Published in final edited form as:

Breast J. 2015 July ; 21(4): 377–386. doi:10.1111/tbj.12418.

Breast cancer chemoprevention among high-risk women and those with ductal carcinoma *in situ*

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Abstract

Chemoprevention with the antiestrogens, tamoxifen, raloxifene, and aromatase inhibitors, reduce breast cancer incidence in high-risk women; however, uptake has been poor (<5%) in the prevention setting. We assessed use of antiestrogens for breast cancer prevention, among high-risk women seen at an academic breast center, to observe how uptake rates compare in this setting. We collected data on demographics, breast cancer risk factors, and health behaviors via self-administered questionnaires and medical chart abstraction. Women eligible for chemoprevention with antiestrogens had a 5-year predicted breast cancer risk according to the Gail model of

1.67%, history of lobular or ductal carcinoma *in situ* (LCIS/DCIS), and/or *BRCA* mutation. We dichotomized antiestrogen use as ever or never. Predictors of use were evaluated using multivariable log-binomial regression. Of 412 high-risk women enrolled, 316 (77%) were eligible for chemoprevention. Among eligible women, 55% were non-Hispanic white, 29% Hispanic, 8% non-Hispanic black, and 7% Asian. Women were grouped based upon their highest category of breast cancer risk (in descending order): *BRCA* mutation carriers (3%), DCIS (40%), LCIS (22%), and 5-year Gail risk 1.67% (36%). Among those eligible for chemoprevention, 162 (51%) had ever initiated antiestrogen therapy (71% tamoxifen, 23% raloxifene, 5% aromatase inhibitor). Antiestrogen use was highest among women with DCIS (73%). In multivariable analysis, women with a 5-year Gail risk 1.67% had approximately a 20% lower likelihood of antiestrogen use compared to women with DCIS ($p=0.01$). In the primary prevention setting, excluding women diagnosed with DCIS, antiestrogen use was 37%. Multivariable analysis showed differences in uptake by education and potentially by race/ethnicity. Among high-risk women seen at a breast center, antiestrogen use for chemoprevention was relatively high as compared to the published

literature. Clinicians can support high-risk women by effectively communicating breast cancer risk and enhancing knowledge about the risks and benefits of chemoprevention.

Keywords

selective estrogen receptor modulator (SERM); aromatase inhibitor (AI); chemoprevention; breast cancer; tamoxifen; raloxifene; high-risk

Introduction

Risk assessment and interventions for breast cancer prevention are underutilized among high-risk women in the United States (1). Among U.S. women age 35-79 years, approximately 15% meet high-risk criteria, defined as having at least a 1.67% 5-year risk of developing breast cancer or a lifetime risk of 20% or greater, and are potentially eligible for chemoprevention (2). The U.S. Food and Drug Administration (FDA) has approved two selective estrogen receptor modulators (SERMs), tamoxifen and raloxifene, for breast cancer chemoprevention. In the primary prevention setting, tamoxifen administered for five years decreases the risk of invasive breast cancer by approximately 30-40% (3-8). Evaluation of tamoxifen use in women with ductal carcinoma *in situ* (DCIS), demonstrates a reduction in ipsilateral and contralateral invasive breast cancers (9-12). Randomized clinical trials of raloxifene in high-risk postmenopausal women report similar risk reduction benefits (13-15). In the Study of Tamoxifen and Raloxifene (STAR) trial, raloxifene is 24% less effective than tamoxifen at preventing invasive breast cancers, but with fewer adverse events (15). Some of the common side effects include hot flashes, vaginal discharge, and sexual dysfunction. Rare but serious side effects are uterine cancer and thromboembolic events (4, 6, 7). In the prevention setting, there are trials actively investigating the use of aromatase inhibitors (AIs) among high-risk postmenopausal women. Early results show exemestane reduces invasive breast cancer incidence by 65% among high-risk women and those with DCIS as compared to placebo (16).

