

## Racial/Ethnic Differences in Use and Duration of Adjuvant Hormonal Therapy for Breast Cancer in the Women's Health Initiative

Jennifer C. Livaudais, Andrea LaCroix<sup>1,2</sup>, Rowan T. Chlebowski<sup>3</sup>, Christopher I. Li<sup>1,2</sup>, Laurel A. Habel<sup>4</sup>, Michael S. Simon<sup>5</sup>, Beti Thompson<sup>1,2</sup>, Deborah O. Erwin<sup>6</sup>, F. Allan Hubbell<sup>7</sup>, and Gloria D. Coronado<sup>8</sup>

### Abstract

**Background:** Five-year breast cancer survival rates are lower among Hispanic and African-American women than among Non-Hispanic White women. Differences in breast cancer treatment likely play a role. Adjuvant hormonal therapies increase overall survival among women with hormone receptor-positive breast cancer.

**Methods:** We examined racial/ethnic differences in use and duration of adjuvant hormonal therapy among 3,588 postmenopausal women enrolled in the Women's Health Initiative (WHI) Extension Study. Women diagnosed with hormone receptor-positive localized or regional stage breast cancer after study enrollment were surveyed between September 2009 and August 2010 and asked to recall prior use and duration of adjuvant hormonal breast cancer therapy. ORs comparing self-reported use and duration with race/ethnicity (Hispanic, African-American, Asian/Pacific Islander vs. Non-Hispanic White) were estimated using multivariable-adjusted logistic regression.

**Results:** Of the 3,588 women diagnosed from 1994 to 2009; 3,039 (85%) reported any use of adjuvant hormonal therapy, and 67% of women reporting ever-use who were diagnosed before 2005 reported using adjuvant hormonal therapy for the optimal duration of 5 years or more. In adjusted analysis, no statistically significant differences in use or duration by race/ethnicity were observed.

**Conclusions:** This study did not find significant differences in use or duration of use of adjuvant hormonal therapy by race/ethnicity.

**Impact:** Findings should be confirmed in other population-based samples, and potential reasons for discontinuation of therapy across all racial/ethnic groups should be explored. *Cancer Epidemiol Biomarkers Prev*; 22(3): 365–73. ©2012 AACR.

### Introduction

African-American and Hispanic women with breast cancer have lower age-adjusted 5-year survival rates compared with non-Hispanic White women (75% and 83% vs. 88%, respectively; ref. 1). Even after controlling for differences in tumor stage, hormone receptor status, socioeconomic factors, and surgical and radiation treatment, disparities in breast cancer survival for African-American

and Hispanic women persist (HR = 1.5 and 1.1, respectively; ref. 2). Remaining differences may be explained by differences in the use of adjuvant breast cancer treatments, including chemotherapy and hormonal therapy, not captured in population-based cancer registries (2–5).

Adjuvant hormonal therapy is associated with improved disease-free and overall survival among women with hormone receptor-positive breast cancer, irrespective of age, menopausal status, lymph node status, or chemotherapy use (6, 7). The optimal duration of use for adjuvant hormonal therapy is 5 years (6, 7), and early discontinuation and nonadherence to adjuvant hormonal therapy have been associated with increased mortality (8). A small number of studies to date have documented racial/ethnic differences in use of adjuvant hormonal therapy, indicating that, compared with non-Hispanic White women, Chinese (9, 10), African-American (3, 11, 12), and Hispanic women (10, 11) are significantly less likely to use adjuvant hormonal therapy in multivariable analyses.

To our knowledge, few previous studies have examined racial/ethnic differences in duration of adjuvant

**Authors' Affiliations:** <sup>1</sup>Fred Hutchinson Cancer Research Center; <sup>2</sup>University of Washington School of Public Health, Seattle, Washington; <sup>3</sup>David Geffen School of Medicine, University of California, Los Angeles, Los Angeles; <sup>4</sup>Kaiser Division of Research, Oakland, California; <sup>5</sup>Karmanos Cancer Center, Detroit, Michigan; <sup>6</sup>School of Public Health and Health Professions, State University of New York at Buffalo, Buffalo, New York; <sup>7</sup>School of Medicine, University of California, Irvine, Irvine, California; and <sup>8</sup>The Center for Health Research, Kaiser Permanente Northwest, Portland, Oregon

**Corresponding Author:** Jennifer C. Livaudais, Fred Hutchinson Cancer Research Center and University of Washington, Seattle, WA 98109. Phone: 917-538-0435; E-mail: jclivaudais@gmail.com

doi: 10.1158/1055-9965.EPI-12-1225

©2012 American Association for Cancer Research.

hormonal therapy use. Consequently, we examined this issue in a cohort from the ethnically diverse Women's Health Initiative (WHI) Extension Study. In light of persistent survival disparities for African-American and Hispanic women in the United States, we examined whether these groups of women in WHI were less likely than non-Hispanic White women to report: (i) use of adjuvant hormonal therapy, and (ii) duration of adjuvant hormonal therapy for  $\geq 1$ ,  $\geq 3$ , and  $\geq 5$  years.

## Materials and Methods

### Study setting

The WHI population represents a large, ethnically diverse national cohort of women, first recruited between 1993 and 1998, and followed for the development of breast cancer and other end points, including death. Recruitment methods for the original WHI cohorts have been described in detail elsewhere (13). Briefly, participants were recruited from areas surrounding 40 clinical centers at major academic health centers in 24 states and the District of Columbia. These areas included urban, suburban, and rural populations. Enrollment of racial/ethnic minority groups proportionate to the racial/ethnic distribution in the U.S. population among women ages 50 to 79 years was a priority. Initial contact from most clinics was made through a mass mailing of a recruitment brochure, providing information on the WHI. Women who returned postcards expressing interest were contacted by telephone interviewers who established eligibility over the phone. Three clinic visits were then conducted to enroll women in the clinical trial component and one visit was conducted to enroll women in the observational study. Those women who were found ineligible for the clinical trials at any point during the screening visits were offered participation in the observational study. In total, 68,133 women were randomized to participate in one or more of the clinical trials and 93,676 were enrolled in the observational study.

