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The Association between Pre-treatment Occupational Skill Level and Mood and Symptom Burden in Early-stage, Postmenopausal, Breast Cancer Survivors during the First Year of Anastrozole Therapy

Bethany D. Nugent, Ph.D(c), BSN, RN¹, Susan M. Sereika, Ph.D¹, Margaret Rosenzweig, Ph.D, CRNP-C, AOCN, FAAN¹, Michael McCue, Ph.D², John D. Merriman, Ph.D, RN¹, and Catherine M. Bender, Ph.D, RN, FAAN¹

¹University of Pittsburgh School of Nursing, Pittsburgh, PA, U.S.A

²University of Pittsburgh School of Health and Rehabilitation Sciences, Pittsburgh, PA, U.S.A

Abstract

Purpose—Previous research has explored occupational activity of breast cancer survivors but has not examined the influence of occupational level on symptoms prospectively. The purpose of this study was to examine the relationship between occupational classification and changes in mood and symptom burden for postmenopausal breast cancer survivors during the first year of anastrozole therapy.

Methods—This was an exploratory secondary analysis in 49 postmenopausal women receiving anastrozole therapy for early-stage breast cancer. Participants reported their occupation at baseline and completed self-report questionnaires measuring mood and symptom burden at baseline, 6 and 12 months. Occupation was classified according to 4 major Skill Levels delineated by the International Standard Classification of Occupations (ISCO).

Results—Breast cancer survivors employed at occupational Skill Levels 1 through 3 reported significantly higher depressive symptoms, fatigue, and total symptoms on average than those employed at ISCO Skill Level 4. After adjusting for multiple comparisons, this pattern remained for the musculoskeletal, vasomotor, and gastrointestinal symptom subscales.

Conclusions—Breast cancer survivors employed at lower Skill Levels (i.e., ISCO 1–3) reported poorer mood and greater symptom burden than breast cancer survivors employed at a higher Skill Level (i.e., ISCO 4). Assessing baseline occupation of occupationally active breast cancer survivors may improve understanding of the association between types of occupations and

Correspondence concerning this manuscript should be addressed to Catherine M. Bender, School of Nursing, University of Pittsburgh, 415 Victoria Bldg., 3500 Victoria St. Pittsburgh, PA 15261, Contact: cbe100@pitt.edu; 412-624-3594; F: 412-383-7293.

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Compliance with ethical standards

Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards

Informed consent: Informed consent was obtained from all individual participants included in the study.

mood and symptom trajectories and may inform development of interventions to mitigate symptom severity in order to help breast cancer survivors maintain optimal occupational function and adherence to therapy.

Keywords

occupational skill; employment; cognitive function; breast cancer survivors; anastrozole therapy

Introduction

Returning to and sustaining employment for cancer survivors is challenging indeed; approximately 40% of all cancer survivors never return to work.[1] Of cancer survivors who remain working, up to 13% stop working within 4 years of diagnosis.[2] Three main categories of factors influence cancer survivors' ability to return to work and maintain pre-diagnosis occupational roles: disease and treatment-related factors (e.g. cancer site, disease stage, treatment, symptoms); work-related factors (e.g. workload, job demands, social climate, employer support); and person-related factors (e.g. age, gender, education level). [1,3,4] Disease and treatment-related symptoms may influence the ability of cancer survivors to return to work, maintain pre-diagnosis levels of work productivity and advance in careers. Disability and unemployment in cancer survivors results in lost potential and tremendous personal and societal costs. Few studies have examined the relationship between disease and treatment symptoms and the ability to maintain occupational roles and no studies to date have examined this relationship in postmenopausal women during aromatase inhibitor (AI) therapy for early-stage breast cancer. Understanding the relationship between work-related factors and symptoms is crucial in preventing work disability, maintaining occupational roles, and achieving career potential.

