Prediction, Communication, and Distribution of Breast Cancer Risk

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Abstract

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Hispanic women represent the only racial/ethnic group in the United States (US) for which breast cancer is the most frequently diagnosed cancer and leading cause of cancer deaths. Despite the availability of tools to assess breast cancer risk, relatively little is known about the performance of current breast cancer risk prediction models and distribution of breast cancer risk in Hispanic women. Furthermore, there is limited evidence on the utility of decision aids designed to help women at high risk for breast cancer make informed choices about chemoprevention. To address these gaps, the overall goal of the proposed research work was threefold: 1) evaluate breast cancer risk projections for Hispanic women; 2) assess the distribution of breast cancer risk among Hispanic women; and 3) assess the impact of a web-based, tailored decision aid for women at high risk for breast cancer. We used data from two nationally representative datasets with information on US Hispanic women, and a randomized trial of women at high risk of breast cancer. Statistical analyses included multivariate linear, logistic, and Cox regression techniques. Findings from this work contribute valuable information on the use of estimates of breast cancer risk in research, clinical practice and public health. First, the National Cancer Institute's Breast Cancer Risk Assessment Tool (BCRAT), the most widely used breast cancer risk prediction model, underestimates risk of developing invasive breast cancer in US Hispanic women. Second, the risk of developing invasive breast among

Hispanic women, based on the BCRAT, is significantly lower compared to non-Hispanic white women, though breast cancer risk also significantly differs between certain Hispanic subgroups. Third, personalized decision aids may be effective tools to provide useful information about women's risk of developing specific types of breast cancer, as well as to facilitate informed medical decisions, reduce patients' decisional conflict, and empower patients to choose a treatment strategy that best reflects their own values. Together, these results improve our understanding of the prediction and distribution of breast cancer risk among US Hispanic women, and help identify ways in which breast cancer risk can be communicated to help inform women about their treatment options.

TABLE OF CONTENTS

LIST OF FIGURES

Figure Number Page

LIST OF TABLES

Table Number Page

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DEDICATION

To Dad, Mom, Jacob, Veronica and Samantha.

BACKGROUND

Hispanic women represent the only racial/ethnic group in the United States (US) for which breast cancer is the most frequently diagnosed cancer and leading cause of cancer deaths (1). Recent trends suggest that, despite an overall decline in breast cancer incidence among US women, the rate of incident breast cancer across all stages of the disease has declined at a slower pace for US Hispanic women (2). Further, regardless of having a lower incidence rate of breast cancer, Hispanic women are more likely to be diagnosed with larger tumors and/or metastatic disease (3, 4) and, consequently, are 20% more likely to die from breast cancer than non-Hispanic white women (5).

Prior research has identified several well-known breast cancer risk factors including age, race/ethnicity, age at menarche, menopausal status, parity, lifestyle (i.e. diet) and family history of breast cancer (6-8). However, differences between Hispanic and non-Hispanic white women have previously been reported, both in the distribution and magnitude of association with breast cancer risk factors, such as family history and reproductive factors (9-13). Also, other factors unique to Hispanics, including migration history and acculturation, have been shown to modify breast cancer risk (14-16). Therefore, the ability to identify Hispanic women at high risk of developing breast cancer, based on risk factors specific to that population, would have substantial public health implications.

The National Cancer Institute's Breast Cancer Risk Assessment Tool (BCRAT), also known as the Gail model (17), was developed to project a woman's individualized risk of developing breast cancer. Specifically, the model projects absolute risk of invasive breast cancer, such that a woman with a specific risk factor profile will develop invasive breast cancer over a defined time period (7). The BCRAT has been validated for predicting breast cancer risk for non-

Hispanic white women (18-21) and has been adapted to project breast cancer risk specific to African-American (22) and Asian-American women (23). However, there is great uncertainty about use of the model for Hispanics (24), as the BCRAT has never been validated for Hispanic women.

The lack of evidence on the performance of the BCRAT for Hispanic women has limited clinicians, researchers, and the public to generalizing estimates from the BCRAT, designed for breast cancer prediction in non-Hispanic white women (17), to Hispanic women and women of other racial/ethnic backgrounds (7). Understanding the performance of the BCRAT in Hispanics may help explain differences in the distribution of breast cancer risk among Hispanic subgroups and increase our understanding of the heterogeneity in breast cancer incidence and mortality (25). Further, estimates from the BCRAT have tremendous clinical and practical use, such as identifying women at high risk for breast cancer, counseling and educating women in regard to breast cancer prevention and treatment options, and as an aid in clinical decisions (22).

Evidence suggests that approximately 15% of all US women aged 30-84 may be at high risk of breast cancer (26), based on a BCRAT 5-year risk $\geq$1.67%. Both the American Society of Clinical Oncology (ASCO) and National Comprehensive Cancer Network (NCCN) recommend that women who meet this high-risk threshold, among other criteria, consider prophylactic treatment with tamoxifen or raloxifene to reduce the risk of developing invasive breast cancer in the future (27, 28). However, there is a paucity of information on the distribution of breast cancer risk among Hispanic women and number of Hispanic women who are high-risk for breast cancer, based on the BCRAT (26). Such knowledge is essential for breast cancer prevention efforts targeting Hispanic women, as it could lead to increased understanding of the efficacy of current chemoprevention agents for the Hispanic population (7, 22).

Moreover, for those women who are eligible for tamoxifen or raloxifene, the decision to use prophylactic chemoprevention is a preference-sensitive decision, relying on patients' understanding the facts relevant to their medical decision (29). Each woman must weigh the risks and benefits of chemoprevention for herself and make a decision that is aligned with her own values and preferences. Decision aids have been shown to be useful in providing such evidence-based information about a health condition and the associated uncertainties, and guidance in the steps of decision making that enable patients to be active, informed participants (30, 31). Accordingly, in addition to tools that identify women eligible for breast cancer chemoprevention, research on decision aids that help individuals of all races and ethnicities make specific and deliberate choices about their breast cancer prevention options are needed (31).

