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BRIEF REPORT

# Randomized Controlled Trial of Cognitive Behavioral Stress Management in Breast Cancer: A Brief Report of Effects on 5-Year Depressive Symptoms

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***Objective:*** Survivors of breast cancer experience stress and are at risk for depressive symptoms following primary treatment. Group-based interventions such as cognitive–behavioral stress management (CBSM) delivered postsurgery for nonmetastatic breast cancer (BCa) were previously associated with fewer depressive symptoms over a 12-month follow-up; few studies have examined the longer-term benefits of such psychosocial interventions. This 5-year follow-up study of a previously conducted trial (#NCT01422551) tested whether group-based CBSM following surgery for nonmetastatic BCa was associated with fewer depressive symptoms. ***Methods:*** Women ($N = 240$) with Stage 0-IIIb BCa were recruited 2–10 weeks postsurgery and randomized to a 10-week CBSM intervention group or a 1-day psycho-educational control group. Women were recontacted 5 years poststudy enrollment and reconsented to participate in the follow-up study ($N = 130$). Depressive symptomatology was assessed using the Center for Epidemiologic Studies-Depression scale (CES-D). ANOVA and ANCOVA analyses were employed to test for group differences on the CES-D at 5-year follow-up accounting for relevant covariates. ***Results:*** Participants assigned to CBSM reported significantly fewer depressive symptoms ($M = 9.99$, $SE = 0.93$) at the follow-up compared with those in the control group ($M = 12.97$, $SE = 0.99$), $p = .030$. With covariates, the group difference remained significant, $p = .012$. ***Conclusion:*** Women who received CBSM postsurgery for BCa reported fewer depressive symptoms than those in the control group in this 5-year follow-up. Psychosocial interventions early in treatment may influence long-term psychological well-being in BCa survivors.

*Keywords:* breast cancer survivors, depressive symptoms, cognitive–behavioral stress management

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Breast cancer survivors (BCS) are at risk for mood disorders such as depression, for which rates are as high as 14.9%–19.2% in oncology populations (Mitchell et al., 2011). In BCS, depression is associated with negative outcomes such as sleep disturbances, pain, fatigue, poor quality of life (QOL; Reyes-Gibby et al., 2012), and reduced long-term treatment adherence (van Wilgen, Dijkstra,

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Stewart, Ranchor, & Roodenburg, 2006). Psychosocial interventions are effective during treatment for early stage breast cancer (BCa) and are shown to alleviate depressive symptoms (Jacobsen & Jim, 2008; Li, Fitzgerald, & Rodin, 2012). Specifically, during BCa treatment, cognitive–behavioral stress management (CBSM) improved QOL and reduced cancer-related anxiety and depressive symptoms (Antoni et al., 2001; Antoni et al., 2006a,2006b). Recent analyses revealed additional CBSM effects on sleep quality and fatigue-related interference (Vargas et al., in press). Despite these findings, there is a need to examine the more long-term effects of psychosocial interventions delivered during primary treatment for BCa (Ganz et al., 2002). As CBSM targets factors contributing to depressive symptoms including cognitive appraisal, coping, social support, and distress (Bigatti, Steiner, & Miller, 2012), it is possible that early intervention provides a long-term protective effect against depressive symptoms. This study tested whether women with BCa assigned to CBSM following surgery report fewer depressive symptoms at 5-year follow-up.

## Method

### Participants and Procedures

This study was a 5-year follow-up from a single center, single blind, randomized controlled trial approved by the Institutional Review Board and conducted within the Psychology Department at the University of Miami from 1998–2005. Participants were 240 women with Stage 0-IIIb BCa randomized to a 10-week group-based CBSM intervention ($N = 120$) or a 1-day psycho-educational control group ($N = 120$) 2–10 weeks postsurgery. Exclusionary criteria included present or past major depressive disorder, psychosis, or suicidality. Women completed three follow-up assessments during the study period. Details of the parent study are described in the initial interim reports (Antoni et al., 2006a) and recent reports with the final sample (Vargas et al., in press; National Institutes of Health Clinical Trial *NCT01422551*).

A follow-up assessment was added to the protocol and conducted 5-years post enrollment. Participants ($N = 240$) were recontacted and asked to participate in a study involving a questionnaire about depressive symptoms and general health status. Participants were reconsented and mailed the completed questionnaire by blinded research assistants.