At the closeout of the clinical trial and observational study components of the WHI study in March 2005, all participants were invited to participate in an additional 5 years of observational study. A total of 115,400 women agreed to participate in the WHI Extension Study, and these participants were followed through the end of 2010, by completing annual surveys mailed to their homes. The Institutional Review Board and Office of Management and Budget at the Fred Hutchinson Cancer Research Center (Seattle, WA) approved all study procedures.

### Study sample

Between September 2009 and August 2010, a medication inventory survey was mailed to all Extension Study cohort participants. All women in the cohort who were documented in WHI records to have been diagnosed with first primary breast cancer since enrollment in WHI were also sent a supplementary questionnaire to collect information about their use of and duration of adjuvant hormonal therapy after breast cancer diagnosis. WHI staff

mailed the supplementary breast cancer treatment questionnaire to a total of 6,584 women. Nonresponders were sent a follow-up mailing, and additional attempts were made by telephone to reach the remaining nonresponders after the second mailing. As of September 2010, a total of 5,712 WHI Extension Study participants had completed and returned the supplementary breast cancer treatment questionnaire (response rate = 87%); 5,581 had a diagnosis of breast cancer, confirmed by the WHI Clinical Coordinating Center after being verified by centrally trained WHI physician adjudicators who reviewed pathology reports (14). At the time of analysis, the most recent adjudication of breast cancer outcomes occurred in August 2009.

### Inclusion/exclusion criteria

Of the 5,581 participants with confirmed diagnosis of breast cancer responding to the questionnaire, 4,041 had hormone receptor-positive breast cancer, and of these, 3,635 had localized or regional stage tumors. A total of 3,581 women self-identified as non-Hispanic White, Hispanic, African-American, or Asian-American, reflecting 65% of the original WHI sample, would have been eligible for inclusion in our analysis, had they all continued participating in WHI through the Extension study. In other words, 35% of women diagnosed with hormone receptor-positive breast cancer after initial study enrollment were eventually lost to follow-up, including 34% of non-Hispanic White women, 44% of Hispanic women, 49% of African-American women, and 38% of Asian-American women.

Our final sample consisted of 3,575 of women who also had nonmissing information on use of adjuvant hormonal breast cancer therapy, including 3,295 non-Hispanic White, 63 Hispanic, 151 African-American, and 66 Asian-American women (including 42 Japanese, 20 Chinese, 3 Filipina, and 1 other Asian woman).

### Data measures

**Use of adjuvant hormonal therapy.** The breast cancer treatment supplemental questionnaire administered in 2009/2010 asked the participants to report their use of adjuvant hormonal breast cancer treatments after diagnosis, and women were asked to check "yes or no" for use of tamoxifen, toremifene, anastrozole, exemestane, or letrozole. Women who indicated that they had ever taken any of these adjuvant hormonal therapies since breast cancer diagnosis were classified as "users." "Nonusers" indicated no use of any of these medications.

**Duration of adjuvant hormonal therapy use.** Women reporting use of one or more types of adjuvant hormonal therapy were asked to indicate, for each type, how long in total they had taken that medication (<1 month, 1–5 months, 6–11 months, 1–2 years, 3–4 years, or  $\geq 5$  years). The total length of time that each woman used adjuvant hormonal therapy was calculated conservatively. We assigned the lower bound value of each of the response categories (0 months, 1 month, 6 months, 1 year, 3 years, or

5 years), and summed responses across all medications for each woman (duration of tamoxifen + toremifene + anastrozole + exemestane + letrozole).

**Self-reported race/ethnicity.** Self-reported race/ethnicity was available from an eligibility screener completed by all participants before WHI study enrollment. If women were of mixed race/ethnicity, they were asked to report which group they identified with most. Categories of interest for our analysis included non-Hispanic White, Hispanic, African-American, and Asian-American (including Chinese, Japanese, Filipina, or other Asian).

**Covariates.** Covariates of interest as potential confounders included age at breast cancer diagnosis, calendar year of diagnosis (by 4-year intervals), marital status, household income, highest level of education completed, and type of health insurance, collected from women during their baseline survey after WHI study randomization/enrollment. Weight and height were measured [to calculate body mass index (BMI) in kg/m<sup>2</sup>], and history of breast cancer in female relatives was collected during this time. For women diagnosed with a first primary breast cancer during study follow-up, tumor stage, tumor size, histology type, and tumor grade were adjudicated by WHI physicians, and available in participant records. Barriers to use of adjuvant hormonal therapy were assessed with the breast cancer treatment supplementary questionnaire. Women were asked to check "yes" or "no" to a list of prespecified barriers to use: physician did not recommend, concerned about side effects, concerned about cost, lack of insurance coverage, discouraged by family, discouraged by friends, inconvenient to use, and concerned about missing work. We created a single summary measure of barriers: women who reported "yes" to any barrier were classified as having "one or more barriers" versus women who did not report "yes" to any barriers ("no barriers").

### Statistical analysis

Summary statistics are presented according to (i) race/ethnicity and (ii) use of adjuvant hormonal therapy, by comparing women with respect to age at diagnosis, year of diagnosis, marital status, household income, education level, type of health insurance, original WHI cohort, BMI, family history of breast cancer in a female relative, Surveillance Epidemiology and End Results (SEER) summary stage, tumor size, histology type, tumor grade, and self-reported barriers to use. Descriptive statistics are based on nonmissing values, and percentages of cases with missing data are reported in table footnotes.  $\chi^2$  tests were used to assess significant differences between groups with respect to categorical variables, and *t* tests were used to assess differences with respect to continuous variables (2-tailed significance level  $P < 0.05$ ).