Based upon this evidence, the U.S. Preventive Services Task Force and other professional organizations recommend that clinicians discuss chemoprevention with high-risk women (17-19). Despite the significant reduction in risk from these chemopreventive agents, prevalence of tamoxifen use is less than 5% for the primary prevention of breast cancer (20). Reasons for lack of antiestrogen use in the primary care setting include inadequate time for counseling, insufficient knowledge and information about risk-reduction strategies, and public misconceptions about chemoprevention risks (21-23). Our goal was to determine antiestrogen use for breast cancer risk reduction among women seen in an academic breast center, where breast surgeons and medical oncologists provide specialized risk counseling. We assess demographic and clinical factors that influence antiestrogen use among a multi-ethnic population of women at high risk of developing breast cancer.

Materials and Methods

Study Population

We conducted a retrospective cohort study of high-risk participants enrolled in the Herbert Irving Comprehensive Cancer Center (HICCC) breast database. At the breast center of Columbia University Medical Center in New York, NY, we approached women seen for initial consultation by a breast surgeon or medical oncologist for enrollment. The HICCC breast database identifies and provides follow-up of patients with a breast cancer diagnosis or women at high risk for breast cancer development. Inclusion criteria includes approval of study participation from the patient's primary treating breast surgeon or medical oncologist and the patient's ability to provide written informed consent in English or Spanish. We obtained Institutional Review Board approval prior to enrollment into the database. High-risk is defined as a woman with either a family history of breast cancer, personal history of atypical ductal or lobular hyperplasia (ADH/ALH), lobular or ductal carcinoma *in situ* (LCIS/DCIS), or known deleterious *BRCA1* or *BRCA2* mutation. In this study, our analysis is limited to those women who met high-risk criteria for breast cancer development.

We determined antiestrogen eligibility based upon current guidelines for breast cancer chemoprevention (3, 9), which include a 5-year predicted Gail risk $\geq 1.67\%$, history of LCIS, known *BRCA* mutation carrier status, or history of estrogen receptor positive (ER+) and/or progesterone receptor positive (PR+) DCIS. Antiestrogen ineligible women included those who had undergone prophylactic bilateral mastectomies, women with ER- and PR- DCIS, and women less than 35 years of age who did not meet other high-risk criteria. In addition, women could not have any medical contraindications to a SERM such as a history of deep vein thrombosis, pulmonary embolism, stroke, transient ischemic attack, or uterine cancer.

Data Collection

We collected demographic, breast cancer risk factor, and medical data through a self-administered questionnaire and medical chart review. Self-reported data, completed at time of enrollment into HICCC breast database, included age, race/ethnicity, highest educational level completed, annual household income, reproductive history, family history of breast cancer, and lifestyle behaviors. We extracted medical data from the most recent clinic notes in the electronic medical record, which included referral to medical oncology, number of prior breast biopsies, *BRCA* genetic testing, presence of benign breast disease or DCIS, medications, prior or current antiestrogen use, type of antiestrogen, duration of use, and early discontinuation. If self-reported data was incomplete for height and weight, we used the measurements from the medical chart to complete the data in order to calculate body mass index (BMI).

The main outcome was antiestrogen use, defined as any prior or current antiestrogen use for breast cancer chemoprevention. We dichotomized antiestrogen use as ever/never. We determined risk of invasive breast cancer in patients with a strong family history and/or atypical hyperplasia, using the model developed by Gail *et al.* to numerically estimate the absolute 5-year and lifetime risk (25). Women were grouped based upon their highest category of breast cancer risk (in descending order): *BRCA* mutation, DCIS, LCIS, and 5-

year Gail risk 1.67%. For the purposes of this analysis, we combined the risk categories of LCIS and *BRCA* mutation carriers due to small numbers. We conducted a secondary analysis of antiestrogen use in the primary prevention setting, which excluded women with DCIS, in order to distinguish between treatment patterns for non-invasive breast cancer and chemoprevention patterns for high-risk women.