Annually, over 100,000 postmenopausal women in the United States are diagnosed with estrogen receptor positive breast cancer, the most common breast cancer diagnosis.[5] This type of cancer is commonly treated with AI, an endocrine therapy prescribed after initial surgery and taken daily for 5 or more years; since AI are taken orally and often without concurrent chemotherapy many maintain occupational roles during treatment. Thus, breast cancer survivors receiving AI are an ideal cohort to study when examining factors that may influence the symptom experience and maintenance of occupational roles throughout active cancer treatment.

Aromatase inhibitors have side effects including changes in mood, cognitive complaints, dyspareunia, diarrhea, gynecological complaints, hot flashes, arthralgia, and musculoskeletal difficulties including osteopenia and fractures. [6–8] These symptoms are not usually severe enough to be dose-limiting, but may be bothersome and affect employment. In the general population, mood disorders (e.g. anxiety; depression) are a major cause of loss in work productivity.[9] Fatigue is an independent predictor of a cancer survivors' ability to return to work.[4] The relationship between disease and treatment-related symptoms and women's occupational role may depend on each woman's day-to-day activities. The International Standardized Classification of Occupations (ISCO) has grouped occupations into four Skill

Levels based on the general physical and cognitive requirements associated with occupational role. [10]

Work-related factors are complex and multifactorial. However, evaluation of job classification and the accompanying tasks involved is an important step in clearly understanding which cancer survivors may have greatest difficulty in maintaining occupational roles. Studies examining employment rarely take into consideration how cancer and its treatment may interfere with a survivor's ability to perform certain job tasks. One study examining job tasks in men with prostate cancer found increased difficulty in maintaining occupational roles particularly when the jobs involved highly physical tasks. [11] Difficulty concentrating and learning new things were also associated with maintenance of occupational roles.[11]

Previous studies of breast cancer survivors who maintained occupational roles found that they experienced greater age-adjusted work limitations than non-cancer controls; moreover, these limitations were predicted by fatigue level [12] and patient-reported cognitive limitations at work [13]. No study prospectively examined the role of symptoms in maintenance of occupational roles for breast cancer survivors. This study's aims were to 1) examine differences in changes in mood (depressive symptoms and anxiety) for breast cancer survivors during the first year of AI therapy between occupational classifications (Skill Level 4 versus Skill Levels 1–3) before therapy; and 2) examine differences in changes in reported symptom burden during the first year of AI therapy between those employed at Skill Level 4 and those employed at lower Skill Levels (Skill Level 1–3) before therapy.

Methods

This study was part of a larger longitudinal study, approved by the University of Pittsburgh Institutional Review Board, and examines cognitive function in postmenopausal women with early-stage breast cancer receiving AI therapy (R01 CA107408). Informed consent was obtained from all individual participants included in the study. Recruitment occurred between 2005 and 2012 through the University of Pittsburgh Cancer Institute Magee Women's Breast Cancer Program. The parent study assessed cognitive function at baseline (pre-AI therapy) and at 6 and 12 months after therapy initiation. Data for the current study are drawn from the baseline, 6-month, and 12-month assessments.

Participants

Parent study inclusion criteria were women who were: postmenopausal with breast cancer stages I–IIIa; post-surgery; age ≥ 75 years; able to speak and read English; educated ≥ 8 years; without history of neurological illness or previous cancer (except non-melanoma skin cancer); not currently receiving hormone replacement therapy; and not hospitalized for psychiatric illness within two years. The subset of women considered for inclusion in this secondary analysis received AI without chemotherapy (n=158) and had completed symptom questionnaires at baseline (i.e., pre-AI therapy), and at 6 months and 12 months post-AI initiation. They also reported at baseline that they were currently employed outside the home. After applying these criteria, 49 women were included in our analysis.

Instruments

Demographic and clinical characteristics—Participants completed a demographic questionnaire at baseline, which assessed age, race, marital status, education, employment, and occupation. Clinical characteristics were collected and verified using medical records.