To address these gaps in the literature, the overall goal of the research projects was threefold: i) evaluate the performance of BCRAT for US Hispanic women; ii) examine the distribution of breast cancer risk, based on the BCRAT, among Hispanic subgroups; iii) assess the impact of a web-based, personally-tailored decision aid developed to inform women at high risk of breast cancer about the risks and benefits of prophylactic tamoxifen and raloxifene use. Our results will contribute valuable information about the validity of current risk assessment models for US Hispanics, as well as the use of BCRAT risk estimates for breast cancer prevention and medical decision making, in general. Ultimately, the knowledge generated may be useful for developing cancer control and prevention strategies that target Hispanic women at high risk of developing breast cancer. If so, these efforts have the potential to lead to a reduction in breast cancer mortality among Hispanic women.

SPECIFIC AIMS

Study One: ***Evaluating breast cancer risk projections for Hispanic women***

Specific Aim 1. To evaluate the performance of current breast cancer risk prediction models for Hispanic women. The predictive accuracy of the NCI Breast Cancer Risk Assessment Tool (BCRAT), and an updated version of the BCRAT, will be measured for Hispanic and non-Hispanic white participants in the WHI, focusing on the relative risk feature, calibration, and discriminatory accuracy.

Study Two: ***The Impact of a web-based, tailored decision aid on women at high risk for breast cancer***

Specific Aim 2. To assess the impact of the Guide to Decide (GtD) decision aid on women at high risk of developing breast cancer. We will evaluate the impact of the GtD, a web-based, personally-tailored decision aid designed communicate information on breast cancer risk and prophylactic tamoxifen and raloxifene use, on participants' decisional conflict and treatment decision behavior, as well as the association between these outcomes with patient satisfaction with the decision aid and preparation for decision making.

Study Three: ***Risk of developing invasive breast cancer risk in Hispanic women: A look across Hispanic subgroups***

Specific Aim 3. To evaluate the distribution of breast cancer risk among women in different Hispanic subgroups. Based on data from the 2000 and 2005 National Health Interview Survey (NHIS) Cancer Control Module surveys, we will assess the distribution of 5-year and lifetime risk of breast cancer across women from six Hispanic subgroups.

THEORETICAL FRAMEWORK

The Quality in the Continuum of Cancer Care (QCCC) (Figure 1) is a framework that was developed to fulfill four conceptual needs: i) to emphasize the relationship of services and processes of cancer care to outcomes; ii) to identify the potential failures that can occur between and during different processes of care; iii) to consider the factors that impact care; and iv) to suggest strategies to improve cancer care performance (32). As a heuristic approach for health services research, the QCCC served to help guide and explain the application of the present research projects to the processes in breast cancer care.

The QCCC outlines the span of services that comprise the cancer care continuum, including risk assessment, primary prevention, screening, detection, diagnosis, treatment, recurrence surveillance and end-of-life care. Further, the framework points out failures that can occur along cancer care continuum, which fall into two categories: i) breakdowns in particular types of care delivered to individuals at various points in their cancer care; and ii) breakdowns during the transitions between types of care (32). Thus, in applying the QCCC framework to this body of work, we focused on the first two types of care in the continuum (risk assessment and primary prevention), the transition between these types of care, and the potential system failures involved.

Assessment of a woman's individualized risk of developing breast cancer, based on the NCI BCRAT, has been used to determine eligibility for clinical trials, use of prophylactic chemoprevention, and use of magnetic resonance imaging as an adjunct to mammography (20, 26, 33). Nevertheless, for Hispanic women, evidence on the validity of the BCRAT for this population was lacking. This has led to both types of failure described above, whereby: i) the lack of knowledge on the performance of the BCRAT for Hispanic women has led to a

breakdown in the first type of care (risk assessment) for this population; and ii) the inability to properly apply BCRAT estimates to Hispanic women has hindered us from identifying Hispanic women who may be eligible to access prophylactic chemoprevention counseling and/or treatment (primary prevention) and, thus, the process of care between risk assessment and primary prevention of breast cancer.

Results from this body of research will help address these failures in the cancer care continuum. By evaluating the performance of the BCRAT for US Hispanic women, we provide evidence on the validity of using the BCRAT in Hispanic women populations. Further, these results allow us to provide an estimate of the number of US Hispanic women, overall and across different subgroups, that may be eligible for prophylactic tamoxifen and raloxifene use.

The second application of the QCCC to this body of research pertains to the next type of care in the continuum, primary prevention. Specifically, chemoprevention and the tools for counseling women at high risk for breast cancer about the decision to take chemopreventive agents. While the transition between risk assessment and primary prevention is critical, once this step occurs, the quality of care will largely depend on a women's knowledge of the risks and benefits of using chemoprevention to reduce the risk of future breast cancer and, ultimately, the decision to uptake the chemoprevention. Hence, the failure that can occur in this stage is a breakdown in the type of care (primary prevention in the form of chemoprevention counseling and/or treatment).

Decision aids are designed to help prepare individuals to make specific and deliberate choices about their care by providing accurate, balanced information on treatment options and outcomes (31). Subsequently, to circumvent failure in this type of breast cancer care, we provide evidence on the impact of the Guide to Decide, a web-based, tailored decision aid designed to inform

women at high risk of breast cancer about the risks and benefits of prophylactic tamoxifen and raloxifene use (34). Results from this study highlight the use of a decisional support tool, the Guide to Decide, for providing useful information to women at high risk of developing breast cancer who are faced with a decision around chemoprevention (35).

Overall, the QCCC provides a systematic approach for assessing how the results of this research may lead to improvements in different types and processes of care within the continuum of care for breast cancer (32). The emphasis on risk assessment and primary prevention as the initial steps in this continuum underscores the importance of these types of care in achieving quality breast cancer outcomes. Ultimately, the QCCC framework posits that by identifying and addressing limitations in current breast cancer care and processes, findings from this research work may lead to improvements that impact the burden of breast cancer.