Statistical Analysis

We examined differences in distribution of risk factors between women who had ever taken or not taken an antiestrogen using chi-square statistics or Fisher's exact test, as appropriate. We used log-binomial regression models to estimate relative risks (RRs) and 95% confidence intervals (95% CI) for each patient characteristic with antiestrogen use. We used log-binomial regression to obtain unbiased estimates of the relative risk due to having a common outcome event. A final multivariable model was constructed with *a priori* adjustment for the following variables: risk category (5-year Gail risk 1.67%, LCIS/*BRCA* mutation or DCIS), age, and race. Variables that had an association of $p < 0.15$ in univariable analysis and changed the estimates of the risk category by more than 10% in the multivariable model were also included: menopausal status, family history of breast cancer, nulliparity and number of medications. We used the same model criteria for our secondary analysis among women in the primary prevention setting, those with either a 5-year Gail risk 1.67% or LCIS/*BRCA* mutation. However, we excluded age and menopausal status from the final primary prevention multivariable model due to the correlated nature of Gail risk and the effect of age. All statistical analyses were carried out with SAS 9.2 (SAS Institute, Cary, NC) and a $p < 0.05$ was considered statistically significant in all analyses.

Results

From March 2007 to April 2013, 1619 consecutive women seen in the breast center for initial consultation with a breast surgeon or medical oncologist were approached for participation in the HICCC breast database. Of these, 1448 (89%) enrolled and 1036 patients with a diagnosis of invasive breast cancer were excluded from this analysis. Of 412 high-risk women enrolled (Figure 1), 316 (77%) were eligible for an antiestrogen for breast cancer chemoprevention, including those with a 5-year Gail risk score 1.67% (35.8%, including 30.1% with atypical hyperplasia), LCIS (21.5%), DCIS (40.2%), and *BRCA* mutation carriers (2.5%). Among the women with DCIS, 81% opted for breast conserving surgery and 19% had a unilateral mastectomy, with antiestrogen usage rates of 76.5% and 58.3%, respectively. The majority (96.8%) of the study population had at least one prior breast biopsy. Eighty percent of women who were eligible for an antiestrogen saw a medical oncologist in addition to the breast surgeon. The proportion of women eligible to receive antiestrogens was higher among non-Hispanic whites (84%) compared to non-Hispanic blacks (76%) and Hispanics (64%) ($p < 0.001$). The main reasons for antiestrogen ineligibility included 5-year Gail risk $< 1.67\%$ (40%), age younger than 35 years without LCIS, DCIS or a *BRCA* mutation (24%), history of ER- and PR- DCIS (17%), opting for bilateral mastectomies (11%), or medical contraindications to an antiestrogen (8%). Among Hispanics, 53% were ineligible for chemoprevention due to having a Gail risk $< 1.67\%$.

Among women who were eligible for an antiestrogen, the median age was 53.3 years (range: 26.2 to 87.6 years). The study population was diverse by race/ethnicity, 55% non-Hispanic white, 29% Hispanic, 8% non-Hispanic black, and 7% Asian, and by educational background and income level (Table 1). In terms of breast cancer risk factors, 29.5% had a family history of breast cancer, 24% were nulliparous, and about 19% of women used hormone replacement therapy (HRT).

Fifty-one percent of antiestrogen eligible patients had prior or current SERM or AI use, including 115 (71%) on tamoxifen, 38 (23%) on raloxifene, and 9 (6%) on an AI. Early antiestrogen discontinuation was 17%, primarily (75%) among women taking tamoxifen. Median time to discontinuation was approximately 1.73 years (range: 0.25 to 4.92 years). In univariable analysis (Table 1), we found medical oncology referral and breast cancer risk category to be the strongest predictors of antiestrogen use. A medical oncologist saw nearly all of the antiestrogen users (97.5%). We saw higher antiestrogen use in women with DCIS (73%) compared to LCIS and *BRCA* mutation carriers (43%) or women with a 5-year Gail risk 1.67% (32%) ($p<0.001$). In addition, antiestrogen use was positively associated with current number of medications. Parous women were more likely to have ever taken an antiestrogen than nulliparous women ($p=0.01$).