To examine the association of race/ethnicity with (i) use of adjuvant hormonal therapy, and (ii) duration of adjuvant hormonal therapy among users ( $\geq 1$  year,  $\geq 3$  years,  $\geq 5$  years), we used logistic regression with robust variance adjustment in Stata/SE version 11.0. Non-Hispanic

White women served as the referent exposure category for each analysis. Covariates adjusted for included factors associated in bivariate analysis with race/ethnicity, and with the outcome of interest among the referent group (non-Hispanic White women); age at diagnosis, year of diagnosis (4-year intervals), marital status, and SEER summary stage (for all analyses), in addition to household income, type of health insurance, histology type, and tumor grade (for analysis of differences in use).

Analyses for duration of  $\geq 1$ ,  $\geq 3$ , and  $\geq 5$  years were restricted to women diagnosed before 2009, 2007, and 2005, respectively, to ensure equal opportunity for all women included in the analysis to have used adjuvant hormonal therapy for the specified number of years by the time they were interviewed in 2009 to 2010.

We proposed, *a priori*, to explore whether the relationship between race/ethnicity and use of adjuvant therapy varied according to (i) educational level (college education vs. less than college education), (ii) family history of breast cancer in a female relative, or (iii) self-reported barriers to use of adjuvant hormonal therapy ( $\geq 1$  barrier vs. no barriers). Interactions for each of these variables were explored (Wald test significance level  $P < 0.05$ ). A statistically significant interaction was identified according to barriers to use [ $P_{\text{interaction}} < 0.001$  (Hispanic);  $< 0.001$  (African-American); and  $< 0.001$  (Asian-American)], and results were stratified according to this factor.

## Results

### Participant characteristics

A total of 3,575 participants from the WHI Extension Study who responded to the breast cancer treatment questionnaire met the eligibility criteria (see Table 1). The mean age at breast cancer diagnosis was 69 years [age range, 50–91 years; (SD) = 7]. Non-Hispanic White women made up the majority of the sample (92%), followed by African-American (4%), Asian-American (2%), and Hispanic women (2%). On average, non-Hispanic White women were the oldest (69.4 years;  $P < 0.001$ ), African-American women were the least likely to be married (49%;  $P < 0.001$ ), and Asian-American women were of the highest income (65% above \$50,000/year;  $P < 0.001$ ) and education levels (59% completed college or beyond;  $P < 0.001$ ). The majority of participants had some type of private health insurance at baseline (88%), and this was most common among Asian-American women (100%;  $P < 0.001$ ). Compared with other racial/ethnic groups, greater percentages of African-American women were diagnosed with regional stage breast cancer (30%;  $P = 0.044$ ), and with high-grade tumors (35% grade 3;  $P < 0.001$ ).

A total of 2,985 (83%) reported use of adjuvant hormonal therapy for breast cancer. More than one-third of these women (36%) reported use of more than one type of adjuvant hormonal therapy, whereas the remaining women reported exclusive use of one therapy; tamoxifen (31%), anastrozole (26%), letrozole (6%), exemestane (1%), and toremifene ( $< 1\%$ ). Compared with nonusers, users of

**Table 1.** WHI: Characteristics of women diagnosed with hormone receptor-positive breast cancer from 1994 to 2009 (N = 3,575)