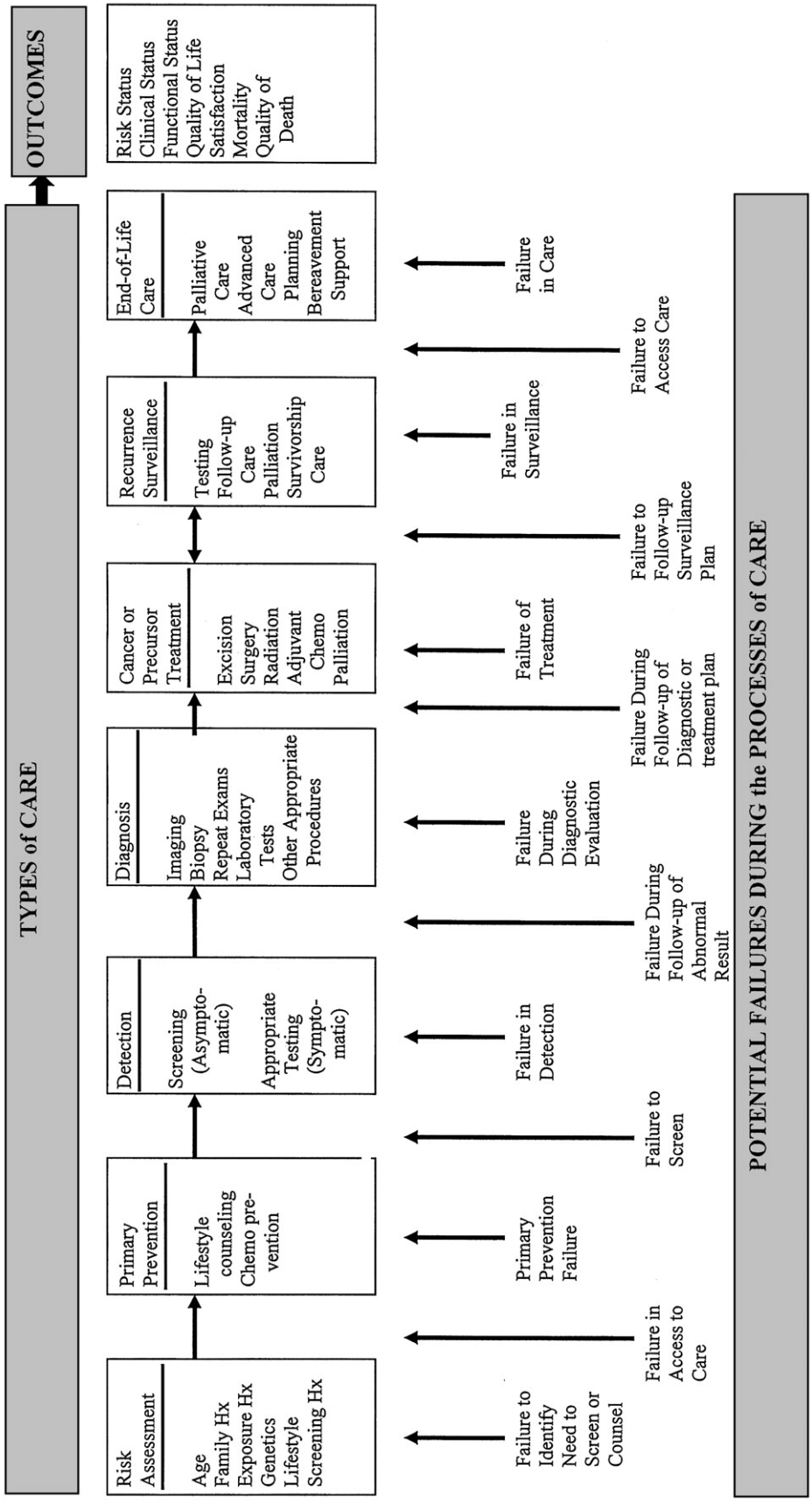

Figure 1. Quality in the Continuum of Cancer Care

Evaluating breast cancer risk projections for Hispanic women[1]

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ABSTRACT

Purpose: For Hispanic women, the Breast Cancer Risk Assessment Tool (BCRAT; "Gail Model") combines 1990-1996 breast cancer incidence for Hispanic women with relative risks for breast cancer risk factors from non-Hispanic white (NHW) women. BCRAT risk projections have never been comprehensively evaluated for Hispanic women.

Methods: We compared the relative risks and calibration of BCRAT risk projections for 6,353 Hispanic to 128,976 NHW postmenopausal participants aged 50 and older in the Women's Health Initiative (WHI). Calibration was assessed by the ratio of the number of breast cancers observed with that expected by the BCRAT (O/E). We re-evaluated calibration for an updated BCRAT that combined BCRAT relative risks with 1993-2007 breast cancer incidence that is contemporaneous with the WHI. Cox regression was used to estimate relative risks. Discriminatory accuracy was assessed using the concordance statistic (AUC).

Results: In the WHI Main Study, the BCRAT underestimated the number of breast cancers by 18% in both Hispanics (O/E=1.18, p=0.06) and NHWs (O/E=1.18, p<0.001). Updating the BCRAT improved calibration for Hispanic women (O/E=1.08, p=0.4) and NHW women (O/E=0.98, p=0.2). For Hispanic women, relative risks for number of breast biopsies (1.71 vs. 1.27, p=0.03) and age at first birth (0.97 vs. 1.24, p=0.02) differed between the WHI and BCRAT. The AUC was higher for Hispanic women than NHW women (0.63 vs. 0.58, p=0.03).

Conclusions: Updating the BCRAT with contemporaneous breast cancer incidence rates improved calibration in the WHI. The modest discriminatory accuracy of the BCRAT for Hispanic women might improve by using risk factor relative risks specific to Hispanic women.