Occupational classification—Participants reported their occupation on a baseline demographic questionnaire, which was re-coded using the International Standard Classification of Occupations (ISCO) [14] Skill Level, which formed fewer, more homogenous groups in terms of the tasks/skills required. This allowed for simpler and meaningful comparisons across skill groupings. The ISCO has four distinct occupational Skill Levels:

Skill Level 1: Skill Level 1 [14] occupations typically involve performance of simple and routine physical or manual tasks and may require physical strength and/or endurance. Some Skill Level 1 jobs require basic literacy or numeracy but this is not a major component of the work. Examples of Skill Level 1 occupations include cleaners, freight handlers, garden laborers, and kitchen assistants.

Skill Level 2: Skill Level 2 [14] occupations typically involve performance of tasks such as operating machinery/equipment; driving vehicles; maintenance of electrical and mechanical equipment; and manipulation, ordering and storage of information. Many Skill Level 2 occupations require relatively advanced literacy and numeracy, good interpersonal communication, and a high level of dexterity. Examples of Skill Level 2 occupations include butchers, bus drivers, secretaries, clerks, sales assistants, police officers, hairdressers, electricians and mechanics.

Skill Level 3: Skill Level 3 [14] occupations typically involve performance of complex technical and practical tasks using extensive factual, technical and procedural knowledge in a specialized field. Skill Level 3 occupations generally require a high level of literacy and numeracy and well-developed communication skills, including the ability to understand complex written material, prepare reports and communicate with distressed individuals. Examples of Skill Level 3 occupations include managers, laboratory technicians, legal secretaries, commercial sales representatives, and computer technicians.

Skill Level 4: Skill Level 4 occupations typically involve performance of tasks requiring complex problem solving and decision making based on extensive theoretical and factual knowledge in a specialized field. Occupations at Skill Level 4 generally require advanced literacy and numeracy, and excellent communication skills, including the ability to understand complex written material and communicate complex ideas in writing and orally. Examples of Skill Level 4 occupations include sales managers, engineers, secondary education teachers, doctors, nurses, and computer systems analysts.

For this analysis, Skill Levels 1 to 3 were considered as one group due to sample distribution and compared to Skill Level 4. Higher Skill Levels involve greater complexity and range of tasks. Skill Level 4 occupations typically necessitate, at minimum, a bachelor's degree, while lower Skill Level occupations often require an associate's degree, vocational training,

or high school education. Individuals with at least bachelor's degrees generally have occupations requiring higher Skill Level [10]; thus, women in occupational roles that require Skill Level 4 may experience different difficulties than breast cancer survivors in lower Skill Level occupations, given the complexity required to maintain these occupational roles.

Depressive symptoms—Symptoms of depression were assessed using the Beck Depression Inventory-II (BDI-II)[15], a 21-item Likert scale questionnaire measuring affective and somatic depressive symptoms. Total scores range from 0 to 63, with higher scores indicating greater depressive symptoms. The BDI-II has high internal consistency (Cronbach alpha = 0.91) [16] and one-week test-retest reliability (Pearson $r = 0.93$) [15] indicating that it is not overly sensitive to daily mood variations.

Anxiety—Anxiety symptoms were measured using the Profile of Mood States-Short Form (POMS-SF) tension-anxiety subscale, which has good internal consistency (Cronbach's alpha = 0.80) and product moment correlation (Pearson $r = 0.85$) in a sample of breast cancer patients. [17] The tension-anxiety subscale consists of 9 items with total subscale scores ranging from 0 to 36, with higher scores indicating greater anxiety.

Fatigue—Fatigue was measured using the POMS-SF fatigue-inertia subscale, which has been used to measure fatigue in cancer patients with excellent internal consistency (Cronbach alpha= 0.89) [17], 48-hour test-retest reliability (Pearson $r = 0.74$), and construct validity demonstrated through inter-instrument correlational analysis with other subscales of the POMS-SF explaining 83% of the variance in responses [18]. The fatigue-inertia subscale consists of 7 items with total subscale scores ranging from 0 to 28, with higher scores indicating greater fatigue.