	Non-Hispanic White 3,295 (92%) n (%) <sup>a</sup>	Hispanic 63 (2%) n (%) <sup>a</sup>	African- American 151 (4%) n (%) <sup>a</sup>	Asian- American 66 (2%) n (%) <sup>a</sup>	P	Nonuse of adjuvant hormonal treatment 590 (17%) n (%) <sup>a</sup>	Use of adjuvant hormonal treatment 2,985 (83%) N (%) <sup>a</sup>	P
Sociodemographic characteristics								
Age at diagnosis (mean ± SD)	69.4 ± 7.2	66.0 ± 6.2	67.6 ± 6.8	68.5 ± 7.8	<0.001	71.4 ± 7.6	68.9 ± 7.0	<0.001
Year of diagnosis								
1994–1997	247 (7.5)	5 (7.9)	14 (9.3)	0	0.263	62 (10.5)	204 (6.8)	0.015
1998–2001	1,112 (33.8)	25 (39.7)	40 (26.5)	26 (39.4)		185 (31.4)	1,018 (34.1)	
2002–2005	1,125 (34.1)	20 (31.8)	60 (39.7)	24 (36.4)		205 (34.7)	1,024 (34.3)	
2006–2009	811 (24.6)	13 (20.6)	37 (24.5)	16 (24.2)		138 (23.4)	739 (24.8)	
Marital status <sup>1</sup>								
Single, widowed, divorced	1,043 (31.8)	18 (29.0)	75 (50.7)	17 (25.8)	<0.001	226 (38.4)	927 (31.2)	0.001
Married or living with partner	2,242 (68.2)	44 (71.0)	73 (49.3)	49 (74.2)		362 (61.6)	2,046 (68.8)	
Household income <sup>2</sup>								
Less than \$20,000	272 (8.7)	8 (14.0)	24 (17.0)	6 (9.2)	<0.001	76 (13.6)	234 (8.3)	<0.001
\$20,000–\$49,999	1,395 (44.8)	27 (47.4)	63 (44.7)	17 (26.2)		260 (46.5)	1,242 (44.1)	
\$50,000–\$99,999	1,043 (33.5)	17 (29.8)	44 (31.2)	28 (43.1)		164 (29.3)	968 (34.3)	
\$100,000 or more	406 (13.0)	5 (8.8)	10 (7.1)	14 (21.5)		59 (10.6)	376 (13.3)	
Education level <sup>1</sup>								
Less than high school	54 (1.7)	6 (9.5)	9 (6.1)	0	<0.001	10 (1.7)	59 (2.0)	0.368
High school diploma/vocational	1,602 (48.8)	30 (47.6)	78 (52.7)	27 (40.9)		305 (52.0)	1,432 (48.2)	
College degree	931 (28.4)	17 (27.0)	18 (12.2)	28 (42.4)		159 (27.1)	835 (28.1)	
Masters or doctoral degree	693 (21.1)	10 (15.9)	43 (29.0)	11 (16.7)		113 (19.2)	644 (21.7)	
Type of health insurance								
HMO or other private	2,900 (88.6)	51 (82.3)	121 (82.3)	63 (95.4)	<0.001	497 (84.5)	2,638 (89.1)	0.001
Public (Medicare, Medicaid, VA)	267 (8.1)	2 (3.2)	17 (11.6)	3 (4.6)		72 (12.2)	217 (7.3)	
Other	36 (1.1)	4 (6.4)	0	0		6 (1.0)	34 (1.2)	
None	71 (2.2)	5 (8.1)	9 (6.1)	0		13 (2.2)	72 (2.4)	
Original WHI cohort								
Clinical trial	1,398 (42.4)	32 (50.8)	91 (60.3)	28 (42.4)	<0.001	259 (43.9)	1,290 (43.2)	0.76
Observational cohort	1,897 (57.6)	31 (49.2)	60 (39.7)	38 (57.6)		331 (56.1)	1,695 (56.8)	
Health-related and tumor characteristics								
Body mass index <sup>1</sup> (BMI) in kg/m <sup>2</sup> (mean ± SD)	27.8 ± 5.6	30.1 ± 6.1	30.8 ± 6.0	26.0 ± 3.6	<0.001	27.8 ± 5.6	27.9 ± 5.6	0.787
Obese <sup>1</sup> (BMI ≥ 30 kg/m <sup>2</sup> )	959 (29.4)	25 (40.3)	73 (48.3)	9 (13.9)	<0.001	180 (30.8)	885 (29.9)	0.678
Family history of breast cancer in female relative	759 (23.0)	12 (19.1)	30 (19.9)	12 (18.2)	0.544	131 (22.2)	682 (22.9)	0.733
SEER Summary stage								
Localized	2,600 (78.9)	50 (79.4)	106 (70.2)	56 (84.8)	0.044	553 (93.7)	2,259 (75.7)	<0.001
Regional	695 (21.1)	13 (20.6)	45 (29.8)	10 (15.2)		37 (6.3)	726 (24.3)	
Tumor size (in cm) <sup>3</sup>								
<1 cm	1,062 (33.2)	22 (34.9)	40 (27.2)	20 (31.3)	0.485	308 (53.8)	836 (28.8)	<0.001
≥1cm	2,141 (66.8)	41 (65.1)	107 (72.8)	44 (68.8)		264 (46.2)	2,069 (71.2)	
Histologic type <sup>1</sup>								
Ductal	2,075 (63.2)	39 (62.9)	88 (58.7)	51 (77.3)	0.244	370 (62.9)	1,883 (63.3)	<0.001
Lobular/mixed lobular	879 (26.8)	17 (27.4)	42 (28.0)	10 (15.1)		120 (20.4)	828 (27.8)	
Other specified histology	331 (10.1)	6 (9.7)	20 (13.3)	5 (7.6)		98 (16.7)	264 (8.9)	
Tumor grade <sup>4</sup>								
Grade I	1,046 (34.2)	24 (39.3)	33 (26.2)	27 (42.9)	<0.001	239 (44.6)	891 (32.1)	<0.001
Grade II	1,444 (47.1)	28 (45.9)	49 (38.9)	29 (46.0)		219 (40.9)	1,331 (47.9)	
Grade III	572 (18.7)	9 (14.8)	44 (34.9)	7 (11.1)		78 (14.6)	554 (20.0)	

<sup>a</sup>Percentages based on nonmissing values.<sup>1</sup><1% missing; <sup>2</sup>5.5% missing; <sup>3</sup>2.7% missing; and <sup>4</sup>7.4% missing.

**Table 2.** WHI: Self-reported barriers to use of adjuvant hormonal therapy among women diagnosed with hormone receptor-positive breast cancer ( $N = 3,575$ )

	Non-Hispanic White 3,295 (92%)	Hispanic 63 (2%)	African- American 151 (4%)	Asian- American 66 (2%)	<i>P</i>
	<i>n</i> (%) <sup>a</sup>	<i>n</i> (%) <sup>a</sup>	<i>n</i> (%) <sup>a</sup>	<i>n</i> (%) <sup>a</sup>	
Potential barriers to use of adjuvant hormonal therapy					
Physician did not recommend	397 (12.1)	2 (3.2)	26 (17.2)	8 (12.1)	0.038
Concerned about side effects	375 (11.4)	10 (15.9)	12 (8.0)	7 (10.6)	0.382
These medications cost too much	166 (5.0)	5 (7.9)	9 (6.0)	2 (3.0)	0.595
Insurance would not cover these medications	40 (1.2)	2 (3.2)	3 (2.0)	1 (1.5)	0.473
Discouraged by family	10 (0.3)	0	1 (0.7)	0	0.797
Discouraged by friends	9 (0.3)	0	0	0	0.857
Taking these medications would be inconvenient	8 (0.2)	1 (1.6)	0	0	0.169
Concerned about missing work	3 (0.1)	0	0	0	0.968
Reported at least one barrier to use	883 (26.8)	17 (27.0)	45 (29.8)	17 (25.8)	0.871

<sup>a</sup>Percentages based on non-missing values.

adjuvant hormonal therapy were younger, more likely to be married (69% vs. 62%;  $P = 0.001$ ), and had higher household incomes (48% above \$50,000 vs. 40% above \$50,000;  $P < 0.001$ ). Users were also more likely to have regional stage breast cancer (24% vs. 6%;  $P < 0.001$ ), tumors  $\geq 1$  cm (71% vs. 46%;  $P < 0.001$ ), and tumors of high grade (20% vs. 15%;  $P < 0.001$ ). Characteristics of this sample are further described in Table 1.

