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Race and Patient-reported Symptoms in Adherence to Adjuvant Endocrine Therapy: A Report from the Women’s Hormonal Initiation and Persistence Study

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Abstract

Background: Adjuvant endocrine therapy (AET) improves outcomes in women with hormone-receptor positive (HR+) breast cancer (BC). Suboptimal AET adherence is common but data are lacking about symptoms and adherence in racial/ethnic minorities. We evaluated adherence by race and the relationship between symptoms and adherence.

Methods: The Women’s Hormonal Initiation and Persistence (WHIP) study included women diagnosed with non-recurrent HR+ BC who initiated AET. AET adherence was captured using validated items. Data regarding patient (e.g., race), medication-related (e.g., symptoms), cancer care delivery (e.g., communication), and clinicopathologic factors (e.g., chemotherapy) were collected via surveys and medical charts. Multivariable logistic regression models were employed to calculate odds ratios and 95% CIs associated with adherence.

Results: Of the 570 participants, 92% were privately insured and nearly 1/3 were Black. Thirty-six percent reported nonadherent behaviors. In multivariable analysis, women less likely to report adherent behaviors were Black (vs. White) (OR: 0.43, 95% CI: 0.27–0.67, $p < 0.001$) and with greater symptom burden (OR: 0.98, 95% CI: 0.96–1.00, $p < 0.05$). Participants more likely to be adherent were overweight (vs. normal weight) (OR: 1.58, 95% CI: 1.04–2.43, $p < 0.05$), sat 6 hours a day (vs. 6 hours) (OR: 1.83, 95% CI: 1.25–2.70, $p < 0.01$), and were taking aromatase inhibitors (vs. Tamoxifen) (OR: 1.91, 95% CI: 1.28–2.87, $p < 0.01$).

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Conclusion: Racial differences in AET adherence were observed. Longitudinal assessments of symptom burden are needed to better understand this dynamic process and factors that may explain differences in survivor subgroups.

Impact: Future interventions should prioritize Black survivors and women with greater symptom burden.

Keywords

Breast Cancer; Adjuvant Endocrine Therapy; Symptoms; Disparities; Adherence

Introduction

Adjuvant endocrine therapy (AET) has made dramatic progress in the treatment of hormonal receptor positive (HR+) breast cancer (BC). Thus, the National Comprehensive Cancer Network (NCCN) recommends AET [tamoxifen or aromatase inhibitors] for hormone receptor positive (HR+) breast cancer (BC).^{1, 2} Adherence to the full course of AET (5 years) is critical to reduce the risk of BC recurrence by 40% and to improve mortality by 31%.^{3, 4} Despite these benefits, up to 50% of women prematurely discontinue AET. Given the high rate of premature treatment discontinuation during the minimum 5-year course, identifying women at risk of discontinuation (i.e. non-adherence) early in their treatment regimen may provide insight to inform timely interventions.^{5, 6} Additionally, non-adherence to daily AET regimens is suboptimal and ranges from 50% to 91%.^{5, 7}

Medication adherence is “the process by which medication is taken as prescribed and encompasses phases of ‘initiation’ (i.e., first dose), ‘implementation’ (taking prescribed doses and taking doses for required length of time) and ultimately ‘discontinuation’”.⁸ Non-adherence in these phases is linked to poor outcomes.⁹ Explanations for non-adherence behaviors are complex and vary depending on the phase (e.g., implementation, discontinuation, etc.).^{10, 11} Thus, it is important to have studies that examine adherence across the spectrum of behaviors. AET medication related symptoms, such as hot flashes or bone pain, are commonly reported reasons for non-adherence,^{12, 13} yet many large-scale adherence studies have not captured patients’ reported symptoms or implementation behaviors in samples that include substantial numbers of minority women.^{14–16} As a result, little is known about symptom burden in minority women prescribed AET.

Though not always consistent across studies, reports suggest that African American (Black) women, are more likely to be non-adherent than their Non-Hispanic White (White) counterparts.^{17–19} Suboptimal AET adherence in Black women is characterized by lower rates of treatment initiation, greater delays to initiate therapy after prescription (implementation), and failure to complete the full course of therapy (persistence).^{20, 21} However, little is known about Black women’s adherence to their treatment regimens; particularly early in their treatment experience or whether if accounting for medication (i.e., symptom burden) and psychosocial factors such as medication beliefs would diminish some of the previously observed disparities. Addressing these areas will aid in the development of future interventions that seek to improve AET adherence. This report will fill important gaps regarding implementation adherence behaviors among Black and White women to inform

interventions that can be implemented early in their treatment course. Using a multifaceted framework of adherence, aims are to: 1) test differences in adherence by race, 2) identify factors related to adherence and 3) understand how symptoms impact AET adherence.

Materials and Methods

The Women's Hormonal Initiation and Persistence (WHIP) study is a prospective study of Black and White women prescribed AET.²² This study was registered at clinicaltrials.gov and approved by the institutional review boards (IRB) at participating sites and were conducted in accordance with recognized ethical guidelines; study protocols met the standards of the Health Insurance Portability and Accountability Act. The study design, recruitment strategies, and study sample have been previously described.²² Briefly, eligibility criteria included being diagnosed with HR+ breast cancer within one-year of study enrollment, 21 years of age, and having filled a prescription script based on pharmacy records for any type of AET (e.g. tamoxifen) within one-year post-diagnosis and within three months of the baseline interview. Pharmacy records were used to confirm that women had current AET prescription at the time of interview. Trained clinical research assistants (CRA) screened and obtained written informed consent from patients. CRAs completed standardized computer-assisted telephone interviews with some women while others elected to complete the survey on-line via a secured link. As displayed in Figure 1, 1,443 women registered for the study; 464 were ineligible and 379 declined; 600 women consented and 595 completed baseline interviews (Figure 1). The analytical samples for this study focused solely on women who self-identified as either Black or White (N=570).