### Study Conditions

The CBSM intervention was a 10-week group based intervention for women undergoing BCa treatment (Antoni, 2003). CBSM incorporates cognitive–behavioral therapy (e.g., cognitive reframing, assertiveness training) and relaxation training (e.g., progressive muscle relaxation) to decrease stress and negative mood. The control group was a 1-day psychoeducational (PE) "self-help" seminar in a classroom setting within the corresponding 10-week intervention period. Women were provided with general information about BCa care, health, and stress management summaries, but there were no structured opportunities to practice these techniques.

### Measures and Analyses

**Depressive symptoms.** At 5-year follow-up the 20-item Center for Epidemiologic Studies–Depression Scale (CES-D) was self-administered (Radloff, 1977). Scores range from 0–60, with higher scores indicating greater depressive symptoms over the past week. The CES-D has been shown to be reliable for use with women with BCa (Hann, Winter, & Jacobsen, 1999) and showed good reliability in the present sample (Cronbach's alpha = .90).

**Demographic and covariate data.** Self-reported demographics (i.e., socioeconomic markers, medical/treatment factors) were collected at baseline. Although the CES-D was not administered at baseline, depressive symptoms were measured via interview with the Hamilton Depression Rating Scale (HDRS Hamilton, 1960) and used as a covariate in adjusted analyses. At 5-year follow-up, women reported on BCa recurrence and medical status.

**Statistical analyses.** Chi-square goodness of fit tests and one-way ANOVAs (SPSS v.19) determined whether women who participated in the follow-up study were characteristically different from those who did not participate. A univariate ANOVA determined whether women assigned to the CBSM intervention versus the PE control condition differed on 5-year depressive symptoms. ANCOVAs assessed group differences on 5-year depressive symptoms while controlling for *demographic* (age at baseline, race/ethnicity, income, education), *cancer-related* (stage of BCa, chemotherapy, radiation therapy, hormone therapy, recurrence, time from surgery to baseline), *health-related* (psychotropic medication use, comorbidities), and *psychosocial* (baseline HDRS) factors added individually to the model. In an effort to determine whether the relationship between study condition and 5-year CES-D scores was related to baseline distress levels, we ran a moderated regression analysis with baseline HDRS as the moderator. Women were classified in high (HDRS $>$ 7) and low (HDRS $<$ or = 7) baseline HDRS subgroups (Hamilton, 1960) and covariates from the primary analysis were included.

## Results

### Sample Characteristics

Of the 240 women recontacted to participate in the follow-up study, 75 (31.3%) were unreachable, 11 (4.6%) had requested no further contact, nine (3.8%) did not return the questionnaire, eight (3.3)% were not interested, and seven (2.9)% were deceased. The present sample includes 130 (54.1%) women from the previous study ($N =$ 70 CBSM intervention; $N = 60$ PE control). See supplemental CONSORT figure. Participation in the follow-up study was not significantly related ($p > .05$) to original study condition (CBSM vs. PE). There were no significant study group differences on demographic characteristics, medical or treatment-related factors, psychosocial status, or use of psychotropic medications. See Table 1 for descriptive details by study condition (CBSM vs. PE).

Women from the parent study (Vargas et al., in press) who participated in the 5-year follow-up study were older at baseline[1] than those who did not participate, $F(1, 238) = 6.73$, $p = .010$, and had less days elapsed from the initial surgery to baseline assessment, $F(1, 229) = 16.66$, $p < .001$. Age at baseline and days from surgery to baseline were included as covariates in all additional analyses. Participants and nonparticipants were not different on

[1] The interaction between age and study group in predicting 5-year CES-D was not significant ($p > .05$).

Table 1
*Means, Standard Deviations, and Frequencies of All Study Covariates by Group*