Only 5% of women reported that cost was a barrier to use, followed by no insurance coverage (1%), discouragement from family (<1%), discouragement from friends (<1%), inconvenience of use (<1%), and concern over missing work (<1%; see Table 2). The most commonly cited barriers for all racial/ethnic groups were lack of physician recommendation (12%) and concern about the side effects (11%). Lack of physician recommendation was most commonly cited by African-American women, and least commonly cited by Hispanic women (17% vs. 3%;  $P = 0.038$ ). In contrast, concern over side effects was least commonly cited by African-American women, and most commonly cited by Hispanic women (8% vs. 16%,  $P =$  not significant). Twenty-seven percent of women reported experiencing at least one barrier to adjuvant hormonal therapy use.

### Multivariable logistic regression

**Use of adjuvant hormonal therapy.** In multivariable-adjusted analysis, no statistically significant differences in use of adjuvant hormonal therapy were observed between non-Hispanic White and Hispanic [(OR) = 1.20; 95% confidence interval; (CI) 0.51–2.84], African-American (OR = 0.96; 95% CI, 0.54–1.70) or Asian-American women (OR = 0.79; 95% CI, 0.40–1.56; see Table 3).

**Use of adjuvant hormonal therapy among women with no self-reported barriers.** Restricting the sample to women without any self-reported barriers to use, no

statistically significant differences in use were observed between non-Hispanic White and African-American women (OR = 1.07; 95% CI, 0.43–2.66; see Table 3). While there was a trend toward decreased use among Hispanic (OR = 0.58; 95% CI, 0.19–1.77) and Asian-American women (OR = 0.75; 95% CI, 0.28–1.96), these results were not statistically significant.

**Table 3.** WHI: Logistic regression: adjuvant hormonal therapy use among women with hormone receptor-positive breast cancer

	All women	
	<i>n</i> (%)	aOR <sup>a</sup> (95% CI)
Entire sample	( $N = 3,104$ )	
Race/ethnicity		
Non-Hispanic White	2,403 (83.7)	Ref
Hispanic	49 (87.5)	1.20 (0.51–2.84)
African-American	98 (84.5)	0.96 (0.54–1.70)
Asian-American	50 (80.7)	0.79 (0.40–1.56)
No self-reported barriers	( $N = 2,277$ )	
Non-Hispanic White	1,923 (91.1)	Ref
Hispanic	36 (87.8)	0.58 (0.19–1.77)
African-American	74 (92.5)	1.07 (0.43–2.66)
Asian-American	41 (89.1)	0.75 (0.28–1.96)

<sup>a</sup>Adjusted for age at diagnosis (continuous years), marital status, household income, type of health insurance, SEER stage, histology, tumor grade, and year of diagnosis (4-year intervals)

### Multivariable logistic regression (duration among ever-users)

**≥1 year duration.** Among ever-users diagnosed before 2009, there were no statistically significant racial/ethnic differences in duration of 1 year or more between non-Hispanic White and Hispanic (OR = 1.15; 95% CI, 0.40–3.30) or African-American women (OR = 1.09; 95% CI, 0.57–2.10; see Table 4). There was a trend toward decreased likelihood of 1 year or more duration among Asian-American women (OR = 0.61; 95% CI, 0.26–1.40), although the result was not statistically significant.

**≥3 years duration.** Among ever-users diagnosed before 2007, there were no statistically significant racial/ethnic differences in duration of 3 years or more observed between non-Hispanic White and African-American (OR = 0.94; 95% CI, 0.56–1.58) or Asian-American women (OR = 0.74; 95% CI, 0.36–1.54; see Table 4). There was a trend toward an increased likelihood of 3 years or more duration among Hispanic women (OR = 2.19; 95% CI, 0.76–6.36), although the result was not statistically significant.

**≥5 years duration.** Among ever-users diagnosed before 2005, there were no statistically significant racial/ethnic differences in duration of 5 years or more observed between non-Hispanic White and Hispanic (OR = 0.98; 95% CI, 0.49–1.98), African-American (OR = 0.84; 95% CI, 0.52–1.36), or Asian-American women (OR = 0.97; 95% CI, 0.49–1.92; see Table 4).

### Discussion

A large proportion (83%) of women participating in the WHI Extension Study diagnosed with hormone receptor-positive breast cancer between 1994 and 2009 reported using adjuvant hormonal therapy after breast cancer diagnosis. This proportion was consistent across diagnosis years (1994–2001: 83%; 2002–2009: 84%). Sixty-seven percent of women reporting ever-use, who were diagnosed before 2005, used adjuvant hormonal therapy for

the optimal duration of 5 years or more, and there were no statistically significant racial/ethnic differences in duration of use for ≥1, ≥3, or ≥5 years.

Our results can be compared with findings from a small number of studies that have explored racial/ethnic differences in adjuvant hormonal therapy use. One study including women diagnosed at municipal hospitals, tertiary referral centers, and community hospitals throughout the New York City, found that African-American or Hispanic race/ethnicity was associated with nonuse of adjuvant therapy compared with non-Hispanic White race (OR = 2.0; ref. 15). While our findings were inconsistent with this result, in their multivariable analysis, the New York study explored nonuse of radiation therapy, hormonal, and chemotherapy combined, grouped African-American and Hispanic women together, and included women less than 50 years of age at diagnosis (15).