INTRODUCTION

Breast cancer is the most commonly diagnosed cancer and leading cause of cancer-related death among Hispanic women in the United States (US) (6, 36). The Breast Cancer Risk Assessment Tool (BCRAT), also known as the “Gail model” (17), estimates a woman’s risk of developing invasive breast cancer over a defined period of time, given her age and risk factor profile (17). For Hispanic women, the BCRAT combines 1990-1996 breast cancer incidence rates from the Surveillance, Epidemiology and End Results (SEER) program for Hispanic women with relative risks for breast cancer risk factors from non-Hispanic white (NHW) women in the Breast Cancer Detection Demonstration Project (17). Several case-control studies suggest that relative risks for family history, reproductive and other factors may differ between Hispanic and NHW women (9-13), calling into question the relative risk assumptions of the BCRAT for Hispanics.

Although BCRAT risk projections have been extensively validated for NHW women (18-21), we are unaware of any study that has comprehensively examined the performance of the BCRAT in a cohort of US Hispanic women. In particular, prospective follow-up is required to evaluate *calibration,* i.e. the similarity between the number of breast cancers that develop in a population with that expected by the BCRAT (37). Adequate calibration is crucial to ensure the validity of BCRAT-based risk thresholds used in clinical practice, such as the American Society of Clinical Oncology (ASCO) guideline that women with a 5-year breast cancer risk greater than 1.67% may benefit from using tamoxifen or raloxifene to prevent breast cancer (38). Calibration may be adversely affected by changes in US breast cancer incidence, which increased through the 1990’s, peaked around 2002, and has since declined (39). For instance, the BCRAT for NHW women, which uses SEER breast cancer incidence from 1983-1987, underestimates breast cancer incidence in many cohorts established in the 1990s (40). In particular, the Women’s

Health Initiative (WHI), when combining women of all races and ethnicities, found 20% underestimation by the BCRAT (41). It has been shown that calibration can be improved by using breast cancer incidence rates contemporaneous to the study cohort (40).

The WHI is one of the few prospective studies with a large cohort of US Hispanic women. Since the Hispanic BCRAT uses relative risks from NHW women, we compared the relative risks, calibration, and discriminatory accuracy of the BCRAT for 6,353 Hispanic participants to 128,976 NHW postmenopausal participants aged 50 and older in the WHI. We also assessed whether updating BCRAT breast cancer incidence rates to SEER rates contemporaneous with the WHI study period (1993-2007) improved calibration.

METHODS

Study Design

The design of the WHI study has been previously described (42-44). Briefly, the WHI is a national, longitudinal health study composed of a set of randomized clinical trials (CT) and an observational study (OS). We used data on 6,353 Hispanic and 128,976 NHW postmenopausal women aged 50-79 without a history of breast cancer or mastectomy (bilateral or unilateral) at enrollment who were followed through March 2005 (WHI Main Study Period). BCRAT risk factors were obtained from the enrollment questionnaire. Mammograms and clinical breast exams were obtained at least biennially for CT participants but not necessarily for OS participants (44). All reported invasive breast cancers were adjudicated locally and again centrally by physician adjudicators (13, 45).

Breast Cancer Risk Assessment Tool (BCRAT)

The BCRAT (17, 21) estimates women's absolute risk of developing invasive breast cancer using age, age at first live birth, age at menarche, number of first-degree relatives with breast cancer, and number of breast biopsies (which is also modified by age). Information on atypical hyperplasia was unavailable in the WHI. When information on a risk factor is missing for a woman, BCRAT imputes the safest level of that risk factor. For both Hispanic and NHW women, relative risks for the model risk factors are based on NHW women in the Breast Cancer Detection Demonstration Project (17). For NHW women, the BCRAT is calibrated to 1983-1987 SEER invasive breast cancer incidence rates for white (not NHW) women. For Hispanic women, the BCRAT is calibrated to 1990-1996 SEER Hispanic invasive breast cancer incidence rates for Hispanic women. We also updated the BCRAT ("Updated BCRAT") by combining BCRAT relative risks with SEER breast cancer incidence from 1993-2007 for Hispanic and NHW women to ensure that breast cancer incidence rates overlap in time with the WHI.

Statistical Analyses

We compared the BCRAT relative risks (RRs) to those estimated for Hispanic and NHW women in the WHI, separately, using Cox proportional hazards models. We assessed the discriminatory accuracy of the models with the concordance statistic, or area-under-the-curve (AUC) statistic (46). Using the BCRAT and the Updated BCRAT, we computed each woman's absolute risk of developing invasive breast cancer from enrollment through 2005. Projections were limited to age 90, since the BCRAT does not project risk past that age. We summed absolute risks over women in each risk factor category i, and also overall, to calculate the expected count (E_i), which was compared with the corresponding observed number of women with incident invasive breast cancer, O_i. For each category, we calculated an observed/expected (O/E) ratio and 95% confidence interval (CI) with a lower limit of $(O/E)\exp(-1.96 \times O^{-1/2})$ and upper limit of

(O/E)exp(+1.96 x $O^{-1/2}$). Analyses were done separately for the BCRAT and the Updated BCRAT.

RESULTS

Compared with NHW women in the WHI, Hispanics women were 3.3 years younger at baseline, 4.4 years younger at breast cancer diagnosis, reported less family history of breast cancer, and fewer breast biopsies (Table 2.1). Relative risks (Table 2.2) for Hispanics in the WHI differed from those in the BCRAT for number of breast biopsies (RR = 1.71 vs. RR = 1.27, p = 0.03) and age at first live birth (RR = 0.97 vs. RR = 1.24, p = 0.02). For NHW women, the BCRAT differed for number of first-degree relatives with breast cancer (RR = 1.31 vs. RR = 2.61, p < 0.001), age at first live birth (RR = 1.13 vs. RR = 1.24, p<0.001) and the interaction between family history and age at first live birth (RR = 1.01 vs. RR = 0.83, p < 0.001). The only relative risk estimate that significantly differed between NHW women and Hispanic women in the WHI was number of breast biopsies (RR = 1.27 vs. RR = 1.71, p = 0.03). The concordance statistic (AUC) of the BCRAT was 0.63 [95% CI: 0.582 to 0.676] for Hispanic women and 0.58 [95%: 0.566 to 0.583] for NHW women in the WHI (p=0.03).