Symptom experience—Symptom burden was measured using the 42-item Breast Cancer Prevention Trial (BCPT) checklist [19-20], which measures symptoms during breast cancer treatment. [20] There are 8 subscales, each representing a clinically relevant cluster of symptoms: cognitive, musculoskeletal, vasomotor, nausea, vaginal, sexual, bladder, and body image. Total scores on the BCPT range from 0 (no symptoms) to 168 (extremely bothersome symptoms). The BCPT subscales demonstrated adequate internal consistency (Cronbach's alpha greater than .70), except the gastrointestinal symptoms (Cronbach's alpha = .624), dyspareunia (Cronbach's alpha = 0.618), weight problems (Cronbach's alpha = 0.616), and gynecological symptoms (Cronbach's alpha = 0.557). To be included in the analysis, women had to have answered at least 80% of the items that made up each score.

Data Analysis

Standard descriptive statistics and frequency distributions were generated to characterize the total sample as well as the two Skill Levels groups. We assessed for differences in demographic and clinical characteristics between the Skill Level groups using two-sample t-tests for continuous variables and Fisher's exact tests for categorical variables. To test the aims of the study we used a repeated measures multivariate analysis of covariance (RM-MANCOVA). The assumption for homogeneity of group variance-covariance matrices were not satisfied for age and years of education. The assumptions of normality of residuals was

met for all independent variables in our model except for years of education, but RM-MANCOVA is robust against violations of normality. To improve the distribution of residuals, we considered the applications of the square root and log base 10 transformations to the data. Analyses using transformed data did not change the conclusions drawn, thus we reported results from untransformed data in their original scaling.

We conducted a RM-MANCOVA to examine relationships between occupational Skill Level and mood (i.e., scores for BDI-II, POMS tension/anxiety subscale) at baseline, 6, and 12 months, after controlling for years of education as a covariate in the model since this was significantly different between the skill level groupings. We examined polynomial contrasts and added a covariate, age, for the analysis of depressive symptoms.[21] Assumptions of the RM-MANCOVA method (i.e., normality, linearity, sphericity, homogeneity of regression slopes, and reliable measurement of the covariate) [22] were met for dependent variables in the model. To protect against inflation of Type I error when looking at multiple dependent variables, we first examined the results of multivariate tests and only if the multivariate test was statistically significant did we proceed to look at results of the univariate tests to see which variables, more specifically, demonstrated statistical significance. For aim 2, we used a RM-MANCOVA to examine changes over time in reported symptom burden overall as well as by specific symptom domains by those employed at Skill Level 4 and those employed at Skill Level 1–3. Partial eta-square values were calculated as a measure of effect size for group mean differences. Two-sided hypothesis testing was conducted at the .05 significance level using IBM® SPSS® Statistics, Version 22.0 (IBM Corp., Armonk, New York).

Results

Participant characteristics

Table 1 summarizes participant characteristics by Skill Level grouping. Approximately 59% of the sample were employed at Skill Level 4, while the rest were employed at Skill Level 1 through 3. As expected, women employed in occupations at Skill Level 4 had significantly more education ($p<.001$) than women employed in lower Skill Level occupations. Thus, years of education was included as a covariate in our model. No other significant differences between occupational skill groups were found.

Occupational Skill Level and Mood

RM-MANCOVA examining the relationship between subjects' Skill Level group and their mood at baseline, 6, and 12 months after beginning AI therapy showed a main effect of group on mood, $F(2,45)=4.86$, $p=.01$, partial $\eta^2=.178$. Compared to individuals employed at Skill Level 4, those employed at the lower Skill Levels reported significantly higher anxiety and depressive symptoms on average. The levels of anxiety ($p=.46$) and depressive symptoms ($p=.17$) did not significantly vary over time. Analysis revealed significant differences in the level of depressive symptoms between lower Skill Levels and Skill Level 4 over the first year of AI therapy, $F(1, 47)=4.29$, $p=.04$, partial $\eta^2=.09$ (Figure 1), but no significant differences for anxiety. See Table 2.