Similar to our findings, data from a large integrated health system documented no differences in use between African-American and non-Hispanic White women with equal access to care (10). There may be similar cultural issues among African-Americans in this study and African-Americans in the WHI, which may explain the lack of variation in use by race. In contrast, 3 other studies reported that African-American women were less likely than non-Hispanic White women to use adjuvant hormonal therapies (3, 11, 12). Two of these studies (3, 12), one reporting on data from the Southern United States and the other reporting on a population from a single institute in Detroit, reported that non-Hispanic White women were more likely to use adjuvant hormonal therapy than African-American women (OR = 4.59 and 2.09, respectively). The third study (11), using data from the National Cancer Database Hospital database, reported a lower likelihood of adjuvant hormonal therapy use among African-American compared with non-Hispanic white women (OR = 0.91).

The WHI Extension cohort included women who agreed to participate in one of the original WHI cohorts,

**Table 4.** WHI: Logistic regression: duration of adjuvant hormonal therapy among women reporting ever-use

	<i>N</i> = 1,993 Duration ≥ 5 years (diagnosed before 2005)		<i>N</i> = 2,481 Duration ≥ 3 years (diagnosed before 2007)		<i>N</i> = 2,929 Duration ≥ 1 year (diagnosed before 2009)	
	<i>n</i> (%)	aOR <sup>a</sup> (95% CI)	<i>n</i> (%)	aOR <sup>a</sup> (95% CI)	<i>n</i> (%)	aOR <sup>a</sup> (95% CI)
Main exposure						
Race/ethnicity						
Non-Hispanic White	1,234 (67.0)	Ref	1,881 (82.2)	Ref	2,436 (90.1)	Ref
Hispanic	26 (68.4)	0.98 (0.49–1.98)	42 (91.3)	2.19 (0.76–6.36)	48 (92.3)	1.15 (0.40–3.30)
African-American	49 (63.6)	0.84 (0.52–1.36)	84 (83.2)	0.94 (0.56–1.58)	111 (91.7)	1.09 (0.57–2.10)
Asian-American	25 (67.6)	0.97 (0.49–1.92)	36 (78.3)	0.74 (0.36–1.54)	44 (86.3)	0.61 (0.26–1.40)

NOTE: <sup>a</sup>Adjusted for age at diagnosis (continuous years), marital status, SEER summary stage, and year of diagnosis (4-year intervals).

were followed through the end of the original study, and agreed to participate in the Extension cohort, which included being followed for an additional 5 years. As a result, our population is a selective sample that may not be representative of the larger population. The women who remained in the sample may be healthier or more likely to use and continue using adjuvant hormonal therapy compared with those women who declined participation or dropped out of the study, leading to a potential underestimation of racial/ethnic differences in use that might exist in the general population. These differences may explain the inconsistency between some of the previous studies and our findings.

Our findings also differ from a population-based study restricted to women ages 50 years and older diagnosed in 1994, reporting that Chinese women were significantly less likely than non-Hispanic White women to use adjuvant hormonal therapy for estrogen receptor-positive tumors (OR nonuse = 2.3; ref. 9). Data from the large integrated health system cited previously also documented that Chinese women were less likely than non-Hispanic White women to initiate adjuvant hormonal therapy (OR = 0.78; ref. 10). However, we were unable to look specifically at use among Chinese-American women in the WHI Extension cohort due to insufficient numbers, and the majority of Asian-American women in our sample were Japanese.

While a variety of factors have been associated with nonadherence to adjuvant hormonal therapy (16) including patient perception of low risk for recurrence (17), experience of adverse events (18–20), older patient age (21, 22), being married within a low SES-Medicaid insured population (23), poor patient-provider communication (24), and psychologic factors (19), only a small number of prior studies on duration of use have reported on racial/ethnic differences. Findings from the National Initiative for Cancer Care Quality revealed no racial/ethnic differences in long-term duration of use ( $\geq 4$  years), although non-White racial/ethnic groups were combined in the multivariable analysis due to small numbers (19). Another recently published study, using data from Kaiser Permanente Northern California, reported a greater likelihood of nonadherence to adjuvant hormonal therapy, defined as less than 4.5 years of use, for African-American women compared with non-Hispanic White women (HR = 1.23; 95% CI, 1.01–1.51; ref. 25). Our findings were not consistent with the latter study, which may also be explained by the selective nature of the WHI Extension cohort.

Some important limitations are worth noting. There were small numbers of minority women in our sample. Perhaps as a result, we did not observe statistically significant differences in use or duration of adjuvant hormonal therapy. In addition, greater proportions of African-American and Hispanic women with breast cancer were lost to follow-up in the WHI Extension cohort compared with non-Hispanic White and Asian-American women. In addition, some WHI participants, particularly

those diagnosed with breast cancer during earlier study years may no longer have been alive at the time our survey was administered in 2009 to 2010. As nonuse of adjuvant hormonal therapy is associated with increased likelihood of mortality (8), women who died or were lost to follow-up before 2009 to 2010 may have been less likely to use adjuvant hormonal therapy. As a result, our estimates of use and duration of adjuvant hormonal therapy in the WHI Extension Study may overestimate use in the full sample of women in WHI with breast cancer, and effect estimates comparing use and duration of use across racial/ethnic groups may be biased toward the null.

In addition, recall of past use, duration, and barriers to use among women diagnosed during earlier study years may be less accurate than recall among women diagnosed during more recent years. Although we did not collect information on dates that adjuvant hormonal therapy was taken, the distribution of breast cancer diagnosis year by 4-year intervals was similar across racial/ethnic groups, so we would expect a similar degree of inaccuracy in recall across groups.