Measures

Selection of measures was guided by our adaption of the Adherence Model by DiMatteo and colleagues and key domains from the WHO Medication Adherence Model.^{23, 24} The primary outcome of implementation adherence assessed if women missed a dose of their medications for reasons identified in prior literature^{13, 25–28} and with validated items.^{29, 30} Unlike prescription-based adherence measures, such as proportion of days covered and medication possession ratio, our outcome offered insight to women's experiences taking AET once in their possession. In other words, this measure assessed women's medication taking behaviors. Participants answered three validated items (yes/no) adapted for our population regarding their medication adherence behaviors within the past two weeks. Queries included if they had stopped their medication due to several reasons (e.g., forgetting, feeling worse, or an inconvenience). Responses were yes versus no; yes responses were coded as "1" and No responses coded as "0." Total scores ranged from 0 to 3 and the mean score was 0.5; therefore, we categorized the outcome for analysis as either "Adherent" (score = 0; no non-adherent behaviors) or 'Nonadherent' (scores = 1–3).

Medication-related factors—were key predictors of interest and included (1) AET drug class (Tamoxifen or Aromatase inhibitors [AI]) and (2) patient-reported AET-related symptoms. Patient-reported AET symptoms were assessed using the Functional Assessment of Cancer Therapy Endocrine Symptoms (Cronbach's alpha=0.79).^{31–33} The scale includes Likert items that asked how frequently they experienced symptoms in the seven days prior to

survey completion. In accordance with published reports,^{34–36} symptoms were grouped according to five clusters; *gastrointestinal symptoms* (i.e., weight gain or loss, vomit, diarrhea, bloating, appetite increase, high cholesterol), *gynecologic symptoms* (i.e., vaginal discharge, vaginal itching/irritation, vaginal bleeding/spotting, vaginal dryness, pain or discomfort during intercourse, loss of interest in sex, breast sensitivity), *neuropsychological symptoms* (e.g. lightheadedness, dizziness, headaches, mood swings, irritability), *vasomotor symptoms* (e.g. hot flashes, cold sweats, night sweats), and *bone symptoms* (e.g. bone loss, joint pain or stiffness).

Individual patient-level factors: included *demographic, clinicopathologic, psychosocial,* and lifestyle factors. *Demographic factors* were age, race, income level (total household income before taxes), insurance type (public vs. private), and employment status (working vs. not working). *Clinicopathologic factors* were abstracted from medical records and included data on cancer stage, surgery type (lumpectomy, mastectomy), and therapy (radiation, hormonal). *Psychosocial factors.* Total self-efficacy was measured using a 12-item scale that assessed women's level of confidence regarding understanding and obtaining health information (Cronbach's alpha=0.87).³⁷ We also employed two subscales of the self-efficacy scale – understanding and participating in care (Cronbach's alpha=.72), and maintaining a positive attitude (Cronbach's alpha=0.85). A three-item scale measured women's health literacy, with higher scores indicating higher literacy (Cronbach's alpha=0.76).³⁸ Beliefs about AET were measured using the Beliefs about Medicine Questionnaire (BMQ)³⁹ and were comprised of two subscales – perceived necessity of medication (e.g. my health in the future will depend on my endocrine therapy) (Cronbach's alpha=0.84) and perceived concerns of taking medication (e.g. my endocrine therapy medications are a mystery to me) (Cronbach's alpha=0.75). Spirituality was measured using Lukwago's Religiosity Scale (Cronbach's alpha=0.95).⁴⁰ Social support and subdomains, emotional and tangible support, were assessed (Cronbach's alpha=0.94, 0.94, and 0.92, respectively).⁴¹ Women reported their level of medical mistrust of the healthcare system using validated scales employed in cancer patients (Cronbach's alpha = 0.80).⁴² *Lifestyle factors* were measured using the International Physical Activity Questionnaire (IPAQ).⁴³ Physical activity was classified as low, moderate, or high based on Metabolic Equivalents (METS). Daily sitting time was classified by the median (>6 hours and ≤6 hours).

Cancer Care Delivery: variables included patients' satisfaction, ratings regarding patient-provider communication, and overall trust in their cancer provider. The patient satisfaction questionnaire, which incorporates multiple domains (e.g. provider communication, access to care), was used to assess women's levels of satisfaction with their care.⁴⁴ An eight-item validated communication scale was adapted to measure women's communication with the provider about AET⁴⁵ (Cronbach's alpha=0.80). Lastly, women rated their trust in their doctors who provided their cancer care (Cronbach's alpha = 0.81).⁴⁶

Statistical Analysis

Descriptive statistics (such as mean and standard deviation, relative frequency) were evaluated for each variable. T-tests were conducted to assess mean differences between AET adherence groups of continuous variables (e.g. religiosity), and chi-square tests were used to

assess the relationships between AET adherence and categorical variables (e.g. race). Summary statistics and p-values are provided in Table 1. All variables in Table 1 superscripted with an 'a' were considered for inclusion in the logistic regression model; those selected to the final model are shown in the Table 3. A stepwise selection forcing the variables race, medication and Endocrine Symptom (ES) total score into the model was used to select variables. The Hosmer and Lemeshow goodness-of-fit test was used to test model fit and AIC was used to compare the fit across models. All models led to a c-statistic of 0.68, indicating similar in-sample predictive performance. Interaction effects between race and ES total symptom score, between race and medication, and between medication and ES total symptom score were tested. The data analysis was based on the complete dataset. Data was treated as missing if less than 70% of item showed response. Furthermore, the analysis was repeated for each ES subscale score using the same procedure. All tests were based on a Type I error of 0.05. All statistical analyses were conducted using SAS version 9.4 (TS1M3).

