, 1992). In terms of education, while two studies found that less education was associated with higher levels of depressive symptoms (Lindviksmoen, et al., 2012; Torres, et al., 2013), several studies found no association between education and patterns of psychological distress (Epping-Jordan, et al., 1999; Maunsell, et al., 1992; Vahdaninia, et al., 2010).

Findings regarding the relationships between clinical characteristics and psychological distress prior to and following breast cancer surgery are inconsistent. In some studies, tumor size and stage of disease were not associated with psychological distress before or after

surgery (Epping-Jordan, et al., 1999; Hartl, et al., 2010; Kissane, et al., 1998; Lam, et al., 2007; Maunsell, et al., 1992), whereas in other studies a positive association was found (Gallagher, et al., 2002; Vahdaninia, et al., 2010). While one study found a decline in depressive symptoms in women following mastectomy (Lindviksmoen, et al., 2012), in other studies (Fallowfield, et al., 1990; Fung, Lau, Fielding, Or, & Yip, 2001; Goldberg, et al., 1992; Hartl, et al., 2010; Kissane, et al., 1998; Lam, et al., 2007; Levy, Herberman, Lee, Lippman, & d'Angelo, 1989; Maunsell, Brisson, & Deschenes, 1989; Medeiros, et al., 2010; Millar, et al., 2005; Moyer, 1997; Parker, et al., 2007; Rijken, de Kruif, Komproe, & Roussel, 1995) no differences in psychological adjustment were found between women undergoing breast conserving surgery (BCS) compared to mastectomy, contrary to early claims that mastectomy was associated with higher rates of depression (Bard & Sutherland, 1955; T. Morris, et al., 1977). Similarly, adjuvant treatment had an effect on levels of depressive symptoms after surgery in some studies (Dean, 1987; Kissane, et al., 1998; Torres, et al., 2013) but not in others (Lam, et al., 2007; Pasacreta, 1997). However, postmenopausal status (Dean, 1987) and physical complaints (e.g., fatigue, pain) (Dean, 1987; Henselmans, Fleer, et al., 2010; Hughson, Cooper, McArdle, & Smith, 1986; Kissane, et al., 1998; Vahdaninia, et al., 2010) were associated with higher levels of psychological distress.

Various psychosocial adjustment characteristics may contribute to the severity and trajectories of psychological distress before and after breast cancer surgery. For example, personality characteristics, such as neuroticism, are associated with higher levels of distress across various phases of the disease trajectory (Hinnen, et al., 2008; Millar, et al., 2005). Similarly, coping mechanisms (Epping-Jordan, et al., 1999; Stanton, et al., 2005), perceived social support (Gallagher, et al., 2002), sense of control (Barez, Blasco, Fernandez-Castro, & Viladrich, 2007; Gallagher, et al., 2002; Henselmans, Fleer, et al., 2010), and illness perceptions (Millar, et al., 2005) are implicated in the patterns of depressive symptoms after breast cancer surgery. In addition, psychiatric history (Dean, 1987; Gallagher, et al., 2002; Maunsell, et al., 1992) and increased levels of preoperative or immediate postoperative distress (Badger, Braden, Mishel, & Longman, 2004; Dean, 1987; Deshields, et al., 2006; Gallagher, et al., 2002; Lam, et al., 2007; Shing, Bonanno, Mancini, & Fielding, 2012; Millar, et al., 2005; Nosarti, et al., 2002) predicted worse psychological outcomes after surgery.

Despite agreement that levels of depressive symptoms decline after breast cancer surgery (Burgess, et al., 2005; Dean, 1987; Epping-Jordan, et al., 1999; Fallowfield, et al., 1990; Gallagher, et al., 2002; Goldberg, et al., 1992; Henselmans, Helgeson, et al., 2010; Hinnen, et al., 2008; Laan & Linden, 2008; Lam, Bonanno, et al., 2010; Lam, et al., 2007; Maunsell, et al., 1989; Medeiros, et al., 2010; Millar, et al., 2005; J. Morris & Royle, 1987; T. Morris, et al., 1977; Nosarti, et al., 2002; Parker, et al., 2007; Vahdaninia, et al., 2010), newer methods of longitudinal data analysis suggest that a large amount of inter-individual variability exists in patients' experiences of depressive symptoms before and after surgery (Deshields, et al., 2006; Gallagher, et al., 2002; Henselmans, Helgeson, et al., 2010; Lam, Shing, et al., 2012; Millar, et al., 2005; Nosarti, et al., 2002). The ability to detect different patterns of adjustment has led to the identification of specific risk factors that identify group membership. Across these studies (Deshields, et al., 2006; Gallagher, et al., 2002;

Henselmans, Helgeson, et al., 2010; Lam, Shing, et al., 2012; Millar, et al., 2005; Nosarti, et al., 2002), women with higher levels of psychological distress had received adjuvant treatment, had a personality consistent with neuroticism, had a lower sense of mastery, and were less optimistic.

The primary limitation with the latter, as well as the aforementioned studies, is that they used general measures of psychological distress (e.g., the General Health Questionnaire) rather than a specific measure of depressive symptoms. In order to better understand the risk factors for and the trajectories of depressive symptoms in patients with breast cancer, symptom-specific instruments (e.g., Center for Epidemiological Studies-Depression Scale (CES-D)) need to be used before and after surgery. Furthermore, newer methods of longitudinal data analysis (e.g., hierarchical linear modeling (HLM)) can be used to identify predictors of initial levels and trajectories of depressive symptoms (Dhruva, et al., 2010; Merriman, et al., 2010).

Only two studies have used HLM to evaluate the trajectories of depressive symptoms in patients with breast cancer (Lindviksmoen, et al., 2012; Schlegel, et al., 2012). In both studies, patients were enrolled during radiation therapy. Therefore, this type of longitudinal analysis of depressive symptoms is lacking in women who were assessed prior to surgery. Knowledge of the predictors of depressive symptoms prior to surgery may improve the identification of high risk women. Therefore, the purposes of this study, in a sample of women who were enrolled prior to breast cancer surgery, were to examine how monthly ratings of depressive symptoms changed from the time of the preoperative assessment to 6 months after surgery and to investigate whether specific demographic, clinical, symptom, and psychosocial adjustment characteristics predicted preoperative levels of and/or characteristics of the trajectories of depressive symptoms over a period of 6 months after the surgery.

