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Pretreatment Predictors of Short-term Nonadherence to Oral Hormonal Therapy for Women with Breast Cancer

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Abstract

Background—Adjuvant treatment with oral hormonal therapy improves clinical outcomes for breast cancer, but women have difficulty adhering to the five-year regimen.

Objective—To explore pretreatment predictors of short-term nonadherence to oral hormonal therapy for women with early stage breast cancer from the pretreatment assessment to six months after initiation of hormonal therapy.

Method—A secondary analysis was performed using data collected from 198 women enrolled in one of two longitudinal studies. Nonadherence was defined as the percentage of prescribed doses of hormonal therapy not taken during the first six months of therapy measured using electronic medication event monitoring. Information on predictor variables was measured at pretreatment using self-report and medical record review. Linear regression analysis was performed to examine associations between predictor variables and six-month nonadherence in a bivariate manner to first identify candidate predictors variables at $p < .20$ and then multivariately considering candidate predictors identified through stepwise and backward elimination regression methods.

Results—Participants were white (98.3%), well educated ($M = 15.0$; $SD = 2.9$ years of schooling), and on average 59.1 years of age ($SD = 7.5$). Mean nonadherence was 11.3%. Stepwise and backward elimination modeling algorithms identified a similar set of predictors associated with six-month nonadherence and explained 13.0% of the variance (adjusted $R^2 = .11$, standard error of the estimate = 0.28). Ductal carcinoma in situ tumor type ($p = .004$) and higher weight concern scores ($p = .003$) were associated with nonadherence.

Discussion—The findings suggest that additional examinations of associations of tumor type and symptom burden with nonadherence are indicated.

Keywords

medication nonadherence; breast neoplasms; tamoxifen; aromatase inhibitors

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For women with breast cancer, adjuvant treatment with oral hormonal agents has been shown to improve clinical outcomes. Five years of tamoxifen, a selective estrogen receptor modifier, is prescribed for pre and perimenopausal women with hormone receptor positive early stage breast cancer (Jonat, Pritchard, Sainsbury, & Klijn, 2006). Aromatase inhibitors (AIs), such as anastrozole, are superior to tamoxifen in reducing the risk of disease recurrence and contralateral disease in postmenopausal women (Newman & Singletary, 2007). Despite the clear therapeutic benefits of oral hormonal therapy, adherence, the "extent to which patients follow the instructions they are given for prescribed treatment" (Haynes, Ackloo, Sahota, McDonald, & Yao, 2008, p. 3), remains challenging for women with breast cancer.

Adherence and persistence to therapy are often examined together in research investigating adherence to oral anticancer agents, but they are distinct concepts (Ruddy, Mayer, & Partridge, 2009). Essentially, adherence measures the percent of correct doses taken as prescribed, whereas persistence assesses the number of days one takes medication (i.e., completion of therapy) (Cramer et al., 2008). Similarly, oral chemotherapies and oral hormonal therapies are often categorized together. Oral chemotherapy is a broad category of drugs of any type taken by mouth to treat cancer (American Cancer Society, 2012). Generally, oral chemotherapies are given for active treatment of cancer; oral hormonal therapies are usually prescribed for prevention of recurrence of breast cancer, and have mechanisms of action that are different from oral chemotherapy. In this report, we focus on short-term (six-month) adherence for women receiving oral hormonal therapy for prevention of recurrence of breast cancer.

A number of patient-, illness-, and treatment-related factors have been shown to affect nonadherence to both tamoxifen and AIs but with varied results. For example, researchers have examined patient-related factors such as age and socioeconomic status (SES) and their relationships to nonadherence to tamoxifen therapy; however, both younger (< 45 years) (Kahn, Schneider, Malin, Adams, & Epstein, 2007; Partridge, Wang, Winer, & Avorn, 2003) and older women (65 to 85 years) (Barron, Connolly, Bennett, Feely, & Kennedy, 2007; Partridge et al., 2003) have been shown to be more likely to discontinue tamoxifen therapy than women ages 45 to 65. Partridge et al. (2003) found that Non-white women were more likely to discontinue tamoxifen therapy than White women. Lebovits et al. (1990) found that women who discontinued oral chemotherapy had a significantly lower SES ($p < .02$) than women who continued their therapy; however, oral chemotherapeutic agents typically have different side effect profiles from those of oral hormonal therapies due to different mechanisms of action that could differentially affect adherence.