Finally, we had to rely on self-reported measures of adjuvant hormonal therapy use and duration. While self-reported use of adjuvant hormonal therapy among breast cancer survivors has been validated against medical records (26–28), at least one study has documented that self-reported duration of adjuvant hormonal therapy overestimates use (29). Our estimate that 67% of women used treatment for the optimal duration of 5 years or more is in fact higher than estimates from studies using prescription records (16). However, there is no reason to expect that overestimation of duration would differ across racial/ethnic groups. Alternatively, the long duration of use observed in WHI could be accurate and simply reflects the unique nature of WHI study participants compared with the general population.

Our study also has several strengths worth noting. We used self-reported information on race/ethnicity rather than administrative-/registry-recorded information, which is subject to misclassification (30, 31). Furthermore, while our study relied on self-reported duration of adjuvant hormonal therapy instead of a more objective measure of adherence taken from pharmacy data or prescription refill information, unlike many prior studies, we were able to examine racial/ethnic differences in duration given the large size and ethnic diversity of the sample. Although we did not have sufficient numbers to explore differences between individual subgroups of Hispanic or Asian-American women, this will be important to examine in future studies.

Furthermore, while both physician recommendations and patient concerns about side effects from adjuvant hormonal therapy have been documented to influence the use of treatment, this information has not been commonly captured. We surveyed participants about barriers they experienced in using adjuvant hormonal therapy, and were able to restrict our analysis to women with no self-reported barriers. This is a particular strength of

our study, as barriers to care differ across racial/ethnic groups.

## Conclusions

Within the WHI Extension Study, 83% of participants diagnosed with hormone receptor-positive breast cancer after study enrollment reported using adjuvant hormonal breast cancer therapy. Among women reporting ever-use who were diagnosed before 2005, 67% reported using adjuvant hormonal therapy for 5 years or more, the optimal duration of use. We observed no statistically significant racial/ethnic differences in adjuvant hormonal therapy use, regardless of barriers. Furthermore, there were no statistically significant differences by race/ethnicity in duration of therapy for  $\geq 1$ ,  $\geq 3$ , or  $\geq 5$  years. Given the unique composition of the WHI Extension Study cohort, these findings should be confirmed in other population-based samples, incorporating more objective measures of adjuvant hormonal therapy use and duration. Reasons for nonuse and discontinuation of use among women from all racial/ethnic groups should be explored.

## Disclosure of Potential Conflicts of Interest

R.T. Chlebowski has honoraria from speakers' bureau from Novartis, AstraZeneca, and Pfizer and is a consultant/advisory board member of

Novartis and Pfizer. No potential conflicts of interest were disclosed by the other authors.

## Authors' Contributions

**Conception and design:** J.C. Livaudais, A.Z. LaCroix, C.I. Li, G. Coronado  
**Development of methodology:** J.C. Livaudais, A.Z. LaCroix, R.T. Chlebowski, B. Thompson  
**Acquisition of data (provided animals, acquired and managed patients, provided facilities, etc.):** A.Z. LaCroix, R.T. Chlebowski, F.A. Hubbell  
**Analysis and interpretation of data (e.g., statistical analysis, biostatistics, computational analysis):** J.C. Livaudais, A.Z. LaCroix, R.T. Chlebowski, C.I. Li, L.A. Habel  
**Writing, review, and/or revision of the manuscript:** J.C. Livaudais, A.Z. LaCroix, R.T. Chlebowski, C.I. Li, L.A. Habel, M.S. Simon, B. Thompson, D. O. Erwin, F.A. Hubbell, G. Coronado  
**Administrative, technical, or material support (i.e., reporting or organizing data, constructing databases):** F.A. Hubbell  
**Study supervision:** F.A. Hubbell, G. Coronado

## Grant Support

The WHI program is funded by the National Heart, Lung, and Blood Institute, NIH, U.S. Department of Health and Human Services through contracts HHSN268201100046C, HHSN268201100001C, HHSN-268201100002C, HHSN268201100003C, HHSN268201100004C, and HHSN271201100004C. Jennifer C. Livaudais was supported by NCRN Grant TL1 RR025016.

The costs of publication of this article were defrayed in part by the payment of page charges. This article must therefore be hereby marked *advertisement* in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

Received October 31, 2012; revised December 11, 2012; accepted December 12, 2012; published OnlineFirst December 28, 2012.