Occupational Skill Level and symptom experience

Total BCPT symptom scores and fatigue levels demonstrated a time effect, $F(2, 94) = 17.0$, $p < .001$, partial $\eta^2 = .266$, and group effect, $F(2, 94) = 4.9$, $p = .009$, partial $\eta^2 = .095$. The univariate tests for time, however, showed that only total BCPT had a significant time effect, $p < .001$, partial $\eta^2 = .181$. See Table 3. The test of between-subject effects showed that there are significant between group differences for both fatigue, $p = .009$, $\eta^2 = .169$, and total BCPT, $p = .023$, partial $\eta^2 = .105$. See Figure 1. More specifically, those at Skill Levels 1 through 3 reported significantly higher levels of fatigue and total symptom scores and this pattern persisted over the 1 year time period.

When exploring differences between the two occupational Skill Levels and the specific symptom domains of the BCPT over time using RM-MANCOVA, we found a significant time effect, $F(16, 28) = 3.4$, $p = .002$, partial $\eta^2 = .661$, and group effect, $F(8, 36) = 2.9$, $p = .014$, partial $\eta^2 = .390$. As summarized in Table 3, univariate tests revealed that musculoskeletal symptoms ($p < .001$), vasomotor symptoms ($p = .001$), dyspareunia ($p < .001$), bladder problems ($p = .017$), and weight concerns ($p = .011$) worsened over the 1-year study time frame. The test of between-subject effects showed that those employed at Skill Level 1 through 3 reported significantly more severe musculoskeletal ($p = .005$), vasomotor ($p = .028$), and gastrointestinal ($p = .010$) symptoms than those employed at Skill Level 4. See Figure 1. Though results were not statistically significant for each of the other BCPT subscales, it is worth noting that mean symptom burden scores for Skill Levels 1 through 3 were consistently higher across all three time points for cognitive complaints, musculoskeletal symptoms, vasomotor symptoms, gastrointestinal symptoms, bladder control, and weight concerns.

Discussion

This study suggests that occupational Skill Level is associated with mood and symptom burden in women receiving AI therapy for breast cancer, with a small effect size. In this longitudinal, observational study, women employed at Skill Levels 1 through 3 reported higher anxiety and depressive symptoms than those employed at the higher Skill Level (4). Women at lower Skill Levels also reported higher levels of symptom burden associated with AI therapy including fatigue, musculoskeletal complaints, vasomotor symptoms, gastrointestinal problems, and total symptom burden. From baseline through the first year of therapy, symptom burden related to AI therapy worsened for both skill-level groupings. However, women in the lower Skill Level grouping reported more severe symptom burden than those employed at the higher level in six (cognitive complaints, musculoskeletal symptoms, vasomotor symptoms, gastrointestinal symptoms, bladder control, and weight concerns) out of eight symptom subscales on the BCPT at each of the three time points measured in the study (baseline, 6 months, and 12 months).

Findings suggest that women employed at lower Skill Levels may be more bothered by symptoms during the first year of AI therapy, which might be related to lower Skill Levels typically involving high levels of physicality. It is also possible that women employed at lower Skill Levels may not have as comprehensive a benefits package or receive accommodations as easily as women employed at the highest Skill Level. With fewer benefits, those employed at lower Skill Levels may not be eligible for paid time off to attend

appointments to adequately address symptoms or may not have employers as willing to implement workplace accommodations, which may contribute to poorer mood and more bothersome symptoms.[23–26] Future research should investigate why breast cancer survivors employed at lower Skill Levels reported more bothersome symptoms than those employed at Skill Level 4. Future work should develop interventions to mitigate symptom burden for women beginning AI therapy who wish to maintain their occupational roles.