The BCRAT underestimated the number of breast cancer diagnoses among Hispanics by 18% (O/E = 1.18, 95% CI = 0.99 to 1.40; p=0.06) (Table 2.3). Underestimation occurred for both the CT and OS, as well as in most BCRAT risk factor categories (Supplemental Table 2.1). For NHW women, the BCRAT also underestimated the number of breast cancer diagnoses by 18% (O/E =1.18, 95% CI = 1.14 to 1.21; p<0.001).

The age-adjusted 1983-1987 SEER breast cancer incidence rate for white women used by the BCRAT is 14.5% lower than the SEER breast cancer incidence rate for NHW women during the

WHI study period 1993-2007 (336 vs. 393/100,000 women/year; p<0.001) (**Figure 2**). The age-adjusted 1990-1996 SEER breast cancer incidence rate for Hispanic women used by the BCRAT is 7.7% lower than the SEER breast cancer incidence rate for Hispanic women during the WHI study period 1993-2007 (217 vs. 235/100,000 women/year; p<0.001). The Updated BCRAT, using 1993-2007 SEER incidence rates, was well-calibrated for both Hispanic women (O/E ratio=1.08, 95% CI = 0.91 to 1.28; p=0.4) and NHW women (O/E =0.98, 95% CI = 0.96 to 1.01; p=0.2) (**Table 3**). The Updated BCRAT showed improved calibration in nearly all risk factor categories for Hispanic and NHW women, except for NHW women with first-degree relatives with breast cancer (**Tables S.2.1 and S.2.2**).

DISCUSSION

In this comprehensive evaluation of the BCRAT for Hispanic women using prospective cohort data, we found that the BCRAT underestimated the number of invasive breast cancers by 18% for both Hispanic and NHW women. The calibration of the BCRAT improved greatly by updating the older SEER breast cancer incidence rates used by BCRAT to rates contemporaneous with the WHI (1993-2007). BCRAT relative risk estimates for number of breast biopsies and age at first birth differed with estimates for Hispanic women from the WHI. The discriminatory accuracy of the BCRAT for Hispanic women was higher than for NHW women, but remained only modest.

Our findings suggest two potential improvements for the BCRAT. Although breast cancer incidence rates in 2007 returned close to the rates observed in 1990, if breast cancer incidence rates increase again in the near future, as expected (39), then serious consideration should be given to recalibrating the BCRAT to more recent rates. Another advantage of recalibrating the BCRAT for NHW women is that it would then conform to rates more specific to NHWs, rather than the 1983-1987 rates, which included Hispanics as “white women”.

Second, discriminatory accuracy may improve by using relative risks specific to each racial/ethnic group. The relative risks for number of breast biopsies may differ between Hispanic and NHW women. Similarly, previous case-control studies (9-13) have reported that several breast cancer risk factors may have different effects In Hispanic women compared with NHW women. Furthermore, Hispanic women likely have unique breast cancer risk factors, such as migration history, degree of acculturation, Hispanic origin, and ancestral genetic admixture (14-16) that are not considered in the current BCRAT. For NHW women, the BCRAT relative risk for family history is much larger than that estimated in our data, but estimates from our data are consistent with those from most cohorts (40, 47) and meta-analyses (48, 49).

Some limitations need to be considered when interpreting our findings. Our analysis limited to postmenopausal women aged 50 or older. There were only 130 Hispanic women with breast cancer, although our findings for Hispanic women are consistent with those from the much larger sample of NHW women. Though the WHI was national study, conducted by 40 Clinical Centers in 24 states and the District of Columbia, Hispanic participants may not be representative of the US Hispanic population. Finally, women in the WHI CT underwent mammography at least biennially, which may have increased the number of breast cancers detected over that expected in the general population with less frequent mammography.

Further development of a more comprehensive model for Hispanic women, that considers breast cancer risk factors distinct to Hispanic women and is validated in a large cohort of US Hispanic women, is warranted.

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Table 2.1. Distribution of BCRAT risk factors and breast cancer outcomes in the WHI

Characteristic	**Hispanic** (n=6,353)		**Non-Hispanic White** (n=128,976)		***p***
BCRAT risk factors[*]	Mean [95% CI]		Mean [95% CI]		
Age at baseline, years	60.20 [60.04, 60.37]		63.51 [63.47, 63.55]		<.001
Age at menarche, years	N	%	N	%	
< 12	1,560	24.8	27,718	21.6	<.001
12-13	3,040	48.2	71,953	56.0	
≥ 14	1,701	27.0	28,848	22.4	
Age at first live birth, years					
< 20	1,087	17.6	14,603	11.5	<.001
20-24	1,869	30.2	51,016	40.0	
25-29/Nulliparous	2,773	44.9	52,436	41.1	
≥ 30	453	7.3	9,484	7.4	
Number of 1st degree relatives with breast cancer					
0	5,318	89.9	103,979	85.1	<.001
1	529	8.9	16,471	13.5	
≥ 2	71	1.2	1,696	1.4	
Number of breast biopsies					
0	4,909	83.2	95,075	78.9	<.001
1	689	11.7	18,955	15.6	
≥ 2	304	5.1	7,949	6.5	
OS Participants	3,479	54.8	73,485	57.0	<.001
CT Participants	2,874	45.2	55,491	43.0	<.001
HT	1,536	53.4	22,006	39.7	
Non-HT	1,338	46.6	33,485	60.3	
Breast Cancer Outcomes and Follow-up Time in WHI Main Study					
Number of Invasive breast cancers	130		4,713		
	Mean [95% CI]		Mean [95% CI]		
Age at diagnosis, years	63.8 [62.7, 65.0]		68.3 [68.1, 68.5]		<.001
Follow-up time, years	7.57 [7.53, 7.62]		8.12 [8.11, 8.13]		<.001

Note: CT = clinical trial; OS = observational study; HT = Hormone Therapy Trial 95% CI = 95% Confidence Interval. *P* value for differences among categorical variables are from chi-square test and for differences among continuous variables are from t-test. [*]Information on presence of atypical hyperplasia was not available in the WHI data.