Results

Sample Characteristics

Participants' ages ranged from 26 to 91 (mean=59, SD=11). Most were employed (58.7%), overweight (66.6%) and 69.5% reported moderate to high levels of physical activity (Table 1). Nearly a third of study participants were Black. Some differences were noted in sample characteristics by race (Table 2). Black participants tended to be younger (mean= 57.4 vs. 59.4, $p=0.044$) and be in a lower category of household income (67.5% vs. 43.0%, $p<0.0001$) than White patients. When compared to their White counterparts, fewer Black women were privately insured (88.2% vs. 93.5%; $p=0.048$), were married (46.3% vs. 71.4%, $p<0.0001$), and had college levels of education or higher (80.9% vs. 87.8%, $p=0.033$). Compared to white women, more black women had chemotherapy (48.3% vs. 36.2%, $p=0.011$) and had a higher BMI (mean=32.1 vs. 27.3, $p<0.0001$). Regarding symptom burden, Black women reported greater overall symptoms (mean= 20.5 vs. 17.2, $p=0.0023$), vasomotor (mean = 4.9 vs. 3.8, $p=0.0018$), neuropsychological (mean= 3.8 vs. 2.8, $p=0.0017$), and gastrointestinal (mean= 4.5 vs. 3.3, $p=0.0015$) symptoms. No differences in bone or gynecological symptom severity were found by race ($p>.05$).

AET Adherence

Most (65.0%) women did not report any non-adherent behaviors. For the remaining women, 22.2% reported one nonadherent behavior, 11.2% reported 2 nonadherent behaviors, and 1.6% reported three nonadherent behaviors.. The most common non-adherent behavior was due to forgetting to take medications (26.4%) followed by missing their medications for reasons other than forgetting (17,3%). It was uncommon for women to cite non-adherence due to feeling worse after taking their medication (5.4%).

Women who were adherent reported lower scores of overall AET symptoms (mean=17.0 vs. 20.2, $p=0.001$) (Table 1). Medication type was associated with regimen adherence, with women on AIs having higher adherence compared to women on tamoxifen (70.9% vs. 53.7%; $p<.0001$). Several patient-level factors were associated with regimen adherence.

White women and women over 50 years of age were more likely to be adherent compared to women who were Black and 50 years old and younger (69.4% vs. 51.9%, $p<0.001$ and 68.9% vs. 49.2%, $p<0.001$, respectively). Compared to women who were employed, those who were not working were more likely to be adherent (73.2% vs. 58.2%, $p<0.0001$). No association was observed between adherence and type of surgery or receipt of radiation, but women who received chemotherapy were less likely to be adherent compared to those without chemotherapy (57.8% vs. 67.8%, $p=0.0241$). Although physical activity was not associated with adherence, adherence was higher among women with ≤ 6 hours per day of sitting than those with > 6 hours per day of sitting (71.3% vs. 55.1%, $p<0.001$).

Several psychosocial factors were associated with adherence, including tangible support ($p=0.020$), medication necessity beliefs ($p=0.027$), medication concerns ($p=0.001$), and religiosity ($p=0.018$). Women's ratings of their communication with their provider was associated with regimen adherence ($p=0.025$).

Table 3 displays six multivariable models for adherence that includes a model adjusting for overall AET symptoms and models accounting for each of the specific five symptom domains (vasomotor, neuropsychological, gynecologic, gastrointestinal, and bone). Each model assessed the odds of adherence (ref: nonadherence). Findings from all models revealed that Black women were less likely to be adherent when compared to White women. For example, in the model that included total AET symptoms, Black women were less likely to be adherent than White women (OR: 0.43; 95% CI: 0.27 to 0.67; $p<0.0001$). Medication type was significant in all models; women taking AI were more likely to be adherent than those taking Tamoxifen (OR=1.91, 95% CI: 1.28 to 2.87; $p < 0.01$). Overweight women had a higher odds of adherence compared to normal weight women (OR=1.58, 95% CI: 1.04 to 2.43; $p<0.05$). Women who were unemployed were more likely to be adherent than employed women (OR=1.57, 95% CI: 1.03 to 2.40; $p<0.05$).

Greater symptom burden was negatively associated with adherence in the total AET symptom and gynecological symptom logistic regression models. For example, in the AET total model the odds of being adherent decreased by a factor of 0.98 for every 1 unit increase in AET total symptoms (95% CI: 0.96 to 1.00; $p<0.05$), while in the AET gynecologic model, the odds of being adherent decreased by a factor of 0.92 for every 1 unit increase in AET gynecologic symptoms (95% CI: 0.87 to 0.96; $p<0.0001$).

Only one psychosocial factor was associated with adherence. Beliefs about AET medication, specifically concern beliefs, was significant in the vasomotor model only. Higher concern beliefs were associated with lower odds of adherence (OR=0.92, 95% CI: 0.86 to 0.99; $p<0.05$). While physical activity was not associated with adherence, women who sat for ≤ 6 hours a day were more likely to adhere to AET in all models.

Discussion

This observational study examined numerous factors that have been hypothesized to be associated with AET adherence in largely White samples but relatively unexamined within the context of racial disparities in adherence. Most of the foundational work related to AET

adherence has been drawn from largely administrative data sources.^{14–16, 47} Guided by our adapted Adherence Model by Bastani and colleagues,²³ this study expands the scope of factors generally examined by collecting data related to patient reported symptoms, psychosocial variables (e.g., medication beliefs, medical mistrust), perceptions of cancer care delivery, and lifestyle factors (physical activity, sitting time). We observed notable differences in regimen adherence behaviors by race, medication-related symptoms, and type of medication that persisted in multivariable models. No interaction effect between race and each symptom domain, or between race and medication, or between medication and each symptom was statistically significant in the models relating symptoms to adherence. Inclusion of data about lifestyle factors suggested opportunities to examine the relationship between BMI, sitting time and adherence among women taking AET. Study findings enhance knowledge about Black women with HR+ BC taking AET and have implications for future approaches to improve cancer prevention and control for BC survivors.