Results of this study may inform future studies of mood and symptom experience in women receiving AI for early stage breast cancer. This study suggests a proxy variable to help predict which breast cancer survivors may experience more severe symptoms and difficulty maintaining occupational roles from diagnosis through early treatment and survivorship. Many clinics routinely screen for symptom severity at office visits, but it is often unclear how the trajectory of mood and symptoms in a patient will develop over time. This study suggests assessment of the woman's occupation at baseline may help predict the severity of symptoms throughout the first year of treatment. Knowing the likely course of symptom severity before treatment provides a window of opportunity to counsel the woman about what she may experience, as well as the opportunity to develop and implement interventions which can prevent or treat these symptoms early, before they interfere with the ability to maintain an occupational role. It would be incorrect to assume that cancer survivors who remain employed during and after treatment have less severe symptoms and that their symptoms do not increase in severity over time. This knowledge is important because other studies have found that severity of symptoms predict poor adherence to treatment [27·28] and who will remain employed [12·24·29].

Studies of cancer survivors found that physical symptoms, depression, and fatigue were associated with ability to return to work.[4] Receiving advice from a healthcare provider about returning to work improves cancer survivors' ability to maintain employment.[24·30] Given that our study found significant associations between occupational Skill Level and both depression and symptom burden, the development of interventions aimed at assisting women, particularly those employed at the lower occupational Skill Levels, may mitigate the severity of symptoms experienced and assist them in maintaining occupational roles.

Study Limitations

The current study has several limitations that are relevant to data interpretation. First, this study is a secondary analysis of a larger study collecting longitudinal data of breast cancer survivors' cognitive function. The occupational skill-level groups were formed post hoc and additional, unmeasured confounding variables may have been associated with Skill Level. Skill Level was classified based on participant's job title at baseline. For our analyses, we assumed that the occupation reported at baseline remained unchanged over the first year of AI therapy. Therefore, we could not evaluate relationships between symptom burden and ability return to work or stay employed. Additionally, due to our limited sample size, we were unable to examine the relationships between symptoms and working full- or part-time. While the relationships between occupational classification and physical and psychological symptoms were statistically significant, the effect sizes were small. Future studies should examine the clinical significance of these relationships.

Future research should incorporate more sophisticated instruments of occupational classification and work function, which may yield a richer picture of occupation and the tasks involved. These instruments may also assess other important factors known to affect cancer survivors' employment status, including the workplace and employer adaptations. [2,24] Lastly, given the small sample size and the distribution of occupational Skill Level, future research with a larger sample size and more diverse occupational Skill Level classifications should be conducted to confirm findings in this exploratory study.

Conclusion

Despite these limitations, this study offers a unique perspective on the association between occupational Skill Level and the symptom burden of postmenopausal women receiving AI therapy for breast cancer. This study highlight the importance of considering the occupation of cancer survivors when assessing the symptom experience and predicting the degree of bother associated with symptoms during the first year of therapy. Future research with a larger, more diverse sample is needed to assess occupational Skill Level based on more specific ISCO occupational classification and to examine what work tasks and aspects of the work environment are most associated with mood and symptom severity. Including as a part of routine clinical care whether or not a breast cancer patient is employed and, if so, whether she is planning to continue working may add to the ability to examine symptoms in the context of a woman's occupation. Clinicians working with cancer survivors might consider asking about occupational function and difficulties to gain perspective on what aspects are most difficult. Finally, it will be important to expand the findings from our study to other cancer populations, and ultimately formulate efficacious interventions to reduce symptom severity and assist survivors in maintaining occupational roles for as long as possible.