Table 2.2 Comparison of RR estimates from the BCRAT and the WHI*

BCRAT Risk Category	BCRAT RR	WHI Hispanic RR [95% CI]	WHI Hispanic $p^{\dagger}$	WHI non-Hispanic White RR [95% CI]	WHI non-Hispanic White $p^{\ddagger}$
Age at menarche	1.10	1.08 [0.85, 1.37]	0.905	1.07 [1.03, 1.11]	0.230
Number of breast biopsies	1.27	1.71 [1.31, 2.24]	0.031	1.27 [1.22, 1.33]	0.994
Age at first live birth (AFB)	1.24	0.97 [0.78, 1.20]	0.024	1.13 [1.09, 1.18]	<0.001
Number of first-degree relatives with breast cancer (FDR)	2.61	2.16 [1.13, 4.13]	0.571	1.31 [1.15, 1.49]	<0.001
AFB*FDR interaction	0.83	0.84 [0.55, 1.29]	0.925	1.01 [0.94, 1.09]	<0.001

* Parameter estimates are Relative Risks (RRs), based on follow-up through the end of WHI Main study only; RR estimates based on comparisons to the referent category for each variable: Age at menarche (≥ 14 years old); Number of breast biopsies (0 biopsies); Age at first live birth (<20 years old); Number of first degree relatives with breast cancer (0 relatives); AFB*FDR (<20 years old and 0 relatives). † Test of difference between WHI Hispanic and Gail Hispanic parameter estimates; ‡ Test of difference between WHI White and Gail White parameter estimates.

Table 2.3 BCRAT and Updated BCRAT observed/expected ratios in the WHI

	Observed breast cancers	BCRAT		Updated BCRAT*	
		Expected breast cancers†	O/E ratio	Expected breast cancers†	O/E ratio
Hispanics					
Main Study (n= 6,353)	130	110	1.18 [0.99, 1.40]	120	1.08 [0.91, 1.28]
Non-Hispanic Whites					
Main Study (n = 128,976)	4,713	4,009	1.18 [1.14, 1.21]	4,788	0.98 [0.96, 1.01]

*For Hispanics, BCRAT is calibrated to 1990-1996 SEER Hispanic women rates and Updated BCRAT is calibrated to 1993-2007 SEER Hispanic women rates. For NHWs, BCRAT is calibrated to 1983-1987 SEER White women rates and Updated BCRAT is calibrated to 1993-2007 SEER non-Hispanic White women rates. †Expected cancers are those estimated by the BCRAT and Updated BCRAT, respectively.

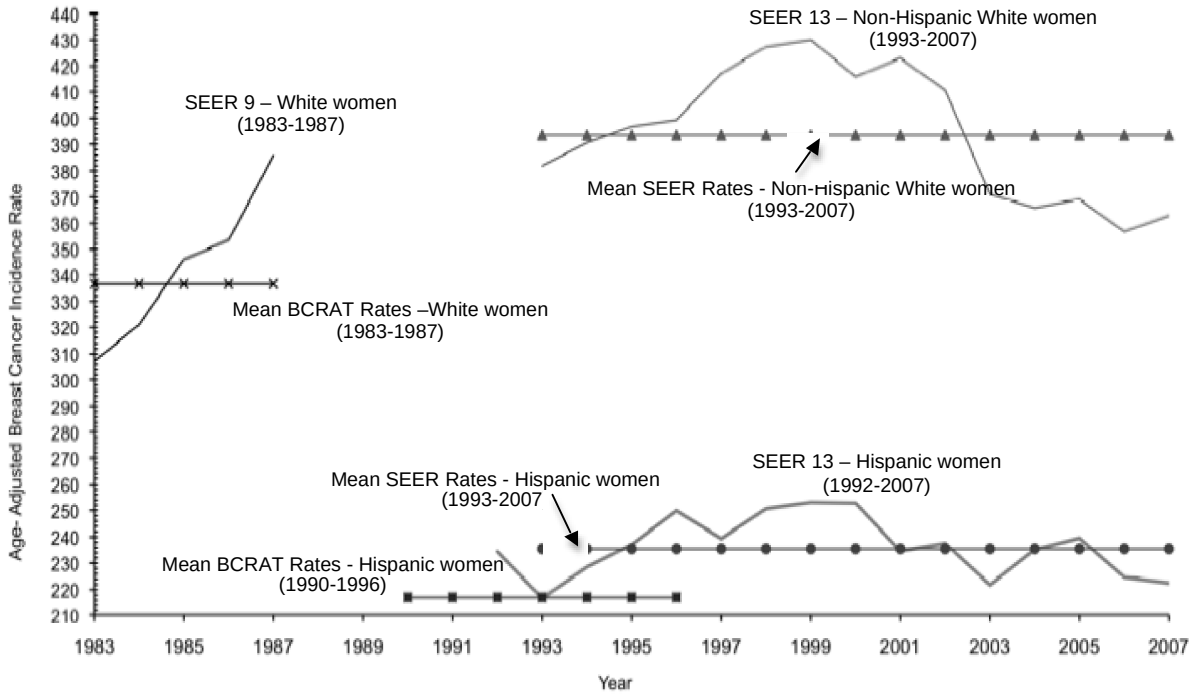

Figure 2.1 Age-adjusted SEER Invasive Breast Cancer Incidence Rates over the BCRAT and WHI time periods. Solid lines show SEER incidence rates of invasive breast cancer for the years used in BCRAT (1983-1987 for White women and 1990-1996 for Hispanic women), as well as for those years available in SEER that cover the WHI study period (1993-2007). Dotted lines show the mean incidence rate of invasive breast cancer over the time periods used in the BCRAT for White women and Hispanic women, and for SEER 1993-2007 for both NHW and Hispanic women. Mean rates were estimated using age-specific invasive breast cancer incidence rates, among women aged 50 and older, based on 5-year age categories (i.e. 50-54 years of age, 55-59 years, 60-64 years, etc.) as used in the BCRAT. Rates are based on SEER 13 registries. All rates are per 100,000 and age-adjusted to the 2000 US Standard Population rates among women age 50 and older.