Methods

Patients and Settings

This descriptive, longitudinal study is part of a larger study that evaluated for neuropathic pain, lymphedema, and other symptoms in a sample of women who underwent breast cancer surgery (McCann, et al., 2012; Miaskowski, et al., 2012; Van Onselen, et al., 2013). Patients were recruited from Breast Care Centers located in a Comprehensive Cancer Center, two public hospitals, and four community practices.

Patients were eligible to participate if they were adult women (≥18 years) who would undergo breast cancer surgery on one breast; were able to read, write, and understand English; agreed to participate; and gave written informed consent. Patients were excluded if they were having breast cancer surgery on both breasts and/or had distant metastasis at the time of diagnosis.

A total of 516 patients were approached to participate and 410 were enrolled in the study (response rate 79.5%). In the current analysis, complete data from 396 women were available. For those who declined participation, the major reasons for refusal were: too busy,

overwhelmed with the cancer diagnosis, or insufficient time available to do the assessment prior to surgery.

Instruments

A demographic questionnaire obtained information on age, marital status, education, ethnicity, employment status, and financial status. Patient's functional status was assessed using the Karnofsky Performance Status (KPS) scale, which ranges from 30 (I feel severely disabled and need to be hospitalized) to 100 (I feel normal, I have no complaints or symptoms). The KPS has well established validity and reliability (Karnofsky, 1977).

The Self Administered Comorbidity Questionnaires (SCQ) is a short and easily understood instrument that was developed to measure comorbidity in clinical and health service research settings (Sangha, Stucki, Liang, Fossel, & Katz, 2003). The questionnaire consists of 13 common medical conditions that were simplified into language that could be understood without any prior medical knowledge. Patients were asked to indicate if they had the condition using a "yes/no" format. If they indicated that they had a condition, they were asked if they received treatment for it (proxy for disease severity) and did it limit their activities (indication of functional limitations). Patients were given the option to add two additional conditions not listed on the instrument. For each condition, a patient can receive a maximum of 3 points. Because the SCQ contains 13 defined medical conditions and 2 optional conditions, the maximum score totals 45 points if the open-ended items are used and 39 points if only the closed-ended items are used. The SCQ has well-established validity and reliability and has been used in studies of patients with a variety of chronic conditions (Brunner, et al., 2008; Cieza, et al., 2006; MacLean, Littenberg, & Kennedy, 2006).

The CES-D consists of 20 items selected to represent the major symptoms in the clinical syndrome of depression. Scores can range from 0 to 60, with scores of ≥16 indicating the need for individuals to seek clinical evaluation for major depression. The CES-D has well-established concurrent and construct validity (Carpenter, et al., 1998; Radloff, 1977; Sheehan, Fifield, Reisine, & Tennen, 1995). Cronbach's alpha for the CES-D was 0.90.

The Spielberger State-Trait Anxiety Inventories (STAI-T, STAI-S) consist of 20 items each that are rated from 1 to 4. Scores for each scale are summed and can range from 20 to 80. A higher score indicates greater anxiety. The STAI-T measures an individual's predisposition to anxiety determined by his/her personality and estimates how a person generally feels. The STAI-S measures an individual's transitory emotional response to a stressful situation. It evaluates the emotional responses of worry, nervousness, tension, and feelings of apprehension related to how a person feels "right now" in a stressful situation. Cuttoff scores of ≥31.8 and ≥32.2 indicate high levels of trait and state anxiety, respectively (Spielberger, Gorsuch, Suchene, Vagg, & Jacobs, 1983). The STAI-S and STAI-T inventories have well-established criterion and construct validity and internal consistency reliability coefficients (Bieling, Antony, & Swinson, 1998; Kennedy, Schwab, Morris, & Beldia, 2001). Cronbach's alphas for the STAI-T and STAI-S were .88 and .95, respectively.

The Lee Fatigue Scale (LFS) consists of 18 items designed to assess physical fatigue and energy.(Lee, Hicks, & Nino-Murcia, 1991) Each item was rated on a 0 to 10 numeric rating

scale (NRS). Total fatigue and energy scores were calculated as the mean of the 13 fatigue items and the 5 energy items. Higher scores indicate greater fatigue severity and higher levels of energy. Respondents were asked to rate each item based on how they felt "right now". The LFS has been used with healthy individuals (Gay, Lee, & Lee, 2004; Lee, et al., 1991) and in patients with cancer and HIV (Lee, Portillo, & Miramontes, 1999; Miaskowski, et al., 2006; Miaskowski & Lee, 1999; Miaskowski, et al., 2008). A cutoff score of ≥4.4 indicates high levels of fatigue (Dhruva, et al., 2010). A cutoff score of ≤4.8 indicates low levels of energy (Dhruva, et al., 2010). The LFS has well established validity and reliability. Cronbach's alphas for the fatigue and energy scales were .96 and .93, respectively.

The Attentional Function Index (AFI) is a commonly used self-report measure of attentional function (Cimprich, Visovatti, & Ronis, 2011). It consists of 16-items that were rated on a 0 to 10 NRS. A higher mean score indicates greater capacity to direct attention (Cimprich, 1992; Cimprich, et al., 2011). Scores are grouped into categories of attentional function (i.e., <5.0 low function, 5.0 to 7.5 moderate function, >7.5 high function) (Cimprich, So, Ronis, & Trask, 2005). The AFI has established reliability and validity (Cimprich, 1992; Jansen, Dodd, Miaskowski, Dowling, & Kramer, 2008). Cronbach's alpha for the AFI was .95.