In multivariable analysis (Table 2), we found that women with a 5-year Gail risk 1.67% or LCIS/*BRCA* mutation had about a 20% lower likelihood of antiestrogen use compared to women with DCIS (RR=0.82, 95% CI=0.70-0.96 and RR=0.84, 95% CI=0.70-1.02, respectively). No other factors were significantly associated with antiestrogen use in multivariable analysis.

We performed a subgroup analysis excluding women with DCIS to evaluate antiestrogen use in the primary prevention setting. Among women with LCIS, a *BRCA* mutation, ADH/ALH, or 5-year Gail risk 1.67%, 37% of women eligible for an antiestrogen had past or current antiestrogen use. Among women who met high-risk criteria by the Gail model, for every percent increase in 5-year Gail risk score, antiestrogen use increased by 17% (RR=1.17; 95% CI=1.03-1.33; Figure 2). In univariable analysis (Table 3), older women were more likely to take an antiestrogen for primary prevention than younger women ($p=0.02$) and higher educational level was associated with antiestrogen use ($p=0.01$). Upon multivariable analysis, however, risk category, race and educational level continued to be associated with antiestrogen use. Although not statistically significant, we did see an increased likelihood of initiation of antiestrogens among non-white women as compared to non-Hispanic white (RR=1.48; 95% CI=0.67-2.36). Women with a grade school or high school education, as well as women with a graduate education, were more likely to initiate antiestrogens for chemoprevention than women with a college education (Grade/High School: RR=2.05; 95% CI=1.08-3.87; Graduate School: RR=2.31; 95% CI=1.26-4.23).

Discussion

Among high-risk women seen at an urban academic breast center, antiestrogen use for chemoprevention was relatively high (51%) compared to the published literature, with 73% antiestrogen usage among DCIS patients (20). Presence of DCIS and medical oncology

referral were the strongest predictors of antiestrogen use. Potential explanations for these findings include self-selection of high-risk women well informed about their breast cancer risk and risk reduction strategies, strength of the recommendations of physicians knowledgeable about breast health, and comfort level of medical oncologists in prescribing antiestrogens.

At our breast center, we found that antiestrogen use among women with DCIS was 73% compared to about 38% in the primary prevention setting. This may reflect the change in the standard of care for DCIS since the publication of the NSABP B-24 trial results in 1999 (9, 26, 27). From 1990 to 2001, investigators found that treatment with adjuvant tamoxifen among DCIS patients increased from 2.3% to 34.4% (26). However, wide variation still exists in physician prescribing practices of tamoxifen for DCIS, from 17% to 74% (27).

An estimated 10 million women in the United States may be eligible to take a SERM for chemoprevention (2). Nevertheless, since their approval by the FDA, use of tamoxifen and raloxifene has been low in the prevention setting. Data from the National Health Interview Survey (NHIS) indicated that the prevalence of tamoxifen use among U.S. women age 40-79 years without a personal history of breast cancer was merely 0.2% in 2000 and decreased to 0.08% by 2005 (28). However, the change in prevalence may be due to women shifting from tamoxifen to raloxifene for chemoprevention (29). Interventions designed to increase antiestrogen uptake for breast cancer chemoprevention, involving reading materials, an educational session or decision aid only, met with limited success in the range of 0.5% to 5.6% (30-34). Therefore, educational materials or decisions aids alone appear to be insufficient for increasing chemoprevention uptake.

Physician recommendation and health care provider communication are among the most influential factors to antiestrogen use (30, 35, 36). Physicians in family medicine, internal medicine, and obstetrics/gynecology reported that one of the primary barriers to breast cancer prevention counseling is insufficient information about risk reduction options, including antiestrogens (22, 23). In a large-scale program, the Ready, Set, GO GAIL! Project, high-risk women were identified using the Gail model in the primary care setting, but only 2% of 868 eligible women agreed to a SERM for chemoprevention (23). In this project, primary care providers predominately conducted the risk counseling, and referred few women for specialized risk counseling to a breast center. In our study, antiestrogen use in the primary prevention setting was 37%, similar to other studies that involved consultation at a specialized breast center where use has ranged from 11% to 58% (35-41). Women seen at breast centers are a highly select group provided specialized risk consultation. Furthermore, medical oncologists may have a higher comfort level in prescribing antiestrogens, which may explain differences in antiestrogen use compared to women counseled in the primary care setting.