Addressing adherence to AET among Black women will be important for future research and clinical practice. Racial disparities have been reported in some studies of adherence outcomes based on pharmacy and medical records,^{48, 49} but limited information has been available about women's reports of their adherence related to their medication behaviors. We found that in contrast to their White peers, Black women were less likely to be adherent when controlling for AET symptoms. While results about racial disparities in AET adherence have been mixed, particularly in Medicare insured samples,⁷ findings are in concert with those that found that Black women had higher rates of non-persistence.¹¹ Explanations of lower pharmacy fills have been attributed in part to financial factors, specifically, lacking insurance or an inability to pay a copay.^{20, 50} In our sample of largely insured women we did not find evidence related to the financial factors measured in our study (e.g., income, concerns about medication affordability). While our findings are in line with those that have relied on pharmacy records to assess prescription refill rates, limited studies have compared racial/ethnic differences in patients' adherence to their daily regimen. Regimen adherence is important because even if women have filled their prescriptions, they may fail to take the medication as prescribed for various reasons (forgetting, etc.).

Although medication symptoms are often widely cited as a reason for premature discontinuation,^{12, 13} there have been relatively few studies that have empirically examined this relationship outside of clinical trials particularly, in samples that include Black women⁵¹ and limited information is available about relationships of symptom severity with AET adherence behaviors. Our study filled research gaps in these areas. The presence of more severe AET symptoms was associated with non-adherence. While studies have focused on the presence (vs. absence) of symptoms^{52, 53} there is emerging data providing information about symptom severity.⁵² In our sample of women, overall severity of AET-related symptoms including, neuropsychological and gynecological symptoms were significantly related to adherence. In the model that included total AET symptoms, the odds of Black survivors' adherence was 56% less than that of White women. These findings warrant future examination to understand the onset of symptoms and symptom management by race, which were beyond the scope of this study (Figure 2). Conversely, Bowels and colleagues found that while most women reported AET-related symptoms, most of those symptoms were not associated with AET non-adherence.⁵⁴ It is possible that severity of effects may relate more

to adherence behaviors than the actual presence or absence of a side effect; however, supporting evidence is mixed⁵⁵ and deserves further exploration. Moreover, women may also have differential thresholds that could be influenced by numerous other factors.

Symptom management is critical in the administration of AET yet empirical data are lacking about its influence on AET adherence. However, Blanchette and colleagues reported that survivors who had a follow-up with their medical oncologists within 4 months of initiating AET were more likely to be high adherers than women who did not. Additionally, measures of symptom management range from a woman's perception of her control over the symptoms^{56, 57} to having a physician's permission to terminate treatment.⁵⁸ We did not collect information on how patients and/or physicians managed AET-related symptoms in this study. We did however, assess women's perceptions of their self-efficacy to manage aspects of their treatment, and interpersonal aspects of care, both of which were significant in bivariate but not in multivariable analyses.

Novel findings related to weight and sedentary behavior were noted in the sample. Women who were overweight or obese and women who are less sedentary were more likely to be adherent. There are several possible explanations for these findings. First, weight gain is a known side effect of AET.^{59, 60} More work in this area is needed to understand the complex relationship between weight and symptoms.

While several factors (i.e., social support) were associated with medication taking behaviors among study participants in bivariate analysis, the strength of these relationships was diminished in multivariable models.¹¹ Women's health beliefs and attitudes toward AET influenced their medication adherence behaviors. Negative attitudes and greater AET concerns are found to be associated with lower adherence,⁶¹ while positive attitudes are positively associated with adherence.⁶² Surprisingly, during the early stages of their treatment regimen, interpersonal aspects of care (e.g. communication) were not strongly associated with regimen adherence. Reports on patient-provider communication and other interpersonal factors have been inconsistent across studies.⁶³ Lower self-efficacy in physician communication was negatively associated with adherence.⁶⁴ Poorer relationships with oncologists are also reported to relate with non-adherence.⁶¹ Provision of information from providers about side effects has been found to be important to women. Qualitative data from Hurtado and colleagues suggested that women reported that they were unprepared about potential side effects, and would have preferred that their providers prepare them for potential issues but more empirical data are needed in this area.⁶⁵ One study of multidisciplinary providers who prescribe AET found that while providers have conversations with their patients about side effects and side effect management, they express concern that there are no widely available systematic side effect assessment tools which contributes to the variation in care BC patients may receive with regard to their AET.⁶⁶ Conversely, in another qualitative study, providers were not particularly concerned about non-adherence although, side effects, considered a rarity, were attributed to non-adherence.⁶⁷ Additional research is needed to understand communication patterns between providers and patients, specifically with regard to adherence and side effects. Further, there is a need to understand the type of information shared with patients and the ways in which this information is presented.

This study has several strengths such as 1) inclusion of substantial proportion of both black and white survivors in the sample, 2) collection of groups of factors hypothesized to be associated with adherence as well as variables reported to be significant in other studies, inclusion of factors not-previously collected in diverse samples, 3) focus on both regimen adherence and AET-symptoms, and 4) measurement of sociocultural factors and patient-reported symptoms in a diverse population of women with breast cancer. There are limitations in our study that should be acknowledged. First, most study participants (89.6%) were insured; therefore, results may not be generalizable to uninsured or underinsured populations. Additionally, our sample is limited to black and white women, limiting the ability to assess adherence in other ethnic or racial groups (e.g. Latinas, Asians). Finally, the study did not include other measures of adherence such as persistence or discontinuation from pharmacy records. However, initiation of AET was confirmed via pharmacy reports and the purpose of this study was to examine medication taking behaviors. Important next steps will be to examine multiple dimensions of adherence.