The relationships between other patient-related factors such as depression and anxiety and nonadherence to tamoxifen therapy are not well defined. Significantly higher tamoxifen nonpersistence (early discontinuation) rates have been shown for women who reported problems with mood (36%) versus women who reported no mood problems (12%) (Demissie, Silliman, & Lash, 2001). Use of antidepressant agents in the year before initiation of tamoxifen therapy has been associated with tamoxifen nonpersistence (Barron et al., 2007). Lebovits et al. (1990) found that women who discontinued self-administered chemotherapy had higher depressive symptom disturbances than women who did not discontinue therapy ($p < .05$). Nonetheless, depression and anxiety are related to nonadherence in individuals with chronic illness (Rubin, 2005) and in women at risk for breast cancer (Cohen, 2002).

Treatment-related factors such as prior chemotherapy (Fink, Gurwitz, Rakowski, Guadagnoli, & Silliman al., 2004) have been reported to be less associated with nonpersistence, or discontinuation of tamoxifen therapy. Positive hormone receptor status

has ben associated with both ongoing tamoxifen use at four years (Kahn et al., 2007) and with stopping tamoxifen therapy by the second year (Fink et al., 2004). Partridge et al. (2003) found that women with mastectomy versus breast conserving surgery were more likely to be nonadherent to tamoxifen therapy. No published reports specifically examining women's menopausal status as a potential predictor of adherence to either tamoxifen or AIs were found.

Side effect severity and discontinuation of tamoxifen has been examined with mixed results (Lash, Fox, Westrup, Fink, & Silliman, 2006; Wickersham, Happ, & Bender, 2012). Fink et al. (2004) reported that side effects were not associated with discontinuation of tamoxifen; however, other researchers have reported that women who experienced side effects were more likely to stop taking tamoxifen (Demissie et al., 2001; Kahn et al., 2007). Grunfeld, Hunter, Sikka, and Mittal (2005) reported that 46% of women who discontinued therapy with tamoxifen did so due to side effects. Hot flushes and night sweats were the primary concern.

Nonadherence or nonpersistence to AIs related to side effects has been evaluated mostly in the context of clinical trials. In the Arimidex, Tamoxifen, Alone or in Combination (ATAC) trial (Baum et al., 2002), fewer women withdrew from therapy with anastrozole compared to tamoxifen; however, higher nonpersistence rates with AIs were noted in similar trials comparing exemestane and letrozole with tamoxifen (Coombes, Hall, & Gibson, 2004; Goss et al., 2003). Younger age, out-of-pocket costs of greater than $30 US per AI prescription, no mastectomy, and higher co-morbid condition burden have been associated with 12-month nonadherence to AI therapy (Sedjo & Devine, 2011). In a qualitative analysis of the medication-taking experiences for women with early stage breast cancer who were midway through a five-year course of anastrozole therapy (Wickersham et al., 2012), most women (11/12) (91.7%) continued to take anastrozole due to a strong belief in its importance despite side effect severity.

Adherence to oral hormonal therapy for women with breast cancer remains difficult. Patient-, illness-, and treatment-related factors have been associated with adherence to oral hormonal therapy with tamoxifen and AIs but with inconsistent findings, and menopausal status was not reported. Further exploration of pretreatment predictors of nonadherence to oral hormonal therapies, including women's menopausal status (pre or postmenopausal), may help identify women with early stage breast cancer who are at risk for nonadherence. Therefore, our purpose was to explore pretreatment patient-, illness-, and treatment-related predictors of short-term nonadherence to oral hormonal therapy for women with early stage breast cancer (Stage I, II, or IIIa) from the pretreatment assessment (prehormonal therapy) to six months after initiation of oral hormonal therapy.

We hypothesized:

1. Older age and marital status (being married) were associated with less nonadherence. The number of years of education, employment status (being employed), and primary occupation were associated with more nonadherence.
2. Tumor type and women's menopausal status (pre or postmenopausal) were associated with nonadherence to hormonal therapy. Lower stage (I/II versus IIIa) of breast cancer was associated with more nonadherence to hormonal therapy.
3. Lower perceived severity of side effects of hormonal therapy, depressive symptoms, fatigue, and anxiety were associated with less nonadherence for women with early stage breast cancer.