Table S.2.1 Results of the BCRAT and Updated BCRAT for Hispanic women in the WHI*

Gail Risk Category	n	No. observed	BCRAT No. predicted	BCRAT O/E ratio	Updated BCRAT No. predicted	Updated BCRAT O/E ratio
Total	6,353	130	110.51	1.18 [0.99, 1.40]	120.53	1.08 [0.91, 1.28]
Age at baseline, years						
50-59	3,212	67	48.51	1.38 [1.09, 1.75]	53.78	1.25 [0.98, 1.58]
60-69	2,467	53	47.85	1.11 [0.85, 1.45]	51.60	1.03 [0.78, 1.34]
≥ 70	673	10	14.14	0.71 [0.38, 1.31]	15.14	0.66 [0.35, 1.23]
Age at menarche, years						
< 12	1,560	35	29.73	1.18 [0.85, 1.64]	32.43	1.08 [0.77, 1.50]
12-13	3,040	65	52.79	1.23 [0.97, 1.57]	57.55	1.13 [0.89, 1.44]
≥ 14	1,701	28	27.29	1.03 [0.71, 1.49]	29.78	0.94 [0.65, 1.36]
Age at first birth, years						
< 20	1,087	21	17.71	1.19 [0.77, 1.82]	19.41	1.08 [0.71, 1.66]
20-24	1,869	42	31.93	1.32 [0.97, 1.78]	34.86	1.20 [0.89, 1.63]
25-29/Nulliparous	2,773	52	47.75	1.09 [0.83, 1.43]	51.99	1.00 [0.76, 1.31]
≥ 30	453	12	10.75	1.12 [0.63, 1.97]	11.69	1.03 [0.58, 1.81]
Number of 1st degree relatives with breast cancer						
0	5,318	98	81.50	1.20 [0.99, 1.47]	88.88	1.10 [0.90, 1.34]
1	529	21	17.45	1.20 [0.79, 1.85]	19.06	1.10 [0.72, 1.69]
≥ 2	71	4	5.08	0.79 [0.30, 2.10]	5.54	0.72 [0.27, 1.92]
Number of breast biopsies						
0	4,909	81	79.17	1.02 [0.82, 1.27]	85.92	0.94 [0.76, 1.17]
1	689	24	15.09	1.59 [1.07, 2.37]	16.31	1.47 [0.99, 2.19]
≥ 2	304	16	8.82	1.81 [1.11, 2.96]	9.53	1.68 [1.03, 2.74]
Age at first birth, years						
< 20						
Number of FDR						
0	929	17	13.47	1.26 [0.78, 2.03]	14.75	1.15 [0.72, 1.85]
1	77	3	2.46	1.22 [0.39, 3.78]	2.71	1.11 [0.36, 3.43]
≥ 2	13	0	0.80	n/a	0.89	n/a
20-24						
Number of FDR						
0	1,565	29	23.07	1.26 [0.87, 1.81]	25.22	1.15 [0.80, 1.65]
1	178	10	5.87	1.70 [0.92, 3.17]	6.40	1.56 [0.84, 2.91]
≥ 2	21	2	1.46	1.37 [0.34, 5.49]	1.59	1.26 [0.31, 5.03]
25-29/Nulliparous						
Number of FDR						
0	2,321	39	35.04	1.11 [0.81, 1.52]	38.13	1.02 [0.75, 1.40]
1	220	7	7.30	0.96 [0.46, 2.01]	7.97	0.88 [0.42, 1.84]
≥ 2	33	1	2.53	0.40 [0.06, 2.81]	2.75	0.36 [0.05, 2.59]
≥ 30						
Number of FDR						
0	374	11	8.42	1.31 [0.72, 2.36]	9.18	1.20 [0.66, 2.17]
1	42	1	1.45	0.68 [0.10, 4.89]	1.58	0.63 [0.09, 4.49]
≥ 2	1	0	0.06	n/a	0.06	n/a

Table S.2.1 continued Results of the BCRAT and Updated BCRAT for Hispanic women in the WHI*

Gail Risk Category	n	No. observed	BCRAT No. predicted	BCRAT O/E ratio	Updated BCRAT No. predicted	Updated BCRAT O/E ratio
Observational Study	3,479	71	59.77	1.19 [0.94, 1.50]	65.05	1.09 [0.86, 1.38]
Clinical Trial	2,874	59	50.74	1.16 [0.90, 1.50]	55.48	1.06 [0.82, 1.37]
HT	1,536	23	26.37	0.87 [0.58, 1.31]	28.85	0.80 [0.53, 1.20]
E only	319	6	5.69	1.05 [0.47, 2.35]	6.24	0.96 [0.43, 2.14]
E + P	470	5	8.01	0.62 [0.26, 1.50]	8.76	0.57 [0.24, 1.37]
Control	747	12	12.67	0.95 [0.54, 1.67]	13.86	0.87 [0.49, 1.52]
Other CT	1,338	36	24.37	1.48 [1.07, 2.05]	26.62	1.35 [0.98, 1.88]

*Supplemental Table 2.1 shows the results of the BCRAT and Updated BCRAT for all BCRAT risk factor categories and categories examined in the WHI, by WHI study period. Notes: n = number of participants; No. = number; O/E ratio = observed/expected ratio; FDR = first-degree relatives; HT = Hormone Therapy Trial; E = Estrogen; P = Progesterone; 95% CI = 95% Confidence Interval