AET adherence is a modifiable factor to reduce morbidity and mortality in breast cancer survivors. To better address AET non-adherence, a full picture of the continuum of adherence behaviors at differential time-periods during the course of treatment is crucial. This can inform appropriate intervention changes as adherence likely changes over time, and is influenced by different factors pending the treatment course. Addressing early non-adherence behaviors may provide an opportunity to mitigate long-term problems of persistence. The impact of symptoms on adherence and the higher symptom report among black women need further investigation. Interventions to manage symptoms and address racial differences are needed.

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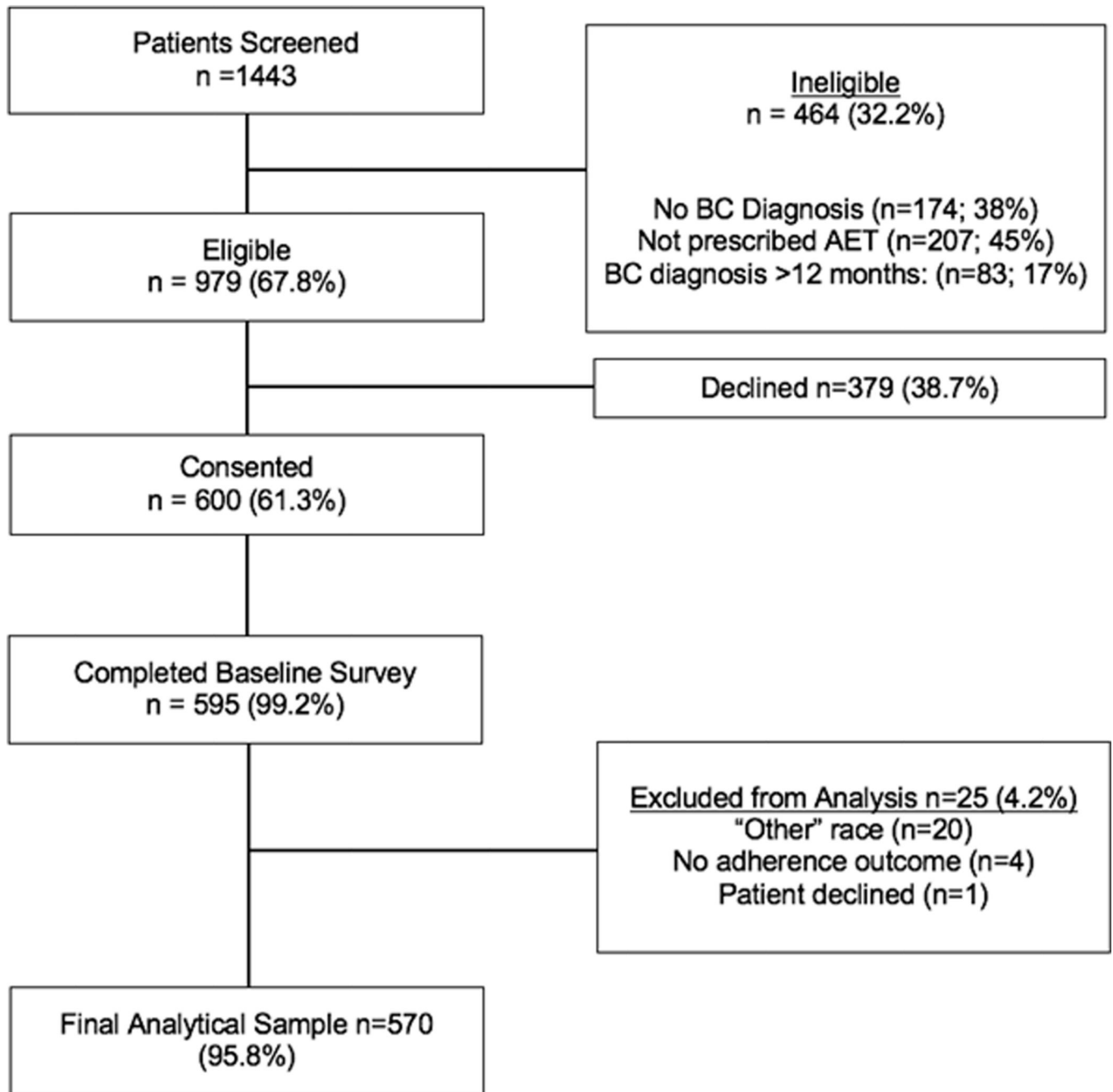