The General Sleep Disturbance Scale (GSDS) consists of 21 items designed to assess the quality of sleep in the past week. Each item was rated on a 0 (never) to 7 (everyday) NRS. The GSDS total score is the sum of the 21 items that can range from 0 (no disturbance) to 147 (extreme sleep disturbance). A GSDS total score of ≥43 indicates a significant level of sleep disturbance (Fletcher, et al., 2008). The GSDS has well-established validity and reliability in shift workers, pregnant women, and patients with cancer and HIV (Lee, 1992; Lee & DeJoseph, 1992). Cronbach's alpha for the GSDS total score was .86.

The occurrence of breast pain prior to surgery was determined by asking the question "Are you experiencing pain in your affected breast?" If women responded yes, they rated the severity of their average and worst pain using a 0 (no pain) to 10 (worst imaginable pain) NRS. Women were asked how many days per week and how many hours per day they experienced significant pain (i.e., pain that interfered with function).

The occurrence of hot flashes and changes in appetite prior to surgery was determined by asking "Did you have hot flashes or changes in appetite in the last week?" If the women responded yes, they rated the severity of each symptom on a 0 to 10 NRS.

The Quality of Life Scale-Patient Version (QOL-PV) is a 41-item instrument that measures four dimensions of QOL in cancer patients (i.e., physical well-being, psychological well-being, spiritual well-being, social well-being), as well as a total QOL score. Each item was rated on a 0 to 10 NRS with higher scores indicating a better QOL. The QOL-PV has well established validity and reliability (Ferrell, Wisdom, & Wenzl, 1989; Padilla & Grant, 1985; Padilla, et al., 1983). Cronbach's alpha for the QOL-PV total score was .86. For the physical, psychological, social, and spiritual well-being subscales, the coefficients were 0.70, 0.79, 0.75, and 0.61, respectively.

Individual items from the QOL-PV were used to assess a number of psychosocial adjustment characteristics (i.e., coping, distress, fear, uncertainty, control). One item asked

patients to rate their difficulty coping as a result of the cancer and its treatment. Another item asked patients to rate the distress associated with their initial cancer diagnosis. Fear was assessed with two questions, one regarding fear of future diagnostic tests and another regarding fear of metastasis. Another question asked patients to rate the level of control over their lives. Finally, one question asked patients to rate the amount of uncertainty they felt about the future. Each item was rated using a 0 to 10 NRS with higher scores indicating a more positive appraisal of a particular characteristic. The specific items were chosen based on the review of the literature of psychosocial adjustment and depression in women with breast cancer (Dean, 1987; Epping-Jordan, et al., 1999; Gallagher, et al., 2002; Henselmans, Helgeson, et al., 2010; Hinnen, et al., 2008; Maunsell, et al., 1989; Millar, et al., 2005; Nosarti, et al., 2002).

Study Procedures

The Committee on Human Research at the University of California, San Francisco and the Institutional Review Boards at each of the study sites approved the study. During the patient's preoperative visit, a staff member explained the study to the patient. For those women who were willing to participate, the staff member introduced the patient to the research nurse who met with the women, determined eligibility, and obtained written informed consent prior to surgery. After providing consent, patients completed the enrollment questionnaires. Patients were contacted two weeks after surgery to schedule the first post-surgical appointment. The research nurse met with the patients either in their home, the Clinical Research Center, or the clinic at one, two, three, four, five, and six months after surgery.

Data Analysis

Descriptive statistics and frequency distributions were generated on the sample characteristics and baseline symptom severity scores using the Statistical Package for the Social Sciences (SPSS) version 19.(SPSS, 2010) For each of the seven assessments of depressive symptoms, a mean CES-D score was calculated for use in the subsequent statistical analyses.

HLM, based on full maximum likelihood estimation, was done in two stages, using the software developed by Raudenbush and colleagues (S. Raudenbush & Bryk, 2002; S. W. Raudenbush, 2001). As previously described (Dhruva, et al., 2010; Langford, et al., 2011; Miaskowski, et al., 2011), during stage 1, intra-individual variability in depressive symptoms over time was examined. Three level 1 models were compared to determine whether the patients' depressive symptoms did not change over time (i.e., no time effect), changed at a constant rate (i.e., linear time effect), or changed at a rate that accelerated or decelerated over time (i.e., quadratic effect). The second stage of the HLM analysis examined inter-individual differences in the trajectories of depressive symptoms by modeling the individual change parameters (i.e., intercept and linear slope) as a function of proposed predictors at level 2. Table 1 presents a list of the proposed predictors that was developed based on a review of the literature on depressive symptoms in women with breast cancer who underwent surgery (Badger, et al., 2004; Bard & Sutherland, 1955; Barez, et al., 2007; Deshields, et al., 2006; Epping-Jordan, et al., 1999; Fallowfield, et al., 1990; Fung, et

al., 2001; Gallagher, et al., 2002; Goldberg, et al., 1992; Hartl, et al., 2010; Henselmans, Fleer, et al., 2010; Hinnen, et al., 2008; Hughson, et al., 1986; Kissane, et al., 1998; Lam, et al., 2007; Lam, Shing, et al., 2012; Levy, et al., 1989; Maunsell, et al., 1989, 1992; Medeiros, et al., 2010; Millar, et al., 2005; T. Morris, et al., 1977; Moyer, 1997; Parker, et al., 2007; Rijken, et al., 1995; Stanton, et al., 2005; Vahdaninia, et al., 2010).

To improve estimation efficiency and construct a model that was parsimonious, exploratory level 2 analyses were completed in which each potential predictor was assessed to determine whether it would result in a better model if it alone were added as a level 2 predictor. Predictors with a t value of <2 were dropped from subsequent model testing. All potential significant predictors from the exploratory analyses were entered into the model to predict each individual change parameter. Only predictors that maintained a statistically significant contribution in conjunction with other variables were retained in the final model. A p-value of < 0.05 indicates statistical significance.

Results

Patient Characteristics

The demographic and clinical characteristics, as well as the preoperative symptom scores for the 396 patients, are summarized in Table 2. On average, patients were 55 years of age, well educated, had a KPS score of 93, and a SCQ score of 4. Most of the women self-identified as White (64.6%) and were post-menopausal (64.8%). A smaller percentage lived alone 94 (24.1%) and were employed (47.5%).