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Figure 1a

Breast Cancer Prevention Trial (BCPT) Symptom Score

Figure 1b

Figure 1.
Trajectory of treatment-related symptoms

Table 1

Demographic and clinical characteristics at baseline by occupational group (N=49)

Characteristic	Skill Levels 1–3 <i>n</i> =20 (40.8%)	Skill Level 4 <i>n</i> =29 (59.2%)	Test Statistic	<i>p</i> -value
	Mean (<i>SD</i>)	Mean (<i>SD</i>)		
Age (years)	59.2 (1.7)	58.2 (0.8)	<i>t</i> =0.54	.631
Education (years)	13.0 (0.4)	17.0 (0.6)	<i>t</i> =5.18	<.001
Weeks since diagnosis (<i>n</i> =48)	8.9 (0.8)	8.6 (0.8)	<i>t</i> =0.23	.815
Weeks since first surgery	5.0 (0.5)	5.1 (0.6)	<i>t</i> =0.14	.888
	Percent (<i>n</i>)	Percent (<i>n</i>)		
Married or partnered (yes)	45.0 (9)	72.4 (21)	--	.075 ^a
White (yes)	100.0 (20)	100.0 (29)	--	1.000 ^a
Natural menopause (yes)	70.0 (14)	86.2 (25)	--	.133 ^a
HRT-ever (yes)	50.0 (10)	51.7 (15)	--	.568 ^a
Mastectomy (versus BCS) (<i>n</i> =47)	10.5 (2)	17.9 (5)	--	.685 ^a
Radiation therapy (yes) (<i>n</i> =46)	84.2 (16)	92.6 (25)	--	.635 ^a
Stage of disease:				
I	90.0 (18)	89.7 (26)	--	.486 ^a
IIa	10.0 (2)	3.4 (1)		
IIb	0.0 (0)	6.9 (2)		

SD standard deviation, *HRT* hormone replacement therapy, *BCS* breast conserving surgery^aFisher's Exact test

Table 2

Occupational skill level and mood over time

Mood	Skill Levels 1–3 <i>n</i> =20 (40.8%)	Skill Level 4 <i>n</i> =29 (59.2%)	Test Statistics	<i>p</i> -value
	Mean (<i>SD</i>)	Mean (<i>SD</i>)		
Depressive symptoms				
Baseline	7.9 (8.4)	3.9 (2.7)	$F_{\text{Group}}(1, 46) = 8.91$	.005
6 months	8.5 (9.4)	2.5 (2.3)	$F_{\text{Time}}(2, 92) = 0.68$	.512
12months	8.3 (9.9)	4.2 (4.3)	$F_{\text{Group} \times \text{Time}}(2, 92) = 1.83$	.166
Anxiety				
Baseline	8.0 (6.1)	6.6 (3.6)	$F_{\text{Group}}(1, 46) = 2.77$	.103
6 months	8.2 (7.4)	5.4 (3.6)	$F_{\text{Time}}(2, 92) = 0.72$	.487
12 months	7.0 (7.6)	5.1 (4.8)	$F_{\text{Group} \times \text{Time}}(2, 92) = 0.79$	.456