Figure 1.
WHIP Study Schema

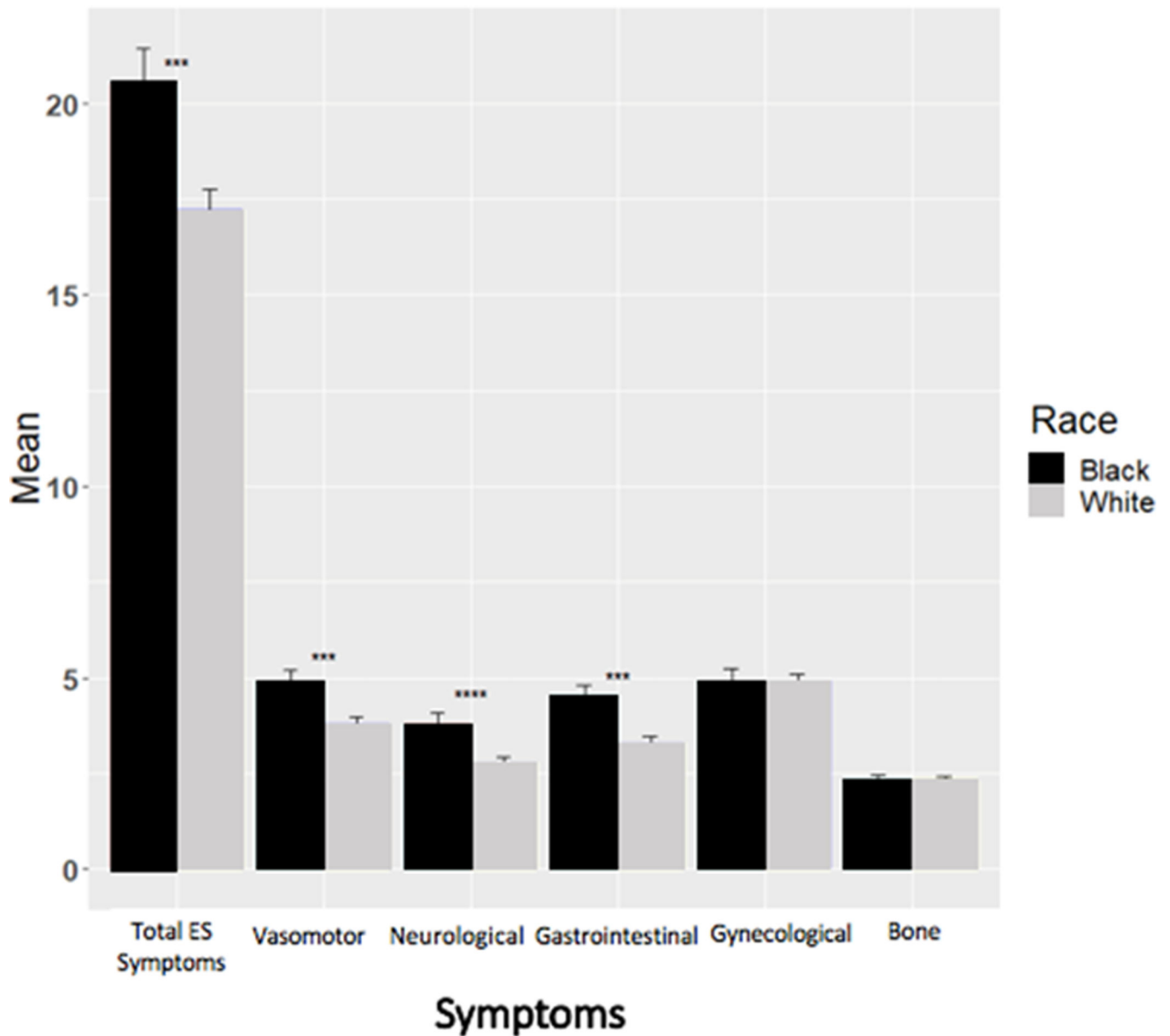


Figure 2.

AET Symptom Severity by Race

Figure 2.: ES total and subscale scores by race. Y-axis shows the mean of ES total and subscale scores. The bar represents standard error. The red represents Black patients, and the blue represents White patients. The x-axis is labelled by the name of ES total and subscales symptoms. T-tests are performed.

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

Table 1:

Descriptive statistics by medication adherence (N=570)

	Medication Adherence			p-value
	All	Nonadherent (N=203)	Adherent (N=367)	
	N (%)	N (%)	N (%)	
Race^a				
Black	162 (28.4)	78 (48.1)	84 (51.9)	<0.001
White	408 (71.6)	125 (30.6)	283 (69.4)	
Age^a				
50+ years	438 (76.8)	136 (31.1)	302 (68.9)	<0.001
50 years	132 (23.2)	67 (50.8)	65 (49.2)	
Insurance				
Both	22 (4.3)	7 (31.8)	15 (68.2)	0.38
Private	470 (92.0)	170 (36.2)	300 (63.8)	
Public	19 (3.7)	4 (21.1)	15 (78.9)	
Marriage				
Married or living with a partner	365 (64.3)	129 (35.3)	236 (64.7)	0.99
Single	203 (35.7)	72 (35.5)	131 (64.5)	
Education				
Less than college	80 (14.2)	30 (37.5)	50 (62.5)	0.81
College or higher	483 (85.8)	171 (35.4)	312 (64.6)	
Income^a				
<100,000/year	267 (49.9)	101 (37.8)	166 (62.2)	0.51
100,000/year	268 (50.1)	93 (34.7)	175 (65.3)	
Home				
Apartment	49 (9.2)	20 (40.8)	29 (59.2)	0.44
House	485 (90.8)	166 (34.2)	319 (65.8)	
Working Status^a				
No	224 (41.3)	60 (26.8)	164 (73.2)	<0.001
Yes	318 (58.7)	133 (41.8)	185 (58.2)	
Stage				
I	308 (59.8)	103 (33.4)	205 (66.6)	0.19
II	164 (31.8)	63 (38.4)	101 (61.6)	
III	43 (8.3)	20 (46.5)	23 (53.5)	
Surgery type				
Lumpectomy	237 (51.1)	77 (32.5)	160 (67.5)	0.62
Mastectomy	198 (42.7)	76 (38.4)	122 (61.6)	
Both	25 (5.4)	11 (44.0)	14 (56.0)	
No surgery	4 (0.8)	1 (25.0)	3 (75.0)	
Chemotherapy^a				