Individual and Mean Changes in Depressive Symptoms

The first stage of the HLM analysis examined how depressive symptoms changed from the preoperative assessment to 6 months after surgery. Two models were estimated in which the individual function of time was linear and quadratic. The goodness-of-fit tests of the deviance between the linear and the quadratic models indicated that a linear model fit the data significantly better than a quadratic model.

Table 3 presents the estimates for the unconditional linear model. Because the model had no covariates, the intercept represents the estimated mean level of depressive symptoms prior to surgery (i.e., 13.830 on a 0 to 60 scale). The estimated linear rate of change in depressive symptoms, for each additional month, was −0.480 ($p<.0001$). Figure 1 displays the trajectory for depressive symptoms from the preoperative assessment to 6 months after surgery. Depressive symptoms decreased over the course of 6 months to a CES-D score of 10.96. It should be noted that the mean depressive symptom scores for the various groups depicted in all the figures are estimated or predicted means.

Inter-individual Differences in the Trajectories of Depressive Symptoms

The second stage of the HLM analysis tested the hypothesis that the pattern of change over time in depressive symptoms varied based on demographic, clinical, symptom, and/or psychosocial adjustment characteristics reported at enrollment. As shown in the final model in Table 3, the characteristics that predicted inter-individual differences in preoperative

levels of depressive symptoms were marital status (married/partnered versus not married/partnered), receipt of adjuvant chemotherapy, as well as preoperative levels of trait and state anxiety, attentional function, sleep disturbance, changes in appetite, number of hours per day in pain, and fear of metastasis. The characteristics that predicted inter-individual differences in the linear slope for depressive symptoms were the patients' depressive symptom scores prior to surgery and the amount of distress associated with the initial cancer diagnosis.

To illustrate the effects of the above predictors on patients' initial levels and trajectories of depression, Figures 2A through 2F display the adjusted change curves for depressive symptoms that were estimated based on differences in trait and state anxiety (i.e., low/high trait/state anxiety calculated based on one standard deviation [SD] below and above the mean STAI-T and STAI-S scores), sleep disturbance (i.e., higher/lower levels of sleep disturbances calculated based on one SD above and below the mean GSDS total score), attentional function prior to surgery (i.e., lower/higher attentional function calculated based on one SD above and below the mean AFI score), hours per day in pain (i.e., fewer/more hours per day in pain calculated based on one SD above and below the mean number of hours per day in pain), and appetite changes (i.e., less/more problems with changes in appetite calculated based on one SD above and below the mean scores on ratings of changes in appetite).

Figures 3A through 3C display the adjusted change curves for depressive symptoms that were estimated based on differences in marital status (i.e., not married-partnered/married-partnered), receipt of adjuvant chemotherapy (i.e., did/did not receive adjuvant chemotherapy), and fear of metastasis (i.e., less/more fear of metastasis calculated based on one SD above and below the mean score for ratings of fear of metastasis). Finally, Figure 4A and 4B display the adjusted change curves for depressive symptoms based on predictors of the linear slope parameters (i.e., CES-D total score prior to surgery, amount of distress associated with the initial cancer diagnosis).

Discussion

This study is the first to use HLM to examine individual trajectories of depressive symptoms prior to and for 6 months following breast cancer surgery and to investigate whether demographic, clinical, symptom, and psychosocial adjustment characteristics predicted preoperative levels of and the trajectories of depressive symptoms over a period of 6 months. Prior to surgery, the patients' mean CES-D score was 13.8 (on a 0 to 60 scale), which is slightly higher than CES-D scores reported in a study that assessed short and long-term psychosocial adjustment in women undergoing different surgical procedures for breast cancer (Parker, et al., 2007). Consistent with previous longitudinal studies (Deshields, et al., 2006; Parker, et al., 2007; Rijken, et al., 1995), overall depressive symptom scores declined over the 6 months following surgery, reaching an average CES-D score of 11.

Only one demographic characteristic (i.e., marital status) predicted preoperative levels of depressive symptoms. In our study, being married/partnered was associated with higher levels of depression prior to surgery (Figure 3A). Our finding is in agreement with one study (Dean, 1987), but not with others that found either no difference (Lam, et al., 2005;

Maunsell, et al., 1992) or that being single was associated with higher levels of depressive symptoms (Parker, et al., 2007). Of note, in the study byDean et al. (1987), women who were clinically depressed prior to surgery were significantly more likely to have sexual problems 12 months after surgery. While problems with sexual activity were assessed in our study, it was not a significant predictor of depressive symptoms. Based on these inconsistent findings, additional research is needed to determine the precise relationships between marital status and depressive symptoms in these women.

This study is the first to report on the association between trait anxiety and depressive symptoms in patients prior to breast cancer surgery. In our study, higher preoperative levels of trait anxiety predicted higher preoperative levels of depressive symptoms. Interestingly, recent work suggests strong associations between neuroticism and trait anxiety (i.e., $r = .622$, $p<.01$) (Perkins, Kemp, & Corr, 2007). In fact, these authors suggested that measures of trait anxiety could be used interchangeably as an estimate of an individual's level of neuroticism. While neuroticism was not assessed in our study, the finding that preoperative levels of trait anxiety was a predictor of the level of depressive symptoms is consistent with studies that found that neuroticism was one of the strongest predictors of higher levels of psychological distress after breast cancer surgery (Henselmans, Fleer, et al., 2010; Hinnen, et al., 2008; Hughes, 1982; Millar, et al., 2005; J. Morris & Royle, 1987).

Consistent with the current DSM-IV criteria for the diagnosis of various types of depressive disorders (American Psychiatric Association, 2000) higher levels of state anxiety, sleep disturbance, and attentional fatigue, as well as longer duration of daily pain and more problems with changes in appetite, were all associated with higher preoperative levels of depressive symptoms. This finding suggests that this constellation of symptoms can be used, independent of demographic and clinical characteristics, to identify groups of women at higher risk for depressive symptoms.