Methods

This investigation was a secondary analysis of two longitudinal cohort studies: (a) *The Anastrozole Use in Menopausal Women (AIM) Study (The AIM Study)*, which examined the effect of anastrozole on cognitive function in women with early stage breast cancer and explores whether anastrozole adherence mediates cognitive function in this sample; and (b) *Predictors of Adherence to Hormonal Therapy in Breast Cancer* (ONS Study), which examined the pattern of adherence, patient and illness/treatment predictors of adherence, and moderation effects between patient factors and illness/treatment factors to hormonal therapy in women with early stage breast cancer. The University of Pittsburgh Institutional Review Board approved both studies. Data for the current investigation were collected from The AIM Study from 2005 to 2011, and from 2007 to 2011 for The ONS Study. The ONS Study was guided by Christensen's (2000) interactionalist framework for adherence, which posits that interaction of patient factors with illness and treatment factors provides the main influence over adherence in persons with chronic illness. We used Christensen's patient by treatment interactionalist framework to guide the organization of our potential predictors for the current study.

Setting and Sample

The present analysis was performed on one pooled dataset of patient-, illness-, and treatment-related data from the pretreatment (prior to initiation of adjuvant therapy) assessments from both The AIM and ONS Studies. Adherence was assessed continuously over the first six months of treatment in both studies; therefore, these data were also pooled together. Both studies included women less than 75 years who are able to speak and read English and who have completed a minimum of eight years of education. Women were excluded for self-reported hospitalization for psychiatric illness within the last two years, prior diagnosis of neurologic illness, distant metastases including the central nervous system, and prior diagnosis of cancer. Because The AIM Study focuses on women who are receiving therapy with anastrozole, only postmenopausal women were included in that study; however, both pre and postmenopausal women were enrolled into The ONS Study. Women who received oral hormonal therapy alone or in combination with chemotherapy were included in the present analysis.

Variables and Measures

Adherence to oral hormonal therapy was continuously assessed with the Medication Event Monitoring System (MEMS™) (AARDEX Group, Ltd.) for 18 months for the ONS study and for the full five years of hormonal therapy for the AIM study. The MEMS™ is a bottle cap fitted with a microprocessor that records the date and time the cap is removed from a medication vial. The MEMS™ records each medication-taking event, including patterns and timing of doses, and allows for detection of missed and extra doses (Cramer, Scheyer, & Mattson, 1990). Nonadherence (dependent variable) was defined as the percentage of prescribed administrations of hormonal therapy not taken during the first six months of therapy. We chose to assess nonadherence during the first six months after initiation of hormonal therapy to understand potential pretreatment predictors of short-term nonadherence. We measured nonadherence as a continuous variable, but when interpreting the results, women with less than 80% adherence were considered nonadherent to be consistent with the current adherence literature for patients with chronic illnesses, including cancer (Osterberg & Blaschke, 2005).

Patient-related variables—Patient-related factors assessed included sociodemographic variables, depressive symptoms, anxiety, and fatigue. Sociodemographic variables included women's employment status, primary occupation, age, total number of years of education,

marital status, and study membership (AIM or ONS). Because the pooled sample of women was 98.3% Caucasian, race/ethnicity was excluded as a predictor variable due its limited variability. Sociodemographic information was collected using the University of Pittsburgh, School of Nursing Center for Research in Chronic Disorders Sociodemographic Questionnaire. Study membership (AIM or ONS) was included as a potential predictor to assess whether study membership affected nonadherence to hormonal therapy.

Women's self-reported depressive symptoms were measured using the Beck Depression Inventory-II, a 21-item, self-report measure on which women rate depressive symptoms and attitudes on a four-point Likert scale (Beck, Steer, & Brown, 1996). The score is the sum of responses for items. The Cronbach's alpha coefficient for 500 outpatients with mental disorders was .92 and for 120 college students was .93. The BDI-II correlates strongly with the major depression episode portion of the Structured Clinical Interview for DSM-IV Axis I Disorders (r = .83) (Sprinkle et al., 2002; Stukenberg, Dura, & Kielcolt-Glaser, 1990) and the Revised Hamilton Rating Scale for Depression (r = .71) (Beck et al., 1996; Spreen & Straus, 1998).

Anxiety was assessed with the Profile of Mood States (POMS) Tension-Anxiety subscale, a 9-item, self-report subscale in which women's adjectives of heightened musculoskeletal tension (somatic and observable) are rated on a five-point Likert scale (McNair, Lorr, & Droppleman, 1992). The score is the sum of responses for items. Reliability estimated using coefficient alpha was .92 and test-retest reliability was .70 in 1000 psychiatric outpatients (McNair et al., 1992). The POMS is sensitive to changes in anxiety levels in patients with cancer (Cassileth et al., 1992). Fatigue was measured using the POMS Fatigue-Inertia subscale, a seven-item, self-report subscale in which adjectives of weariness, inertia, and low energy levels are rated on a five-point Likert scale (Mason, Matsuyama, & Jue, 1995). The score is the sum of responses for items.