Randomized clinical trials of antiestrogens for chemoprevention have not demonstrated a survival benefit (9-16). In addition, the efficacy of antiestrogens for prevention among *BRCA* mutation carriers is unclear (42, 43). Therefore, chemoprevention should be a personal choice based upon informed decision-making about risks and benefits. Within the prevention setting, we found that antiestrogen use was higher with increasing 5-year Gail

risk score and level of education. Breast cancer related anxiety and heightened perceived risk increase the likelihood of SERM use (30, 35), whereas women with low self-perceived breast cancer risk (36, 40, 44) or lack of breast cancer worry (36, 45) are less likely to partake in chemoprevention. Concern about potential side effects, such as endometrial cancer, thromboembolic events and menopausal symptoms, is another main contributor to a woman's unwillingness to initiate antiestrogen therapy (30, 31, 35, 39, 40, 44, 46). Our data lacked information on concerns about side effects so we were unable to assess these issues in our study population.

According to breast cancer chemoprevention guidelines from the American Society for Clinical Oncology (ASCO), tamoxifen is preferred for high-risk premenopausal women and postmenopausal women with a hysterectomy, whereas raloxifene may be preferred for high-risk postmenopausal women with an intact uterus (47). A better understanding of the risk-benefit profile of antiestrogens may influence patient's decisions regarding chemoprevention. Freedman *et al.* recently published models to predict the risks and benefits of SERMs for chemoprevention for women over age 50, based upon age, race/ethnicity, breast cancer risk, and presence of a uterus (48). Tools such as this can aid physicians in providing women with a more personalized risk-benefit profile for SERM use.

Acceptance of chemoprevention may increase with the availability of aromatase inhibitors (AIs) (49). Five years of exemestane reduces invasive breast cancer incidence by 65% compared to placebo among postmenopausal women with DCIS or at high-risk (16). Two ongoing trials of AIs for prevention include the International Breast cancer Intervention Study-II (IBIS-II) trial, which is comparing five years of anastrozole to placebo in high-risk postmenopausal women, and the NSABP B-35 trial, which is comparing tamoxifen to anastrozole in postmenopausal women with DCIS (50). Unlike SERMs, no excess gynecologic or thromboembolic side effects are associated with AIs, but these drugs may cause an increased risk of osteoporosis, musculoskeletal pain/arthritis, and hyperlipidemia. There are no reported trials comparing AIs to SERMs in the primary prevention setting and it remains unclear whether there will be widespread acceptance of AIs for breast cancer chemoprevention.

Our data also show that Hispanics are less likely to be eligible for antiestrogens due to not meeting high-risk criteria according to the Gail model. Current risk estimation methods utilizing the Gail model are potentially missing minority women who could be at high risk for breast cancer. The Gail model recently incorporated the Women's Contraceptive and Reproductive Experiences (CARE) (51) model and Asian American Breast Cancer Study (AABCS) (52) model to provide estimates that are more sensitive for non-Hispanic black and Asian American women, respectively. Few studies have used the Gail model in Hispanic populations (53, 54). Eligibility for chemoprevention among U.S. women varies dramatically by race/ethnicity: 18.7% of non-Hispanic whites, 5.7% of non-Hispanic blacks, and 2.9% of Hispanics (2). Not meeting high-risk criteria may be an initial barrier to chemoprevention uptake among minority groups. Notably, while they may be less likely to be eligible for an antiestrogen. In the primary prevention setting, our data suggested higher initiation among Hispanic and other minorities as compared to non-Hispanic white women, among those eligible for an antiestrogen.