In this study, women who reported more fear of metastasis had higher preoperative levels of depressive symptoms that remained high in the 6 months after surgery. This finding is consistent with another study that found that fear of a cancer recurrence and of the side effects of treatment, assessed at 3 weeks and 3 months after the end of treatment, were the main sources of distress for women with breast cancer (Costanzo, et al., 2007). Similarly, in several studies (Girgis, Boyes, Sanson-Fisher, & Burrows, 2000; Hodgkinson, et al., 2007; Schmid-Buchi, Halfens, Dassen, & van den Borne, 2008), fear of cancer metastasis was one of the primary concerns of breast cancer patients in the years after the initial diagnosis. Additional research is warranted to determine how persistent fears of metastasis and recurrence influence changes in depressive symptoms over time and whether interventions targeted to decrease these fears impact levels of psychological distress.

Women with higher ratings of distress at being diagnosed with breast cancer and a higher CES-D score prior to surgery experienced a sharper decline in levels of depressive symptoms in the 6 months following surgery. The reason why these two characteristics predicted the associated changes in the trajectories of depressive symptoms is not readily apparent. Previous studies found that higher preoperative levels of distress were associated with worse psychosocial adjustment after surgery (Dean, 1987; Hughes, 1982; T. Morris, et

al., 1977). This relationship was replicated when psychological distress was assessed at diagnosis (Nosarti, et al., 2002; Stanton & Snider, 1993) or immediately after surgery (Lam, et al., 2005; Millar, et al., 2005). Because the majority of these studies used generic measures of psychological distress (Dean, 1987; Hughes, 1982; Lam, et al., 2005; Millar, et al., 2005; T. Morris, et al., 1977; Nosarti, et al., 2002; Stanton & Snider, 1993), additional research is needed to examine the impact of anxiety versus depression on the trajectories of depressive symptoms following surgery for breast cancer.

While this study used longitudinal data from a large sample of women, a validated measure for depression, and the HLM analysis to evaluate depressive symptom trajectories, a number of limitations need to be acknowledged. Results of this study are limited in their generalizability by the characteristics of the sample, especially that most of the women were Caucasian, middle-aged, and highly educated. Given that many of the women who declined to participate in the study stated that they were too overwhelmed with the experience of cancer, level of depressive symptoms may be underestimated. Also, assessments during the follow up period were not scheduled to coincide with the initiation of new treatments or disease recurrence that might contribute to patients' levels of distress (Heim, Valach, & Schaffner, 1997; Henselmans, Helgeson, et al., 2010; Hinnen, et al., 2008). Finally, individual items of the QOL-PV scale were used as indicators of psychosocial adjustment. While single items rated on a 0 to 10 NRS are valid measures of subjective states (DeSalvo, et al., 2006; Lundberg & Manderbacka, 1996), it is generally recommended that multidimensional measures be used to assess these types of subjective experiences.

Research is warranted to confirm the predictors of preoperative levels and trajectories of depressive symptoms after breast cancer surgery. Subsequent studies need to evaluate the associations between anxiety, fears of recurrence, and uncertainty, as well as personality characteristics and depressive symptoms. In addition, intervention studies need to be designed and implemented to reduce depressive symptoms in these high risk patients.

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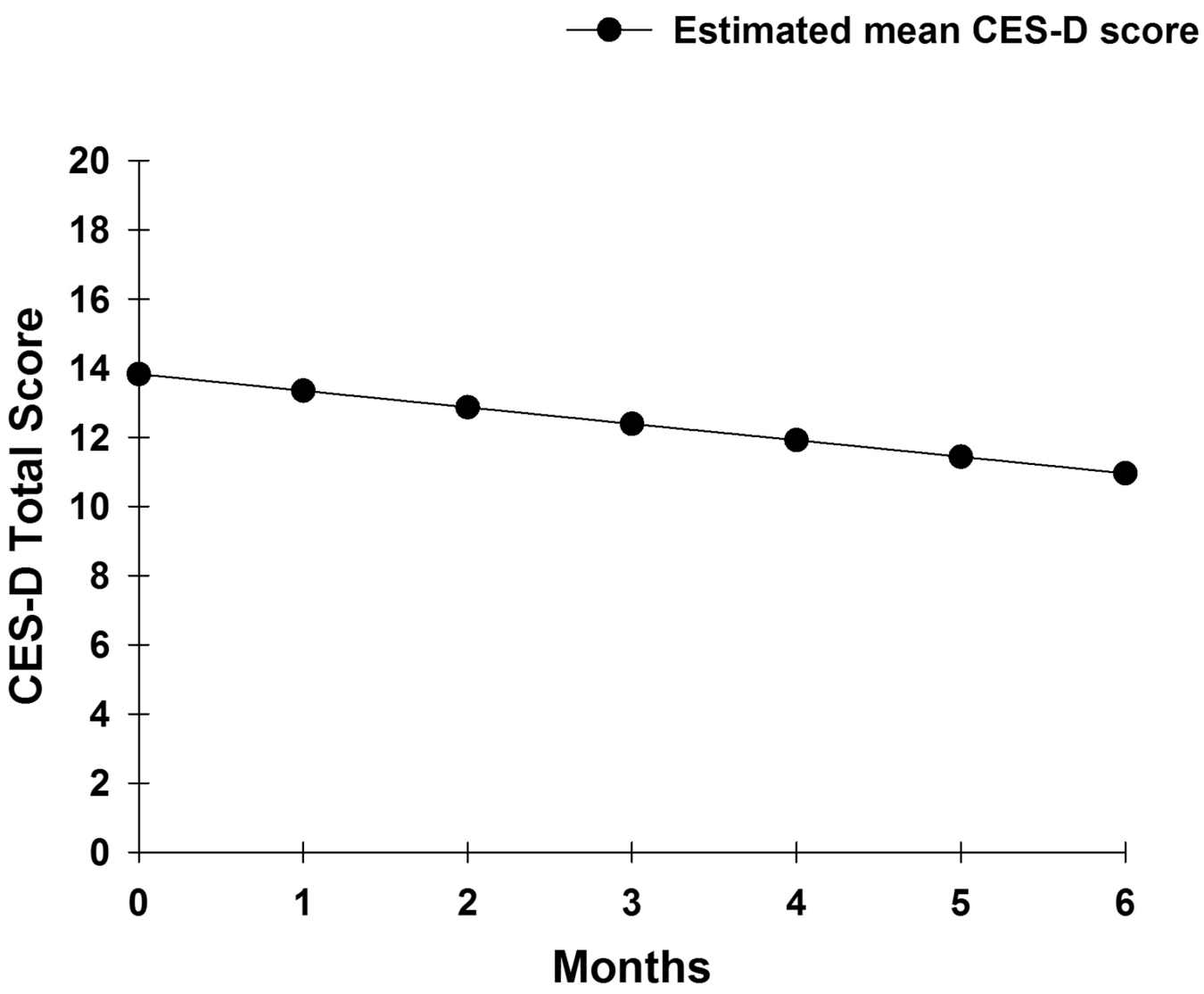