| Variable | Control | Intervention | Statistic | *p* |
|---|---|---|---|---|
| Age at baseline (in years) | 57.43 (8.64) | 56.10 (8.95) | $F$ (1, 128) = 0.74 | .39 |
| Race/ethnicity | | | $\chi^2(3) = 1.41$ | .70 |
| White non-Hispanic | 41 (68.3%) | 52 (74.3%) | | |
| Hispanic | 13 (21.7%) | 14 (20.%) | | |
| African American | 4 (6.6%) | 4 (5.7%) | | |
| Asian | 1 (1.7%) | 0 | | |
| Income (in thousands of dollars) | 75.45 (52.11) | 73.90 (40.26) | $F$ (1, 109) = 0.03 | .86 |
| Education (in years) | 15.27 (2.48) | 15.73 (2.27) | $F$ (1, 128) = 1.23 | .27 |
| Stage at diagnosis | | | $\chi^2(3) = 0.96$ | .81 |
| 0 | 8 (13.3%) | 10 (14.3%) | | |
| I | 27 (45.0%) | 28 (40.0%) | | |
| II | 23 (38.3%) | 28 (40.0% | | |
| III | 1 (1.7%) | 3 (4.3%) | | |
| Received chemotherapy | | | $\chi^2(1) = 0.09$ | .76 |
| Yes | 30 (50.0%) | 37 (52.9%) | | |
| No | 28 (46.70%) | 31 (44.3%) | | |
| Received radiation therapy | | | $\chi^2(1) = 0.01$ | .91 |
| Yes | 33 (55.0%) | 38 (54.3%) | | |
| No | 25 (41.7%) | 30 (42.9%) | | |
| Received anti hormonal therapy | | | $\chi^2(1) = 0.63$ | .43 |
| Yes | 38 (63.3%) | 49 (70.0%) | | |
| No | 20 (33.3%) | 19 (27.1%) | | |
| Breast cancer recurrence at 5 years | | | $\chi^2(4) = .75$ | .86 |
| No, remained cancer free | 53 (88.3%) | 62 (88.6%) | | |
| Yes, recurrence | 2 (3.3%) | 4 (5.7%) | | |
| New primary | 4 (6.7%) | 3 (4.3%) | | |
| Unsure if new primary or recurrence | 1 (1.7%) | 1 (1.4%) | | |
| Days from surgery to baseline | 35.97 (19.71) | 34.66 (19.74) | $F$ (1, 126) = .14 | .71 |
| Baseline anti depressant medication | | | $\chi^2(1) = 0.06$ | .82 |
| Yes | 13 (21.7%) | 14 (20.%) | | |
| No | 47 (78.3%) | 56 (80.0%) | | |
| Baseline anti anxiety medication | | | $\chi^2(1) = .34$ | .56 |
| Yes | 20 (33.3%) | 20 (28.6%) | | |
| No | 40 (66.7%) | 50 (71.4%) | | |
| Baseline sleep medication | | | $\chi^2(1) = .30$ | .59 |
| Yes | 18 (30.0%) | 18 (25.7%) | | |
| No | 42 (70.0%) | 52 (74.3%) | | |
| Baseline pain medication use | | | $\chi^2(3) = 2.06$ | .15 |
| Yes | 28 (46.7%) | 24 (34.3%) | | |
| No | 33 (53.3%) | 46 (65.7%) | | |
| Charlson Comorbidity Index at 5 yrs | 1.11 (2.0) | 1.25 (2.14) | $F$ (1, 123) = 0.15 | .70 |
| Hamilton Depression Rating–Baseline | 7.6 (5.5) | 7.36 (5.67) | $F$ (1, 123) = 0.06 | .81 |

12-month outcomes including negative affect and cancer-specific distress.

## Intervention Effects

The average CES-D score at 5-year follow-up was 11.38 ($SD$ = 7.80). Uncontrolled, women assigned to CBSM reported significantly fewer depressive symptoms at 5-year follow-up ($M$ = 9.99, $SE$ = 0.93) than women in the control group ($M$ = 12.97, $SE$ = 0.99), $F(1, 126) = 4.8$, $p = .030$, partial $\eta^2 = 0.04$. The group difference in CES-D scores at 5-year follow-up remained significant while controlling for baseline depressive symptoms on the HDRS and other previously mentioned covariates: Women assigned to CBSM had significantly fewer depressive symptoms at 5-year follow up ($M$ = 9.22, $SE$ = 0.81) than women in the control group ($M$ = 12.30, $SE$ = 0.86), $F(1, 76) = 6.61$, $p = .012$, partial $\eta^2 = 0.08$. The uncontrolled group difference in CES-D scores of 2.98 ($SE$ = 1.36, $p = .030$, 95% CI [.29, 5.67]) was a small-medium effect ($d = .32$; Cohen, 1988). With 130 participants, the power to detect a group difference of this magnitude of .32 is adequate (93%). When controlling for theoretically supported covariates and baseline depressive symptoms, the group difference in CES-D scores of 3.10 ($SE$ = 1.12, $p = .012$, 95% CI [.72, 5.46]), was a small-medium effect ($d = .34$). With 130 participants and all covariates, the power to detect a group difference of this magnitude was adequate (93%).