A strength of our study is that we were able to capture actual antiestrogen use, whereas previous studies have often focused on hypothetical chemoprevention uptake (33, 44, 45). In addition, we have a relatively large sample and information on women at various levels of breast cancer risk. This was one of the few studies of antiestrogen use with racially and socioeconomically diverse women. However, our high-risk population seen in an urban academic center may not be representative of all high-risk women nationwide. In addition, we are cautious of the conclusions based on our data in the primary prevention setting given our limited sample size. Other limitations include lack of information on reasons for declining antiestrogens, perceived breast cancer risk or worry, and long-term follow-up data on adherence to antiestrogens. Another limitation is possible self-selection of our study population, based upon referral to the breast center or medical oncology. We may have introduced selection and/or referral bias; however, this highlights the importance of the risk counseling and prevention education setting.

Clinicians can support high-risk women by effectively communicating breast cancer risk and enhancing knowledge about the risks and benefits of chemoprevention. Further research should determine how knowledge about breast cancer, actual and perceived breast cancer risk, and risks/benefits of chemoprevention are best communicated to women to improve uptake. Given the efficacy of these chemopreventive agents, increased acceptance of a SERM or AI for breast cancer risk reduction could significantly reduce the public health burden of this disease.

Acknowledgements

This publication was supported by the National Center for Research Resources and the National Center for Advancing Translational Sciences, National Institutes of Health, through Grant Number UL1 RR024156. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH.

Laura Reimers was supported by a training grant from the National Cancer Institute (T32 CA009529).

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Fig 1.

Diagram of study participants by antiestrogen eligibility and antiestrogen use. ER, estrogen receptor; PR, progesterone receptor; HICCC, Herbert Irving Comprehensive Cancer Center.

Fig 2.
Boxplot of continuous 5-year Gail risk by antiestrogen use for primary prevention among women with Gail risk 1.67%.

Table 1

Sociodemographic and clinical characteristics related to antiestrogen use among eligible high-risk women and those with DCIS

Characteristic	Antiestrogen n Eligible (n=316)		Antiestrogen Use (n=162; 51%)		No Antiestrogen Use (n=154; 49%)		P- value
	N	%	N	%	N	%	
Age (years)							0.06
<45	50	15.8	21	13.0	29	18.8	
45-50	62	19.6	25	15.4	37	24.0	
51-60	119	37.7	67	41.4	52	33.8	
>60	85	26.9	49	30.3	36	23.4	
Menopause							0.02
Premenopausal	97	42.5	42	35.3	55	50.5	
Postmenopausal	131	57.5	77	64.7	54	49.5	
Race							0.63*
Non-Hispanic white	174	55.1	83	51.2	91	59.1	
Hispanic	92	29.1	53	32.7	39	25.3	
Non-Hispanic black	26	8.2	13	8.0	13	8.4	
Asian	22	7.0	12	7.4	10	6.5	
Other	2	0.6	1	0.6	1	0.7	
Education (highest level completed)							0.15*
Grade School	14	6.5	9	8.0	5	4.8	
High School	42	19.4	26	23.0	16	15.4	
College	92	42.4	38	33.6	31	29.8	
Graduate School	69	31.8	40	35.4	52	50.0	
Annual Household Income							0.58
0-\$30,000	50	15.8	26	16.1	24	15.6	
\$30,001-\$100,000	57	18.0	30	18.5	27	17.5	
\$100,000+	62	19.6	36	22.2	26	16.9	
Refused	147	46.5	70	43.2	77	50.0	
Insurance							0.05*
Commercial	157	69.5	75	62.5	82	77.4	
Medicare	34	15.0	22	18.3	12	11.3	
Medicaid	23	10.2	17	14.2	6	5.7	
Uninsured	12	5.3	6	5.0	6	5.7	
Medical Oncology Referral							<0.001
Yes	250	79.9	156	97.5	94	61.4	
No	63	20.1	4	2.5	59	38.6	
Body Mass Index (kg/m ²)							0.23
<25	153	49.0	72	44.7	81	53.6	