Figure 1.
Trajectory of depressive symptoms as measured with the Center for Epidemiologic Studies Depression (CES-D) scale over the six months of the study.

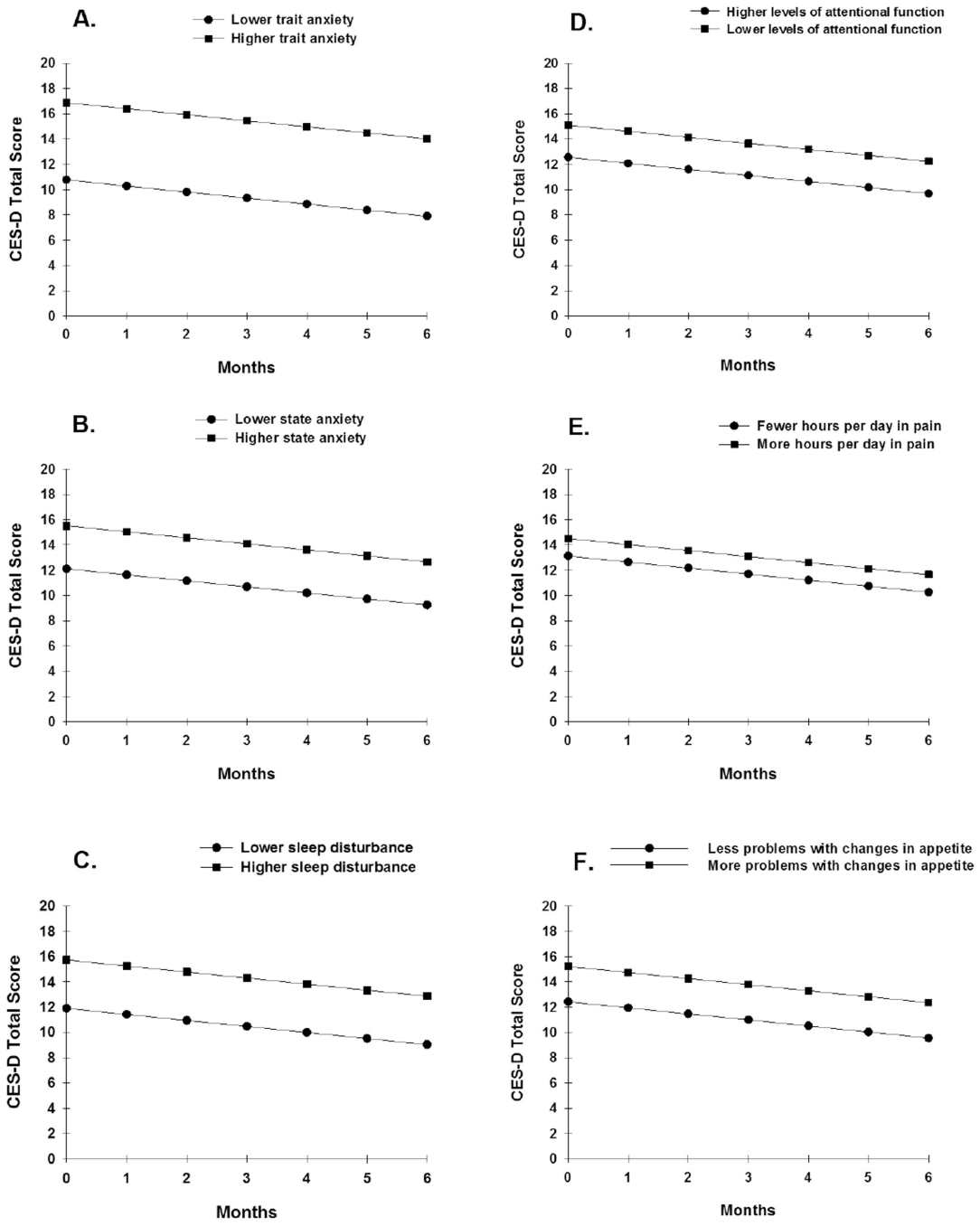

Figure 2.

Influence of trait anxiety score (A), state anxiety score (B), sleep disturbance score (C), levels of attentional fatigue (D), hours per day in pain (E), and changes in appetite (F) on interindividual differences in the intercept parameters for levels of depression.