	Medication Adherence			p-value
	All	Nonadherent (N=203)	Adherent (N=367)	
	N (%)	N (%)	N (%)	
Yes	211 (39.5)	89 (42.1)	122 (57.8)	0.024
No	323 (60.5)	104 (32.2)	219 (67.8)	
Radiation				
Yes	340 (67.2)	124 (36.5)	216 (63.5)	0.614
No	166 (32.8)	56 (33.7)	110 (66.3)	
Medication^a				
AIs	350 (61.8)	102 (29.1)	248 (70.9)	<0.001
Tamoxifen	216 (38.2)	100 (46.3)	116 (53.7)	
BMI^a				
Overweight or Obese	355 (66.6)	124 (34.9)	231 (65.1)	0.368
Underweight or Normal	178 (33.4)	70 (39.3)	108 (60.7)	
Physical Activity Level				
Low	163 (30.5)	60 (36.8)	103 (63.2)	0.900
Moderate	280 (52.4)	102 (36.4)	17 (63.6)	
High	91 (17.1)	31 (34.1)	60 (65.9)	
Daily sitting time^a				
6 hours	327 (57.4)	94 (28.7)	233 (71.3)	<0.001
> 6 hours	243 (42.6)	109 (44.9)	134 (55.1)	
Distress^a				
Under control	321 (56.8)	97 (30.2)	224 (69.8)	0.009
Some distress	168 (29.7)	70 (41.7)	98 (58.3)	
High level of distress	76 (13.5)	34 (44.7)	42 (55.3)	
	Mean (SD)	Mean (SD)	Mean (SD)	p-value
Age	58.9(11.0)	55.9 (11.1)	60.5 (10.6)	<0.001
BMI	28.7 (7.5)	28.8 (7.3)	28.6 (7.6)	0.817
Self-efficacy^a	44.7 (4.0)	44.3 (4.3)	44.9 (3.9)	0.098
Understand Participate in Care	15.0 (1.4)	14.9 (1.5)	15.1 (1.4)	0.046
Maintain Positive Attitude	14.4 (2.0)	14.3 (2.1)	14.5 (2.0)	0.242
Obtaining information	15.2 (1.4)	15.2 (1.6)	15.3 (1.4)	0.293
Medication Concerns^a	11.2 (2.9)	11.7 (3.1)	10.9 (2.8)	0.001
Medication Necessity^a	13.9 (3.0)	13.5 (2.9)	14.1 (3.1)	0.027
Religiosity	26.7 (7.5)	27.7 (7.2)	26.2 (7.7)	0.018
Health Literacy Screening^a	0.9 (1.6)	1.0 (1.6)	0.8 (1.6)	0.193
Perceived Severity^a	37.5 (14.4)	38.3 (14.0)	37.0 (14.6)	0.307
Perceived Susceptibility^a	37.8 (16.4)	39.0 (15.9)	37.1 (16.7)	0.2
Social support	81.8 (18.2)	79.6 (18.9)	83.0 (17.8)	0.031

	Medication Adherence			p-value
	All	Nonadherent (N=203)	Adherent (N=367)	
	N (%)	N (%)	N (%)	
Emotional Support ^a	82.4 (18.5)	80.8 (18.8)	83.4 (18.2)	0.106
Tangible Support ^a	80.5 (23.6)	77.4 (24.9)	82.2 (22.7)	0.02
Trust in primary care ^a	78.6 (15.1)	76.8 (14.4)	79.6 (15.5)	0.04
Communication ^a	33.9 (4.9)	33.3 (5.1)	34.2 (4.7)	0.025
Medical Mistrust ^a	20.4 (4.9)	20.2 (4.5)	20.4 (5.1)	0.639
Total Endocrine Symptoms	18.2 (11.3)	20.2 (11.0)	17.0 (11.3)	0.001
Vasomotor Symptoms	4.1 (3.7)	4.4 (3.4)	3.9 (3.8)	0.128
Neuropsychological Symptoms	3.1 (3.0)	3.5 (3.0)	2.9 (3.0)	0.014
Gastrointestinal Symptoms	3.7 (3.4)	3.9 (3.4)	3.5 (3.4)	0.152
Gynecological Symptoms	4.9 (3.9)	5.8 (4.1)	4.4 (3.7)	<0.001
Bone Symptoms	2.3 (1.9)	2.4 (2.1)	2.3 (1.9)	0.614

Note: N=sample size; SD=standard deviation

Percentages are by columns for all participants and by rows across medication adherence.

T-tests used for continuous variables and chi-square tests used for categorical variables

* p<0.05,

** p<0.01,

*** p<0.001.

^a represents the variables considered for inclusion in the logistic regression model and had to earn their way into the models with stepwise selection.

Table 2:

Descriptive statistics by Race (N=570)

	Race		p-value
	Black (N=162)	White (N=408)	
	N (%)	N (%)	
Age			
50+ years	118 (72.8)	320 (78.4)	0.15
50 years	44 (27.2)	88 (21.6)	
Insurance			
Both	7 (4.9)	15 (4.1)	0.048 *
Private	127 (88.2)	343 (93.5)	
Public	10 (6.9)	9 (2.4)	
Working Status			
No	60 (40.0)	164 (41.8)	0.7
Yes	90 (60.0)	228 (58.2)	
Distress			
Under control	88 (55.3)	233 (57.4)	0.29
Some distress	44 (27.7)	124 (30.5)	
High level of distress	27 (17.0)	49 (12.1)	
Medication			
AIs	96 (60.4)	254 (62.4)	0.65
Tamoxifen	63 (39.6)	153 (37.6)	
BMI (categorized)			
Overweight or Obese	130 (86.7)	225 (58.7)	<0.0001 ***
Underweight or Normal	20 (13.3)	158 (41.3)	
Physical Activity Level			
Low	57 (38.5)	106 (27.5)	0.0065 *
Moderate	76 (51.4)	204 (52.8)	
High	15 (10.1)	76 (19.7)	
Stage			
I	72 (52.9)	231 (64.0)	0.075
II	51 (37.5)	101 (28.0)	
III	13 (9.6)	29 (8.0)	
Surgery type			
Lumpectomy	55 (42.3)	182 (54.5)	0.18
Mastectomy	65 (50.0)	133 (39.8)	
Both	8 (6.2)	17 (5.1)	
No surgery	2 (1.5)	2 (0.6)	
Chemotherapy			
Yes	71 (48.3)	140 (36.2)	0.011 *
No	76 (51.7)	247 (63.8)	
Radiation			