Illness- and treatment-related variables—Information concerning prior hormone replacement therapy in the past three months, stage of breast cancer, tumor type, radiation therapy, and chemotherapy was abstracted from the patient medical record. Because of the small sample sizes of women who underwent hormone replacement therapy in the past three months, received chemotherapy, or received radiation therapy, these variables were excluded as potential predictors. Women's menopausal status (pre or postmenopausal) was determined using a combination of the women's natural menopause status at entry into each study and the MEMS™-monitored medication. If natural menopause status was missing, the MEMS™-monitored medication (e.g., anastrozole, letrozole) determined the woman's menopausal status, since they are prescribed according to menopausal status.

Side effects of hormonal therapy were assessed with the Breast Cancer Prevention Trial (BCPT) Symptom Checklist, a self report measure of the degree that women are bothered by 43 treatment- and menopausal-related symptoms in the past four weeks (Ganz et al., 2000; Stanton, Bernaards, & Ganz, 2005). Women rate symptoms on a five-point Likert scale (0 = *not at all* to 4 = *extremely*). Eight-factor (Stanton et al., 2005; Terhorst, Blair-Belansky, Moore, & Bender, 2010) and seven-factor (Cella et al., 2007) structures have been reported for the BCPT. For consistency, scores on the eight subscales used in The AIM Study were calculated in the present analysis: vasomotor symptoms, gastrointestinal (GI) symptoms, bladder control, cognitive symptoms, weight concerns, musculoskeletal pain, gynecological symptoms, and dyspareunia. Subscale scores are the average score for items in each subscale, and the total score is the average score across all items. Cronbach's alphas for subscale scores range from .43 to .83 for women with breast cancer receiving hormonal therapy. In previous studies, BCPT subscale scores were generally negatively associated with SF-36 Physical Health and Mental Health subscale scores (lower BCPT symptom

subscales were associated with better physical and mental health) (Alfono et al., 2006; Terhorst et al., 2011).

Statistical Analyses

All statistical analyses were performed with IBM® SPSS® Statistics v.20.0 (Armonk, NY). Descriptive statistics were computed to describe the data distributions and to characterize the study samples. The independent samples t-test (or Mann-Whitney U-test, if data were non-normal) and the χ^2 test of independence (or Fisher exact test, if cell sizes were sparse) were used to compare women in The AIM Study with women in The ONS Study at pretreatment to investigate whether certain characteristics may be more associated with study membership. Data were screened for accuracy of input, univariate and multivariate outliers, missing data, multicollinearity and severe violations in the underlying assumptions for multiple linear regression analysis. Linearity of continuous predictor variables was assessed by review of scatterplots. For categorical predictors, sparsely populated categories or cells were collapsed in a meaningful way to limit the sparseness of cells. For example, we collapsed seven categories of types of primary occupation into four categories: (a) higher executive/medium-sized business, teacher, health care professional, (b) administrative/clerical/sales, (c) skilled-manual/non-skilled manual/unskilled, and, (d) homemaker/disabled/student/retired/no occupation.

Multiple linear regression analysis was used to examine patient-, illness-, and/or treatment-related factors that predict short-term nonadherence to oral hormonal therapy for women with early stage breast cancer from prehormonal therapy to six months after initiation of therapy. Statistical analyses for evaluation of candidate predictors were completed in two stages. Bivariate associations between each candidate predictor variable and the outcome variable (nonadherence after six months of initiation of treatment) were first assessed using simple linear regression. The categorical variable for primary occupation was modeled as three indicator variables with administrative/clerical/sales category serving as the reference group. Candidate predictor variables meeting the criteria of $p < .20$ for the bivariate analyses were retained for further consideration in the multivariate analysis using both stepwise and backward modeling algorithms of multiple linear regression to identify the predictors of six-month nonadherence. Candidate predictors were retained in the model if they remained associated at $p < .10$ in the multiple linear regression analysis. Two-way interaction terms were created using the candidate predictor variables identified in the retained model to account for possible nonadditivity.