## References

- Jemal A, Clegg LX, Ward E, Ries LA, Wu X, Jamison PM, et al. Annual report to the nation on the status of cancer, 1975–2001, with a special feature regarding survival. *Cancer* 2004;101:3–27.
- Ooi SL, Martinez ME, Li CI. Disparities in breast cancer characteristics and outcomes by race/ethnicity. *Breast Cancer Res Treat*. 2010;127:729–38.
- Banerjee M, George J, Yee C, Hryniuk W, Schwartz K. Disentangling the effects of race on breast cancer treatment. *Cancer* 2007;110:2169–77.
- Hershman D, McBride R, Jacobson JS, Lamerato L, Roberts K, Grann VR, et al. Racial disparities in treatment and survival among women with early-stage breast cancer. *J Clin Oncol* 2005;23:6639–46.
- Li CI, Malone KE, Daling JR. Differences in breast cancer stage, treatment, and survival by race and ethnicity. *Arch Intern Med* 2003;163:49–56.
- NCCN Guidelines Version 2.2011:Breast Cancer; 2011. Available from: <http://www.nccn.com/patient-guidelines.html>.
- Effects of chemotherapy and hormonal therapy for early breast cancer on recurrence and 15-year survival: an overview of the randomised trials. *Lancet* 2005;365:1687–717.
- Hershman DL, Shao T, Kushi LH, Buono D, Tsai WY, Fehrenbacher L, et al. Early discontinuation and non-adherence to adjuvant hormonal therapy are associated with increased mortality in women with breast cancer. *Breast Cancer Res Treat* 2010;126:529–37.
- Prehn AW, Topol B, Stewart S, Glaser SL, O'Connor L, West DW. Differences in treatment patterns for localized breast carcinoma among Asian/Pacific islander women. *Cancer* 2002;95:2268–75.
- Livaudais JC, Hershman DL, Habel L, Kushi L, Gomez SL, Li CI, et al. Racial/ethnic differences in initiation of adjuvant hormonal therapy among women with hormone receptor-positive breast cancer. *Breast Cancer Res Treat* 2012;131:607–17.
- Freedman RA, Virgo KS, He Y, Pavluck AL, Winer EP, Ward EM, et al. The association of race/ethnicity, insurance status, and socioeconomic factors with breast cancer care. *Cancer* 2011;117:180–9.
- Short LJ, Fisher MD, Wahl PM, Kelly MB, Lawless GD, White S, et al. Disparities in medical care among commercially insured patients with newly diagnosed breast cancer: opportunities for intervention. *Cancer* 2010;116:193–202.
- Hays J, Hunt JR, Hubbell FA, Anderson GL, Limacher M, Allen C, et al. The Women's Health Initiative recruitment methods and results. *Ann Epidemiol* 2003;13(9 Suppl):S18–77.
- Curb JD, McTiernan A, Heckbert SR, Kooperberg C, Stanford J, Nevitt M, et al. Outcomes ascertainment and adjudication methods in the Women's Health Initiative. *Ann Epidemiol* 2003;13(9 Suppl):S122–8.
- Bickell NA, Wang JJ, Oluwole S, Schrag D, Godfrey H, Hiotis K, et al. Missed opportunities: racial disparities in adjuvant breast cancer treatment. *J Clin Oncol* 2006;24:1357–62.
- Chlebowski RT, Geller ML. Adherence to endocrine therapy for breast cancer. *Oncology* 2006;71:1–9.
- Fink AK, Gurwitz J, Rakowski W, Guadagnoli E, Silliman RA. Patient beliefs and tamoxifen discontinuance in older women with estrogen receptor-positive breast cancer. *J Clin Oncol* 2004;22:3309–15.
- Demissie S, Silliman RA, Lash TL. Adjuvant tamoxifen: predictors of use, side effects, and discontinuation in older women. *J Clin Oncol* 2001;19:322–8.
- Kahn KL, Schneider EC, Malin JL, Adams JL, Epstein AM. Patient centered experiences in breast cancer: predicting long-term adherence to tamoxifen use. *Med Care* 2007;45:431–9.
- Lash TL, Fox MP, Westrup JL, Fink AK, Silliman RA. Adherence to tamoxifen over the five-year course. *Breast Cancer Res Treat* 2006;99:215–20.
- Crew KD, Capodice JL, Greenlee H, Brafman L, Fuentes D, Awad D, et al. Randomized, blinded, sham-controlled trial of acupuncture for the management of aromatase inhibitor-associated joint symptoms in women with early-stage breast cancer. *J Clin Oncol* 2010;28:1154–60.
- Owusu C, Buist DS, Field TS, Lash TL, Thwin SS, Geiger AM, et al. Predictors of tamoxifen discontinuation among older women with estrogen receptor-positive breast cancer. *J Clin Oncol* 2008;26:549–55.



23. Kimmick G, Anderson R, Camacho F, Bhosle M, Hwang W, Balkrishnan R. Adjuvant hormonal therapy use among insured, low-income women with breast cancer. *J Clin Oncol* 2009;27:3445–51.
24. Pellegrini I, Sarradon-Eck A, Ben Soussan P, Lacour AC, Largillier R, Tallet A, et al. Women's perceptions and experience of adjuvant tamoxifen therapy account for their adherence: breast cancer patients' point of view. *Psychooncology* 2009;19:472–9.
25. Hershman DL, Kushi LH, Shao T, Buono D, Kershbaum A, Tsai WY, et al. Early discontinuation and nonadherence to adjuvant hormonal therapy in a cohort of 8,769 early-stage breast cancer patients. *J Clin Oncol* 2010;28:4120–8.
26. Maunsell E, Drolet M, Ouhoumane N, Robert J. Breast cancer survivors accurately reported key treatment and prognostic characteristics. *J Clin Epidemiol* 2005;58:364–9.
27. Phillips KA, Milne RL, Buys S, Friedlander ML, Ward JH, McCredie MR, et al. Agreement between self-reported breast cancer treatment and medical records in a population-based Breast Cancer Family Registry. *J Clin Oncol* 2005;23:4679–86.
28. Schootman M, Jeffe DB, West MM, Aft R. Self-report by elderly breast cancer patients was an acceptable alternative to surveillance, epidemiology, and end results (SEER) abstract data. *J Clin Epidemiol* 2005;58:1316–9.
29. Waterhouse DM, Calzone KA, Mele C, Brenner DE. Adherence to oral tamoxifen: a comparison of patient self-report, pill counts, and microelectronic monitoring. *J Clin Oncol* 1993;11:1189–97.
30. Gomez SL, Glaser SL. Misclassification of race/ethnicity in a population-based cancer registry (United States). *Cancer Causes Control* 2006;17:771–81.
31. Gomez SL, Kelsey JL, Glaser SL, Lee MM, Sidney S. Inconsistencies between self-reported ethnicity and ethnicity recorded in a health maintenance organization. *Ann Epidemiol* 2005;15:71–9.