	Race		p-value
	Black (N=162)	White (N=408)	
	N (%)	N (%)	
Yes	87 (64.4)	253 (68.2)	0.43
No	48 (35.6)	118 (31.8)	
Daily sitting time			
6 hours	90 (55.6)	237 (58.1)	0.58
> 6 hours	72 (44.4)	171 (41.9)	
Marriage			
Married or living with a partner	75 (46.3)	290 (71.4)	<0.0001 ***
Single	87 (53.7)	116 (28.6)	
Education			
Less than college	31 (19.1)	49 (12.2)	0.033 *
College or higher	131 (80.9)	352 (87.8)	
Income			
<100,000/year	102 (67.5)	165 (43.0)	<0.0001 ***
>=100,000/year	49 (32.5)	219 (57.0)	
Home			
Apart	30 (20.0)	19 (4.9)	<0.0001 ***
House	120 (80.0)	365 (95.1)	
	Mean ± SD	Mean ± SD	p-value
Age	57.4 ± 11.6	59.4 ± 10.8	0.044 *
BMI	32.1 ± 7.1	27.3 ± 7.3	<0.0001 ***
Self-efficacy	45.0 ± 3.4	44.6 ± 4.3	0.32
Understand Participate in Care	14.9 ± 1.3	15.1 ± 1.5	0.25
Maintain Positive Attitude	14.7 ± 1.8	14.3 ± 2.1	0.038 *
Obtaining information	15.3 ± 1.3	15.2 ± 1.5	0.29
Medication Concerns	11.8 ± 3.1	10.9 ± 2.9	0.0012 **
Medication Necessity	14.1 ± 3.0	13.8 ± 3.0	0.29
Religiosity	32.2 ± 4.2	24.6 ± 7.5	<0.0001 ***
Health Literacy Screening	1.3 ± 2.0	0.7 ± 1.4	<0.0001 ***
Perceived Severity	40.9 ± 13.3	36.2 ± 14.6	0.0005 ***
Perceived Susceptibility	35.4 ± 15.4	38.7 ± 16.8	0.035 *
Social support	83.3 ± 18.0	81.1 ± 18.3	0.2
Emotional Support	83.7 ± 18.0	81.9 ± 18.7	0.3
Tangible Support	82.8 ± 23.2	79.6 ± 23.7	0.15
Trust in primary care	76.0 ± 15.6	79.6 ± 14.8	0.0092 ***
Communication	33.0 ± 4.5	34.2 ± 5.0	0.0076 **
Medical Mistrust	22.1 ± 5.2	19.7 ± 4.6	<0.0001 ***
Total Endocrine Symptoms	20.5 ± 11.7	17.2 ± 11.0	0.0023 *

	Race		p-value
	Black (N=162)	White (N=408)	
	N (%)	N (%)	
Vasomotor Symptoms	4.9 ± 3.6	3.8 ± 3.7	0.0018**
Neuropsychological Symptoms	3.8 ± 3.3	2.8 ± 2.8	0.0017**
Gastrointestinal Symptoms	4.5 ± 3.7	3.3 ± 3.2	0.0015**
Gynecological Symptoms	4.9 ± 3.9	4.9 ± 4.0	0.94
Bone Symptoms	2.3 ± 1.8	2.3 ± 2.0	0.88

Note: N=sample size; SD=standard deviation

T-tests were used for continuous variables and chi-square tests were used for categorical variables

* p<0.05,

** p<0.01,

*** p<0.001.

Table 3:

Multivariable Logistic regression Models for Adherence by AET Symptom Domains

Parameters	Odds ratio estimates (95% CI)					
	Primary model	Subset models				
	Total Endocrine Symptoms	Vasomotor Symptoms	Neuropsychological Symptoms	Gynecologic Symptoms	Gastrointestinal Symptoms	Bone Symptoms
Symptom score	0.98 (0.96, 0.995)*	1.02 (0.96, 1.08)	0.93 (0.87,0.994)*	0.92 (0.87, 0.96)***	0.96 (0.91, 1.02)	0.97 (0.85, 1.11)
Race (Black vs White)	0.43 (0.27, 0.67)***	0.43 (0.28, 0.68)***	0.42 (0.27, 0.66)***	0.42 (0.27,0.65)***	0.42 (0.27,0.78)***	0.46 (0.27, 0.78)**
Working status (No vs. Yes)	1.57 (1.03,2.40)*	1.65 (1.08, 2.52)*	1.60 (1.05, 2.44)*	1.62 (1.06, 2.47)*	1.62 (1.06,2.46)*	-
Medication (AI vs. Tamoxifen)	1.91 (1.28, 2.87)**	1.95 (1.29, 2.94)**	1.94 (1.29,2.93)**	1.98 (1.31, 2.98)**	1.92 (1.28,2.88)**	2.59 (1.52, 4.40)***
BMI (Overweight vs. Normal)	1.58 (1.04, 2.43)*	1.50 (0.98, 2.30)	1.50 (0.98, 2.29)	1.43 (0.93, 2.18)	1.59 (1.03,2.44)*	-
Daily sitting time (6 hours vs. >6 hours)	1.83 (1.25, 2.70)**	1.77 (1.20, 2.62)**	1.86 (1.27, 2.74)**	1.78 (1.21,2.63)**	1.83 (1.24, 2.68)**	2.01 (1.22,3.32)**
Chemotherapy (No vs. Yes)	-	-	-	-	-	1.62 (0.94, 2.71)
Medication Concerns	-	0.92 (0.86, 0.99)*	-	-	-	-
Goodness-of-Fit (p-value)	0.59	0.09	0.40	0.88	0.57	0.39
AIC	660.80	650.93	657.88	657.88	662.63	395.52
C-statistic	0.70	0.69	0.69	0.70	0.69	0.69

Note: Each model controls for race, age, medication and Total Endocrine symptoms or one of the endocrine symptom subscales by default. Stepwise selection was performed in order to determine the inclusion of additional variables.

CI=confidence interval

* p<0.05;

** p<0.01;

*** p<0.001