For all hypotheses, we used Power Analysis and Sample Size Software for Windows (PASS 2011; NCSS Statistical Software, Kaysville, Utah) to determine the smallest detectable effect size in terms of R^2 using a fixed sample size of $N = 198$, desired power of .80, and a level of significance of $p = .01$. A sample size of $N = 198$ achieved .80 power to detect an R^2 of .149 based on 25 predictor variables with a significance level of $p = .01$ for two-sided hypothesis testing, suggesting that a sample size of $N = 198$ was sufficient to correctly reject a false null hypothesis. The number of predictor variables was determined by taking into account the number of potential patient-, illness-, and treatment-related predictors considering for potential interactions. An R^2 of .15 was chosen to allow detection of smaller explained variability in the retained model that may still be clinically meaningful.

Results

A summary of the descriptive statistics for the pooled sample and by study (AIM or ONS) is provided in Table 1. The mean nonadherence for the pooled sample was 11.3%. For The AIM Study, women were 12.8% nonadherent six months after initiation of therapy, and women in The ONS Study were 4.6% nonadherent. Women in the two studies were similar

in terms of self-reported depressive symptoms, anxiety, fatigue, symptoms based on BCPT subscales, and nonadherence. The mean age of the women for the pooled sample was 59.1 years (*SD* = 7.5, range 39–75) and the mean number of years of education was 15.0 (*SD* = 2.9, range 10–26). We found expected significant differences in age and MEMS™-monitored medication at the pretreatment assessment between the two groups ($p = .0001$ for each) because only postmenopausal women participated in The AIM Study, took only anastrozole, and were likely to be somewhat older than women in The ONS Study (the ONS Study sample comprised both pre and postmenopausal women). As anticipated, the proportion of women being postmenopausal differed between the studies because only postmenopausal women were eligible for participation in The AIM Study ($p = .0001$). No women in The ONS Study received mammosite therapy; therefore, the distribution of the type of radiation therapy received also differed between the studies ($p = .026$). There was a significant difference in the number of women with ductal carcinoma in situ (DCIS) between the two groups. No other differences were observed.

Potential predictors that were set aside because coefficients in a simple regression with nonadherence were not significant ($p > .20$) were: age, education, marital/partnered status, occupational categories (high executive vs other; semiskilled vs other), breast cancer stage, infiltrating ductal tumor type, anxiety, vasomotor symptoms, bladder control, and dyspareunia. Correlations among retained candidate predictors identified through screening ($p \leq .20$) using simple regression analysis are shown in Table 2. Candidate categorical predictors of nonadherence included study membership, employment status, primary occupation (homemaker and related categories vs other), DCIS tumor type, and menopausal status. Depressive symptoms, fatigue, GI symptoms, cognitive symptoms, weight concerns, gynecological symptoms, musculoskeletal pain, and total BCPT score were identified as linear predictors of nonadherence. Regression results are summarized in Table 3. Using stepwise multiple linear regression analyses of these candidate predictor variables, DCIS tumor type ($p = .004$) and weight concerns ($p = .003$) were identified as pretreatment predictors of women's nonadherence at six months post treatment (Table 3). Backward multiple linear regression analyses identified a similar set of variables (Table 3). In addition to DCIS tumor type ($p = .004$) and weight concerns ($p = .003$), backward multiple linear regression analysis identified the third dummy-coded primary occupation group (homemaker, student, retired, disabled versus all other categories) as a statistically significant predictor ($p = .05$). When exploring the potential two-way interactions among DCIS tumor type, weight concerns, and the third primary occupation group, no change was observed in the stepwise linear regression model; however, the interaction between DCIS tumor type and the third primary occupation group was statistically significant ($p = .001$) in the backward elimination model.

Discussion

We examined potential patient-, illness-, and/or treatment-related factors and their relationship to short-term nonadherence to oral hormonal therapy for women with early stage breast cancer from the pretreatment assessment (prehormonal therapy) to six months after initiation of therapy. We found that women with DCIS tumor type and higher weight concern scores on the BCPT were associated with greater nonadherence six months after therapy initiation, but no other symptoms were retained in the stepwise or backward-elimination models.