SD standard deviation

Table 3

Occupational skill level and symptom burden over time

Symptom	Skill Levels 1–3	Skill Level 4	Test Statistics	<i>p</i> -value
	Mean (SD)	Mean (SD)		
	<i>n</i> =20 (40.8%)	<i>n</i> =29 (59.2%)		
Fatigue				
Baseline	9.6 (8.8)	3.7 (3.2)	$F_{\text{Group}}(1, 47) = 9.56$	<.001
6 months	6.8 (6.0)	3.6 (3.7)	$F_{\text{Time}}(2, 94) = 1.95$	.009
12 months	8.2 (8.9)	4.0 (3.5)	$F_{\text{Group} \times \text{Time}}(2, 94) = 9.56$	.003
Total BCPT				
Baseline	22.4 (20.1)	14.5 (8.5)	$F_{\text{Group}}(1, 47) = 5.54$	.023
6 months	27.3 (22.3)	16.3 (10.0)	$F_{\text{Time}}(2, 94) = 10.42$	<.001
12 months	30.9 (23.9)	18.9 (11.3)	$F_{\text{Group} \times \text{Time}}(2, 94) = 1.18$	.311
	<i>n</i> =17 (37.8%)	<i>n</i> =28 (62.2%)		
Cognitive				
Baseline	2.1 (3.0)	1.5 (1.5)	$F_{\text{Group}}(1, 43) = 1.08$	.304
6 months	2.2 (2.6)	1.3 (1.7)	$F_{\text{Time}}(1.6, 69.4) = 0.19$	.784
12 months	2.1 (2.4)	1.8 (1.8)	$F_{\text{Group} \times \text{Time}}(1.6, 69.4) = 0.83$	.418
Musculoskeletal				
Baseline	3.9 (3.2)	2.3 (2.3)	$F_{\text{Group}}(1, 43) = 8.91$	.005
6 months	5.6 (4.2)	3.0 (2.7)	$F_{\text{Time}}(2, 86) = 8.39$	<.001
12 months	6.4 (4.3)	3.4 (2.8)	$F_{\text{Group} \times \text{Time}}(2, 86) = 1.28$	.285
Vasomotor				
Baseline	2.1 (2.8)	1.3 (1.2)	$F_{\text{Group}}(1, 43) = 5.19$	.028
6 months	3.3 (3.0)	1.9 (1.7)	$F_{\text{Time}}(2, 86) = 7.90$	.001
12 months	3.8 (3.5)	1.9 (1.4)	$F_{\text{Group} \times \text{Time}}(2, 86) = 1.36$	.261
Gastrointestinal				
Baseline	0.5 (1.1)	0.1 (0.4)	$F_{\text{Group}}(1, 43) = 7.18$	.010
6 months	0.8 (1.0)	0.3 (0.8)	$F_{\text{Time}}(1.7, 72.8) = 2.73$	.080
12 months	1.1 (1.7)	0.3 (0.8)	$F_{\text{Group} \times \text{Time}}(2, 86) = 0.79$	.437
Dyspareunia				
Baseline	0.4 (0.8)	1.4 (2.1)	$F_{\text{Group}}(1, 43) = 3.44$	.071
6 months	1.0 (2.0)	2.1 (2.4)	$F_{\text{Time}}(1.6, 69.3) = 10.44$	<.001
12 months	1.4 (1.9)	2.4 (2.3)	$F_{\text{Group} \times \text{Time}}(2, 94) = 0.00$	1.0
Bladder Control				
Baseline	1.1 (1.9)	0.5 (0.7)	$F_{\text{Group}}(1, 43) = 3.02$	.090
6 months	1.4 (2.1)	0.6 (1.0)	$F_{\text{Time}}(1.6, 68.1) = 4.78$	.017
12 months	1.8 (2.5)	0.8 (1.5)	$F_{\text{Group} \times \text{Time}}(1.6, 68.1) = 1.07$	.336
Weight Concerns				
Baseline	1.9 (2.4)	1.3 (1.4)	$F_{\text{Group}}(1, 43) = 1.68$	.202

Symptom	Skill Levels 1–3	Skill Level 4	Test Statistics	<i>p</i> -value
	Mean (<i>SD</i>)	Mean (<i>SD</i>)		
6 months	2.4 (2.2)	1.5 (1.8)	$F_{\text{Time}}(2, 86) = 4.8$	.011
12 months	2.6 (2.4)	2.0 (1.8)	$F_{\text{Group} \times \text{Time}}(2, 86) = 0.32$	.725
Gynecological				
Baseline	0.2 (0.6)	0.3 (0.5)	$F_{\text{Group}}(1, 43) = 0.02$	.904
6 months	0.4 (0.6)	0.4 (0.8)	$F_{\text{Time}}(2, 86) = 0.40$	.675
12 months	0.4 (0.7)	0.3 (0.7)	$F_{\text{Group} \times \text{Time}}(2, 86) = 0.02$	.942

SD standard deviation; *BCPT* Breast Cancer Prevention Trial Symptom Checklist