In the moderated regression analysis, the baseline HDRS subgroup by study condition interaction was not significant in predicting 5-year CES-D scores ($p = .858$), suggesting that the effects of the intervention on longer term depressive symptoms did not depend on baseline levels of depressive symptoms.

## Discussion

Women who received CBSM intervention reported fewer depressive symptoms than women in the PE control group at 5-year

follow-up. The magnitude of the group difference, confidence intervals, and statistical power suggest the results were both statistically and clinically significant. The average 5-year CES-D score in this study was 11.38 ($SD$ = 7.80), which is comparable with CES-D scores in other posttreatment BCS studies. Other BCS studies have reported CES-D scores of 12.70 up to 6 months posttreatment ($SD$ = 10.73; Deshields, Tibbs, Fan, & Taylor, 2006), 10.50 at > 1-year posttreatment ($SD$ = 8.30; van Wilgen et al., 2006), and 10.30 at 3-years posttreatment, with scores being statistically similar at the > 5-year posttreatment follow-up (Ganz et al., 2002). In two studies with healthy age and gender-matched control samples, the reported CES-D mean was 8.30 (van Wilgen et al., 2006) and 8.67 (Lewinsohn et al., 1997). The mean CES-D scores in both of these healthy samples approached 5-year values reported in our CBSM condition ($M$ = 9.22). Thus, women assigned to CBSM revealed 5-year depressive symptom scores similar to norms for healthy controls, and women in the control group remained within the range of cancer patients undergoing active treatment, scoring nearly 33% higher ($M$ = 12.30) than CBSM cases.

Findings suggest that women given the opportunity to learn stress management while undergoing active treatment may benefit into survivorship. Studies have shown group-based cognitive–behavioral interventions to reduce depressive symptoms in early stage BCa over 1–2 years following treatment (Li, Fitzgerald, & Rodin, 2012; Antoni et al., 2006a). The present study showed that CBSM continued to mitigate depressive symptoms up to 5 years later. As intervention effects on depressive symptoms did not depend on baseline distress levels, our findings are best seen as evidence for an intervention benefit for BCa patients who present with and without elevated depressive symptoms during treatment.

These findings have implications for the clinical management of BCS and risk for depressive symptoms in long-term survivorship (Deshields et al., 2006). Depressive symptoms in BCS have been associated with poorer QOL, less therapy compliance, longer hospital stays, and biological processes related to BCa disease progression (van Wilgen et al., 2006). It has been recommended that cancer survivor care plans include evaluation of the psychosocial burden associated with BCa diagnosis (Ganz & Hahn, 2008). This finding calls attention to the use of approaches such as CBSM early on to optimize mental health outcomes in BCS posttreatment.

This sample was predominately middle class, highly educated, younger than average at diagnosis, and motivated to participate in health-related research, limiting the generalizability of findings. However, approximately one third of the sample identified as an ethnic minority, increasing generalizability to diverse populations of BCS. Neither study group mean exceeded the CES-D cutoff (i.e., ≥ 16); thus, these BCS do not report clinically significant depressive symptoms. Given that women were not aware they would be recontacted 5-years postenrollment, it can be considered a strength that 88% of reachable women participated. Finally, the inclusion of theoretically supported covariates in our analyses indicated that intervention-related differences in depressive symptoms were robust above and beyond phenomena occurring over the survivorship period.

Future research should seek to understand how postsurgical group-based CBSM reduces long-term depressive symptoms. CBSM reduces cancer-specific anxiety and negative affect for at least 12 months (Antoni et al., 2006b), which may equip women for anxiety-provoking stimuli during survivorship, such as awaiting follow-up mammogram results and fears of recurrence. Other CBSM intervention targets are potential mediators, including cognitive restructuring, coping self-efficacy, social support utilization, mood disturbance, and perceived stress management skills (Moyer et al., 2012; Stanton, Luecken, MacKinnon, & Thompson, 2013).

This 5-year follow-up study of women with nonmetastatic BCa showed that participants who received a 10-week CBSM intervention following surgery exhibited fewer depressive symptoms than those in a psychoeducational control group. Implementing psychosocial interventions in the early phases of treatment may influence long-term psychological well-being.

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