Prior reports of the relationship between side effect severity and discontinuation of tamoxifen or AI therapy have been somewhat unclear. The types of side effects that women with breast cancer who are taking oral hormonal therapy have been measured and have included attractiveness (Grunfeld et al., 2005), but this was not found to be a significant

predictor of nonadherence in our study. Other scientists have measured severity of side effects (e.g., severe, moderate, mild, none) (Kahn et al., 2007) or number of side effects (Lash et al., 2006), but we were unable to find specific reports regarding weight concerns and nonadherence for women with breast cancer taking oral hormonal therapy. Our quantitative findings are somewhat consistent with the qualitative analysis of medication-taking for a subset of 12 women who participated in The Aim Study (Wickersham et al., 2012). They provided rich description of their side effects of therapy, which included hot flashes, arthralgias, fatigue, sleep disturbances, and memory problems. Despite severity of their symptoms, most (11 of 12 participants, 91.67%) indicated that their side effects would not stop them from taking their anastrozole. The sentiments expressed by the women in our qualitative study (Wickersham et al., 2012) were consistent with the findings of the present secondary analysis; however, only two of the women in the qualitative analysis mentioned weight gain or weight loss in their descriptions of their medication-taking experiences with anastrozole. It is possible that women who had weight concerns had discontinued therapy with anastrozole before the interviews or attributed weight concerns to another process, such as aging.

The interaction of DCIS tumor type and primary occupation suggests that women with DCIS tumor type and who were homemakers, retired, students, unemployed or disabled were more nonadherent when compared to women with other tumor types and other occupations. This relationship is puzzling. Published reports examining similar interactions were not found. Previous reports of predictors of nonadherence to oral hormonal therapy with tamoxifen or AIs have not addressed employment status or occupation. Information that may further explain our findings might have been missed by our coding scheme. Despite collapsing the categories in a meaningful way to limit sparseness of cells, the third and fourth categories of primary occupations for women in The ONS Study still had sparse cells and may have been too small to detect a meaningful difference. It is important to note that participants in both The AIM and ONS Studies with DCIS also had to have another tumor type to be eligible for those studies; this requirement may have inflated our findings. While our findings suggest that women without DCIS tumor type were more adherent six-months after initiating hormonal therapy, further discrimination of tumor type and its relationship to nonadherence is needed.

The results of our study should be interpreted with several limitations in mind. The most important limitation is the observational design of our study. While our findings have provided insight for future investigations of nonadherence and women with early stage breast cancer receiving hormonal therapy, no associations regarding causality can be made. In addition, nonadherence was longitudinally assessed in The AIM and ONS Studies, but we assessed nonadherence six months after initiation of hormonal therapy to obtain a “snapshot” of which patient-, illness-, or treatment-related factors predicted short-term nonadherence. Some of the predictors we considered could be time-dependent, such as anxiety or depression. All tumor types were examined as candidate predictors, but participants with DCIS also had another tumor type to be eligible for the parent studies.

We chose percentage of nonadherence as the dependent variable, but we did not include examinations of dose intervals (the time between each dose of hormonal therapy), which may provide further information as to patterns of the women’s adherence. Several adherence rates were extremely low (e.g., 1.52%); they were verified to be correct, but the scores may have reflected a testing of the MEMS™ cap, or one use only. It is possible that pill minders were used by the women but not reported, also potentially affecting our findings. In addition, women were aware of the purpose of the MEMS™ cap, which may have motivated them to be more adherent with taking hormonal therapy.

The samples of women from The AIM and The ONS Studies examined in this analysis were uneven. While no unexpected differences between the two groups were noted at pretreatment, it is possible that the sample size of women selected from The ONS Study was too small to generate significant findings. We did not include lobular carcinoma in situ as a type of breast cancer in our analyses because there was only one case in the pooled sample; therefore, the results cannot be generalized to women with that type of breast cancer. Additionally, all women in our sample were white and well educated. Racial/ethnic disparities in treatment could have an effect on nonadherence and should be further investigated.

Our findings suggest future directions of inquiry with regard to nonadherence for women with early stage breast cancer who receive therapy with oral hormonal agents and for nursing practice. First, we did not include type of surgery for breast cancer, social support, and beliefs about medicines in our analyses, which could provide additional insight for potential predictors of nonadherence. We used multiple linear regression analysis with a continuous nonadherence variable; other approaches could include logistic regression using 80% and/or 90% as cut-offs for adequate adherence. Future studies should also include exploration of employment and types of primary occupation and their relationship to nonadherence, as well as the effects of nonadherence on clinical outcomes and predictors of nonadherence for women with breast cancer taking oral chemotherapies or targeted therapies. Suggestions for nursing practice include: (a) asking women targeted questions about their experiences with specific side effects (e.g., weight concerns), rather than about side effects as a whole; and, (b) discussing women's beliefs about their illness and the relationship of those beliefs to medication-taking behaviors (including adherence). Our study offers insight into potential predictors of nonadherence for women participating in one of two large cohort studies. The findings suggest additional examinations of work and symptom burden and their relationship to nonadherence are indicated.