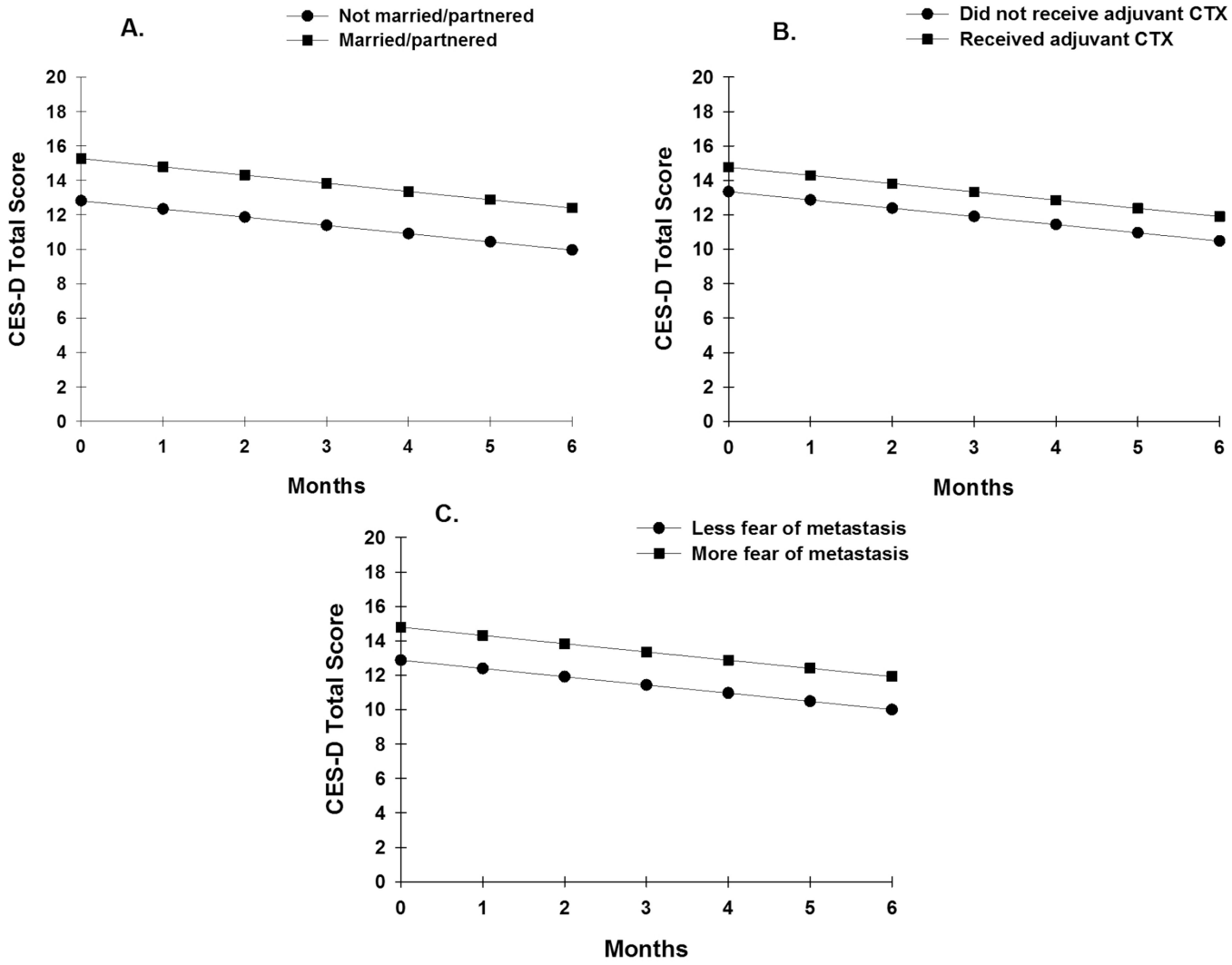

Figure 3.

Influence of marital status (A), receipt of adjuvant chemotherapy (CTX) (B), and fear of metastasis (C) on interindividual differences in the intercept parameters for depressive symptoms.