Characteristic	Antiestrogen Eligible (n=316)		Antiestrogen Use (n=162; 51%)		No Antiestrogen Use (n=154; 49%)		P- value
	N	%	N	%	N	%	
25-30	79	25.3	42	26.1	37	24.5	
>30	80	25.6	47	29.2	33	21.9	
Risk Category							<0.001
5-year Gail Risk 1.67%	113	35.8	36	22.2	77	50.0	
LCIS or BRCA mutation	76	24.0	33	20.4	43	27.9	
DCIS	127	40.2	93	57.4	34	22.1	
Family History of Breast Cancer							0.46
Yes	87	29.5	44	27.7	43	31.6	
No	208	70.5	115	72.3	93	68.4	
Nulliparous							0.01
Yes	75	24.0	29	17.9	46	30.5	
No	238	76.0	133	82.1	105	69.5	
Hysterectomy							0.60
Yes	34	10.8	16	9.9	18	11.7	
No	282	89.2	146	90.1	136	88.3	
Number of Medications							0.02
0	45	19.5	18	15.0	27	24.3	
1-3	125	54.1	62	51.7	63	56.8	
4	61	26.4	40	33.3	21	18.9	
Hormone Replacement Therapy Use							0.13
Yes	42	19.1	26	35.1	12	22.6	
No	178	80.9	48	64.9	41	77.4	

* p-value was calculated using Fisher's exact, otherwise Pearson chi-square test was used.

Table 2

Multivariable model of association between sociodemographic and clinical factors and antiestrogen use among high-risk women and those with DCIS

Characteristic	Multivariable		
	RR	95% CI	p-value
Age (years)			
	1.		
<45	0		
45-50	1.02	(0.80-1.29)	0.88
51-60	1.04	(0.82-1.31)	0.77
>60	0.98	(0.75-1.28)	0.88
Menopausal Status			
Premenopausal	1.0		
Postmenopausal	1.03	(0.84-1.26)	0.77
Race			
Non-Hispanic white	1.0		
Hispanic	1.06	(0.91-1.24)	0.47
Non-Hispanic black	0.96	(0.72-1.28)	0.79
Asian	1.04	(0.86-1.26)	0.66
Risk Category			
Gail Risk >1.67%	0.82	(0.70-0.96)	0.01
LCIS/BRCA mutation	0.84	(0.70-1.02)	0.07
DCIS	1.0		
Family History of Breast Cancer			
Yes	1.0		
No	1.04	(0.91-1.20)	0.55
Nulliparous			
Yes	0.93	(0.80-1.09)	0.39
No	1.0		
Number of Medications			
0	1.0		
1-3	1.07	(0.91-1.26)	0.40
4	1.14	(0.94-1.39)	0.19

Table 3

Multivariable model of association between sociodemographic and clinical factors and antiestrogen use for primary prevention, high-risk women with Gail risk 1.67%, ADH/ALH, LCIS, or *BRCA* mutation carrier

Characteristic	Antiestrogen Use (n=69; 36.5%)		No Antiestrogen Use (n=120; 63.5%)		Multivariable			
	N	%	N	%	p-value	RR	95% CI	p-value
Age (years)					0.02*			
<45	8	11.6	23	19.2				
45-50	10	14.5	34	28.3				
51-60	32	46.4	45	37.5				
>60	19	27.5	18	15.0				
Menopause					0.001			
Premenopausal	14	29.8	51	58.6				
Postmenopausal	33	70.2	36	41.4				
Race					0.10*			
Non-Hispanic white	34	49.3	75	62.5		1.0		
Non-white	35	50.7	45	37.5		1.4 8	(0.67- 2.36)	0.14
Risk Category					0.12			
Gail Risk 1.67%	22	31.9	57	47.50		0.7 1	(0.40- 1.25)	0.23
ADH/ALH	14	20.3	20	16.7		1.0 8	(0.65- 1.77)	0.78
LCIS/BRCA	33	47.8	43	35.8		1.0		
Education (highest level completed)					0.01*			
Grade/High School	14	31.1	16	19.1		2.0 5	(1.08- 3.87)	0.03
College	12	26.7	45	53.6		1.0		
Graduate School	19	42.2	23	27.4		2.3 1	(1.26- 4.23)	0.01

* Fisher's exact used