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Table 1

Sociodemographic Characteristics

	Pooled Sample (*N* = 198)		**AIM Study (*n* = 162)**		**ONS Study (*n* = 36)**		
Characteristic	***M***	**(*SD*)**	***M***	**(*SD*)**	***M***	**(*SD*)**	***p***
Age (years)	59.1	(7.5)	60.6	(6.1)	52.4	(9.5)	.0001
Education (years)	15.0	(2.9)	15.1	(3.0)	14.8	(2.7)	.64
Adherence	88.7	(1.6)	87.2	(24.6)	95.4	(8.9)	.21
Depression (BDI total score)	6.0	(5.7)	5.8	(5.6)	6.7	(6.0)	.37
Fatigue (POMS fatigue score)	6.1	(6.1)	6.2	(6.1)	5.7	(6.0)	.70
Anxiety (POMS anxiety score)	6.7	(4.6)	6.8	(4.5)	6.5	(5.0)	.38
	n	(%)	*n*	(%)	*n*	(%)	
Marital status							.80
Never married	20	(10.1)	18	(11.1)	2	(5.6)	
Currently married	136	(68.7)	109	(67.3)	27	(75.0)	
Widowed	16	(8.1)	13	(8.0)	3	(8.3)	
Separated	2	(1.0)	2	(1.2)	1	(0.0)	
Divorced	24	(12.1)	20	(12.3)	4	(11.1)	
Employed							.55
Yes	138	(69.7)	111	(68.5)	27	(75.0)	
No	60	(30.3)	51	(31.5)	9	(25.0)	
Ethnicity							.08
White	194	(98.0)	159	(98.1)	35	(97.2)	
African American	3	(1.5)	3	(1.9)	0	(0.0)	
Multi-racial	1	(0.5)	0	(0.0)	1	(2.8)	
Latino	2	(1.0)	1	(0.6)	1	(2.8)	
Primary occupation							.06
1. Higher executive[a]	50	(26.2)	40	(20.9)	10	(5.2)	
2. Administrative[b]	64	(33.5)	51	(26.7)	13	(6.8)	
3. Skilled/nonskilled[c]	24	(12.6)	20	(10.5)	4	(2.1)	
4. Homemaker/other[d]	53	(27.7)	51	(26.7)	2	(1.0)	

Characteristic	Pooled Sample (*N* = 198) *M*	(*SD*)	AIM Study (*n* = 162) *M*	(*SD*)	ONS Study (*n* = 36) *M*	(*SD*)	*p*
Menopausal status							.0001
Premenopausal	16	(8.1)	0	(0.0)	16	(44.4)	
Postmenopausal	182	(91.9)	162	(100.0)	20	(55.6)	
MEMS-monitored medication							.0001
Anastrozole	69	(85.4)	62	(100.0)	7	(19.4)	
Letrozole	9	(3.5)	0	(0.0)	7	(19.4)	
Examestane	2	(1.0)	0	(0.0)	2	(5.6)	
Tamoxifen	19	(9.6)	0	(0.0)	19	(52.8)	
Multiple AIs	1	(0.5)	0	(0.0)	1	(2.8)	
Radiation therapy							.03
Radiation	57	(28.8)	32	(19.8)	25	(69.4)	
Mammosite	12	(6.1)	12	(7.4)	0	(0.0)	
Chemotherapy							.83
Yes	37	(18.7)	25	(15.4)	12	(33.3)	
No	60	(30.3)	39	(24.1)	21	(58.3)	
Stage of breast cancer							.22
LCIS	1	(0.5)	1	(0.6)	0	(0.0)	
I	139	(70.2)	119	(73.5)	20	(55.6)	
IIa	35	(17.7)	26	(16.0)	9	(25.0)	
IIb	12	(6.1)	9	(5.6)	3	(8.3)	
IIIa	11	(5.6)	7	(4.3)	4	(11.1)	
Tumor type							
DCIS	79	(39.9)	71	(43.8)	8	(22.2)	.02
LCIS	7	(3.5)	5	(3.1)	2	(5.6)	.61
Infiltrating ductal	170	(85.9)	142	(87.7)	28	(77.8)	.18
Tubular	6	(3.0)	6	(3.7)	0	(0.0)	.59
Mucinous	2	(1.0)	2	(1.2)	0	(0.0)	1.00
Infiltrating lobular	20	(10.1)	14	(8.6)	6	(16.7)	.22
Combination	1	(0.5)	1	(0.6)	0	(0.0)	1.00
Hormone replacement theory last 3 months							.36