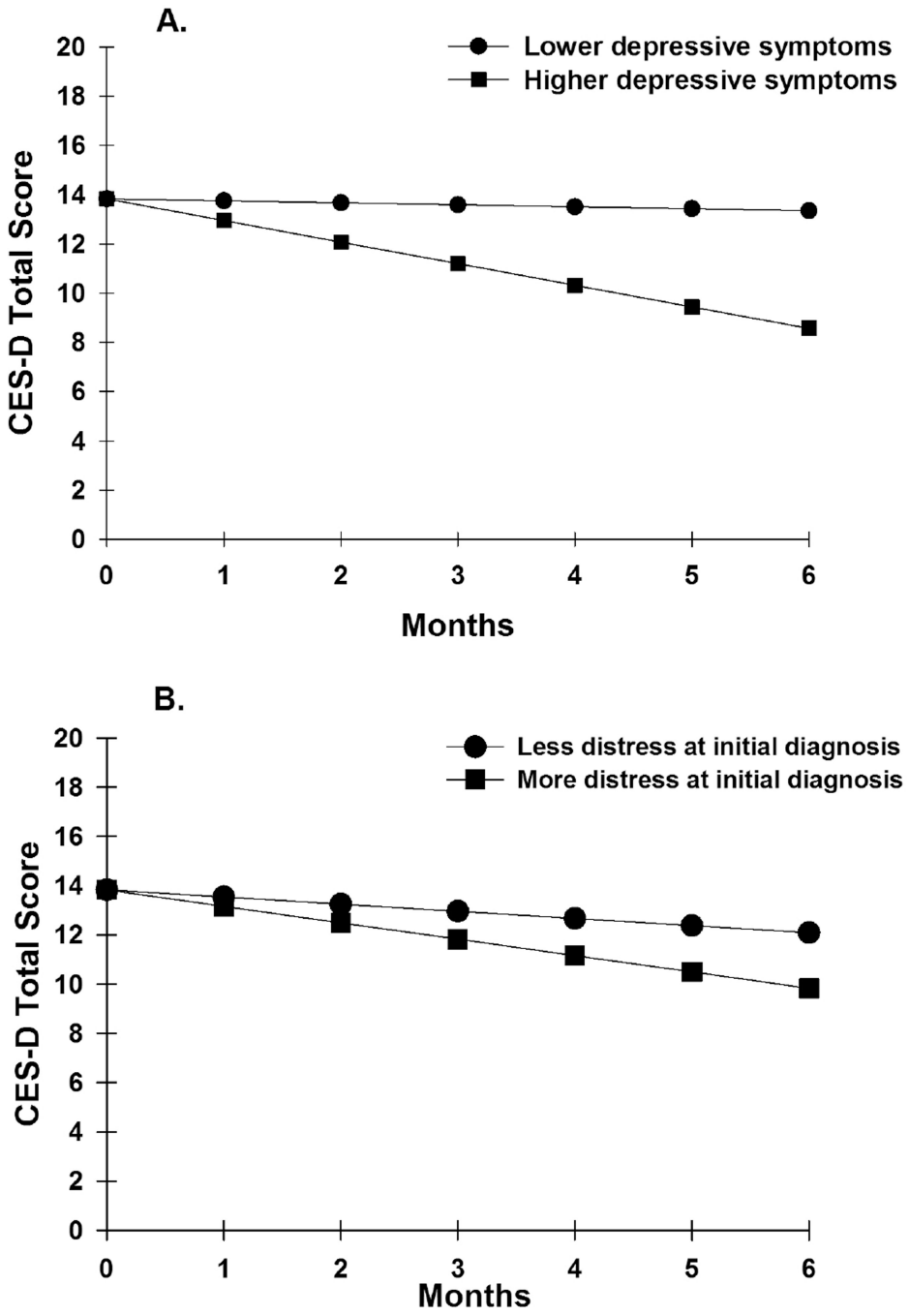

Figure 3.

Influence of baseline levels of depressive symptoms (A) and distress at initial cancer diagnosis (B) on interindividual differences in the slope parameters for depressive symptoms.

Table 1

Potential Predictors of the Intercept (I) and Linear Coefficient (LC) for Depressive Symptoms Using Preoperative Characteristics

Characteristic	I	LC
Demographic characteristics		
Age	■	
Lives alone	■	
Education		
Marital status	■	
Ethnicity	■	
Employment status		
Clinical characteristics		
Body mass index		
Karnofsky Performance Status score	■	
Self-Administered Comorbidity Questionnaire score	■	
Stage of disease		
Neoadjuvant chemotherapy		
Type of surgery		
Sentinel lymph node biopsy		
Axillary lymph node dissection		
Breast reconstruction at the time of surgery		■
Menopausal status		
Adjuvant radiation therapy in first six months		
Adjuvant chemotherapy in the first six months	■	
Symptoms		
Trait anxiety score	■	■
State anxiety score	■	■
Attentional Function Index score	■	■
Lee Fatigue Scale - Fatigue score	■	
Lee Fatigue Scale - Energy score	■	
General Sleep Disturbance Scale score	■	■
Presence of breast pain prior to surgery	■	
Worst pain score	■	
Average pain score	■	
Number of days per week in pain	■	
Number of hours per day in pain	■	
Severity of hot flashes	■	
Severity of changes in appetite	■	
Psychosocial adjustment characteristics		
Difficulty coping as a result of disease/treatment	■	■
Distress of initial diagnosis	■	■
Fear of future diagnostic tests	■	■

Characteristic	I	LC
Fear of metastasis	■	■
Control of things in your life	■	■
Amount of uncertainty about the future	■	■

■ = From the exploratory analysis, had a t value of ≥ 2.

Table 2

Demographic, Clinical, and Treatment Characteristics of the Patients (N = 396)

Characteristic	Mean (SD)
Age (years)	54.9 (11.6)
Education (years)	15.7 (2.6)
Self-Administered Comorbidity Questionnaire score	4.3 (2.8)
Karnofsky Performance Status score	93.2 (10.3)
	%
Non-white	35.4
Married or partnered	41.5
Lives alone	24.1
Employed	47.5
Postmenopausal	62.3
Stage of disease	
0	18.3
I	37.9
IIA, IIB	35.4
IIIA,IIIB,IIIC,IV	8.3
Neoadjuvant chemotherapy	19.8
Type of surgery	
Breast conservation	79.9
Mastectomy	20.1
Sentinel lymph node biopsy	82.4
Axillary node dissection	37.4
Underwent reconstruction at time of surgery	21.6
Received adjuvant radiation therapy in first six months	56.6
Received adjuvant chemotherapy in the first six months	33.6
Symptom severity scores prior to surgery	Mean (SD)
Center for Epidemiological Studies-Depression score	13.7 (9.8)
Trait Anxiety Inventory score	35.3 (9.0)
State Anxiety Inventory score	41.8 (13.5)

Characteristic	Mean (SD)
General Sleep Disturbance Scale score	48.3 (21.6)
Lee Fatigue Scale - Fatigue score	3.1 (2.4)
Lee Fatigue Scale - Energy score	4.9 (2.5)
Attentional Function Index score	6.6 (1.9)

Table 3

Hierarchical Linear Model of Depressive Symptoms

	Coefficient (SE)	
	Unconditional Model	**Final Model**
Fixed Effects		
Intercept	13.830 (.458)$^{+}$	14.791 (.453)$^{+}$
Time[a] (linear rate of change)	−.480 (.074)$^{+}$	−.478 (.068)$^{+}$
Time invariant covariates		
Intercept:		
Married or partnered		2.448 (.526)$^{+}$
Receipt of adjuvant chemotherapy		1.426 (.557)*
Trait anxiety		.348 (.036)$^{+}$
State anxiety		.128 (.024)$^{+}$
Attentional function		−.665 (.174)$^{+}$
Sleep disturbance		.090 (.015)$^{+}$
Changes in appetite		.537 (.108)$^{+}$
Hours per day in pain		.150 (.056)**
Fear of metastasis		.268 (.079)**
Linear:		
Depressive symptoms prior to surgery × time		−.041 (.007)$^{+}$
Distress at initial cancer diagnosis × time		−.070 (.025)**
Variance components		
In intercept	66.038^{+}	10.940^{+}
In linear rate	.749^{+}	.409^{+}
Goodness-of-fit deviance (parameters estimated)	17115.210 (6)	16657.111 (17)
Model comparison (x^2)		458.099 (11)$^{+}$

* $p < 0.05$;

** $p < 0.01$;

$^{+}$ $p < 0.001$

[a] Time was coded zero at the time of the preoperative visit.