Characteristic	Pooled Sample (*N* = 198)		AIM Study (*n* = 162)		ONS Study (*n* = 36)		*p*
	M	(*SD*)	*M*	(*SD*)	*M*	(*SD*)	
Yes	23	(11.6)	20	(12.3)	3	(8.3)	
No	69	(34.8)	65	(40.1)	4	(11.1)	

Note. AI = aromatase inhibitors; BDI = Beck Depression Inventory; POMS = Profile of Mood States; DCIS = ductal carcinoma in situ. Women may have more than one type of breast cancer tumor. Participants with DCIS also had another tumor to be eligible for the parent studies.

[a]Occupations included higher executive/medium-sized business, teacher, health care professional.

[b]Occupations included clerical and sales.

[c]Occupations included skilled-manual, nonskilled manual, and unskilled.

[d]Occupations included homemaker, disabled, student, retired, and no occupation.

Table 2

Correlations, Means, and Standard Deviations (N = 190)

	Measure	1	2	3	4	5	6	7	8	9	10	11	12	13	14
1.	Study Membership	1.00													
2.	Primary Occupation3	−.20	1.00												
3.	Menopausal Status	−.69	.18	1.00											
4.	DCIS	.15	−.03	−.13	1.00										
5.	Infiltrating Lobular	−.02	−.01	−.02	−.22	1.00									
6.	Depressive Symptoms	.05	.01	−.06	.01	.07	1.00								
7.	Fatigue	−.09	.02	.02	−.02	.06	.60	1.00							
8.	GI Symptoms	−.12	.04	.06	−.04	.09	.15	.27	1.00						
9.	Cognitive Symptoms	−.01	.03	.02	−.08	.03	.49	.42	.21	1.00					
10.	MK Pain	−.06	.07	.09	−.11	.06	.50	.55	.24	.44	1.00				
11.	Weight Concerns	−.09	.02	.04	.01	.00	.17	.34	.32	.34	.40	1.00			
12.	Gynecological Symptoms	.04	.02	−.03	−.02	.03	.20	.29	.06	.27	.31	.32	1.00		
13.	BCPT Subscale Score	−.04	.00	.05	−.08	.11	.46	.54	.39	.64	.68	.59	.54	1.00	
14.	Nonadherence	.172	.15	.11	−.20	.12	.10	.13	.14	.09	.12	.21	.11	.15	1.00
M		90.09	.28	.91	.59	.91	5.94	5.95	.17	.72	.78	.27	.22	.47	1.22
SD		19.11	.45	.29	.49	.29	5.72	5.93	.39	.68	.63	.53	.46	.33	.29

Note. BCPT = Breast Cancer Prevention Trial Symptom Checklist; DCIS = ductal carcinoma in situ tumor type; MK = musculoskeletal. Primary Occupation 3 is skilled-manual/non-skilled manual/unskilled.

Table 3

Regression Results (N = 190)

		Stepwise			Backward Elimination		
Variable	**Values**	***b***	***SE***	***p***	***b***	***SE***	***p***
Study	0 = The AIM Study 1 = ONS Study						
Occupation3	0 = All else 1 = Homemaker/student/disabled/retired				.137	.045	.05
Menopausal status	0 = post 1 = pre						
		−.204	.042	.004	−.200	.041	.004
DCIS tumor type	0 = yes 1 = no						
Infiltrating lobular tumor type	0 = yes 1 = no						
Depression	BDI total score						
Fatigue	POMS fatigue score						
GI symptoms	BCPT subscale score						
Cognitive symptoms	BCPT subscale score						
Musculoskeletal pain	BCPT subscale score						
Weight concerns	BCPT subscale score	.209	.039	.003	.207	.038	.003
Gynecological symptoms	BCPT subscale score						
Overall symptoms	BCPT total score						
Interaction: DCIS and occupation3	DCIS × OCCUPATION3				−.250	.077	.001

Note. BCPT = Breast Cancer Prevention Trial Symptom Checklist; BDI = Beck Depression Inventory-II; POMS=Profile of Mood States; DCIS = ductal carcinoma in situ. Stepwise: R^2 = .085 Adjusted R^2 = .075 s = .283, $p < .004$. Backwards Elimination: R^2 = .130, Adjusted R^2 = .111, s = .277, $p < .001$.