Table S.2.2 Results of the BCRAT and Updated BCRAT for non-Hispanic white women in WHI*

Gail Risk Category	n	No. observed	BCRAT No. predicted	BCRAT O/E ratio	Updated BCRAT No. predicted	Updated BCRAT O/E ratio
Total	128,976	4,713	4009.01	1.18 [1.14, 1.21]	4787.75	0.98 [0.96, 1.01]
Age at baseline, years						
50-59	40,648	1,346	1,076.49	1.25 [1.18, 1.32]	1,305.09	1.03 [0.98, 1.09]
60-69	58,729	2,199	1,914.05	1.15 [1.10, 1.20]	2,284.62	0.96 [0.92, 1.00]
≥ 70	29,595	1,168	1,018.35	1.15 [1.08, 1.21]	1,197.89	0.97 [0.92, 1.03]
Age at menarche, years						
< 12	27,718	1,077	924.83	1.16 [1.10, 1.24]	987.89	1.03 [0.96, 1.09]
12-13	71,953	2,596	2,244.61	1.16 [1.11, 1.20]	2,680.01	0.97 [0.93, 1.01]
≥ 14	28,848	1,014	828.23	1.22 [1.15, 1.30]	1,106.38	0.97 [0.92, 1.03]
Age at first birth, years						
< 20	14,603	463	413.57	1.12 [1.02, 1.23]	495.78	0.93 [0.85, 1.02]
20-24	51,016	1,694	1,488.39	1.14 [1.09, 1.19]	1,779.38	0.95 [0.91, 1.00]
25-29/Nulliparous	52,436	2,057	1,688.11	1.22 [1.17, 1.27]	2,014.47	1.02 [0.98, 1.07]
≥ 30	9,484	441	383.76	1.15 [1.05, 1.26]	456.29	0.97 [0.88, 1.06]
Number of 1st degree relatives with breast cancer						
0	103,979	3,575	2,771.35	1.29 [1.25, 1.33]	3,311.89	1.08 [1.04, 1.11]
1	16,471	800	875.14	0.91 [0.85, 0.98]	1,044.28	0.77 [0.71, 0.82]
≥ 2	1,696	92	181.65	0.50 [0.41, 0.62]	215.68	0.43 [0.35, 0.52]
Number of breast biopsies						
0	95,075	3,108	2,703.54	1.15 [1.11, 1.19]	3,207.57	0.97 [0.93, 1.00]
1	18,955	907	708.64	1.28 [1.20, 1.37]	839.41	1.08 [1.01, 1.15]
≥ 2	7,949	397	386.92	1.06 [0.93, 1.13]	457.48	0.87 [0.79, 0.95]
Age at first birth, years						
< 20						
Number of FDR						
0	11,742	362	277.74	1.30 [1.18, 1.44]	333.27	1.09 [0.98, 1.20]
1	1,836	65	94.78	0.69 [0.54, 0.88]	113.57	0.57 [0.45, 0.73]
≥ 2	190	9	21.20	0.42 [0.22, 0.82]	25.11	0.36 [0.19, 0.69]
20-24						
Number of FDR						
0	41,004	1,272	1,000.49	1.27 [1.20, 1.34]	1,196.96	1.06 [1.01, 1.12]
1	6,671	300	350.27	0.86 [0.76, 0.96]	418.53	0.72 [0.64, 0.80]
≥ 2	672	37	75.41	0.49 [0.36, 0.68]	89.54	0.41 [0.30, 0.57]
25-29/Nulliparous						
Number of FDR						
0	42,451	1,579	1,186.81	1.33 [1.27, 1.40]	1,417.25	1.11 [1.06, 1.17]
1	6,604	352	354.65	0.99 [0.89, 1.10]	422.43	0.83 [0.75, 0.92]
≥ 2	685	35	71.39	0.49 [0.35, 0.68]	84.93	0.41 [0.30, 0.57]
≥ 30						
Number of FDR						
0	7,639	332	285.99	1.16 [1.04, 1.29]	340.19	0.98 [0.88, 1.09]
1	1,194	74	67.08	1.10 [0.87, 1.39]	79.83	0.93 [0.74, 1.16]
≥ 2	129	10	10.94	0.91 [0.49, 1.70]	12.89	0.78 [0.42, 1.44]

Table S.2.2 continued Results of the BCRAT and Updated BCRAT for non-Hispanic white participants in WHI*

			BCRAT		Updated BCRAT	
Gail Risk Category	**n**	**No. observed**	**No. predicted**	**O/E ratio**	**No. predicted**	**O/E ratio**
Observational Study	73,485	2,739	2,296.15	1.19 [1.15, 1.24]	2,743.16	1.00 [0.96, 1.04]
Clinical Trial	55,491	1,974	1,712.87	1.15 [1.10, 1.20]	2,044.59	0.96 [0.92, 1.01]
HT	22,006	660	663.12	1.00 [0.92, 1.07]	789.57	0.84 [0.77, 0.90]
E only	4,003	95	120.89	0.79 [0.64, 0.96]	143.97	0.66 [0.54, 0.81]
E + P	7,136	256	215.96	1.18 [1.05, 1.34]	256.96	1.00 [0.88, 1.13]
Control	10,867	309	326.28	0.95 [0.85, 1.06]	388.63	0.79 [0.71, 0.89]
Other CT	33,485	1,314	1049.75	1.25 [1.19, 1.32]	1,255.03	1.05 [0.99, 1.10]

*Supplemental Table 2.2 shows the results of the BCRAT and Updated BCRAT for all BCRAT risk factor categories and categories examined in the WHI, by WHI study period. Notes: n = number of participants; No. = number; O/E ratio = observed/expected ratio; FDR = first-degree relatives; HT = Hormone Therapy Trial; E = Estrogen; P = Progesterone; 95% CI = 95% Confidence Interval

The impact of a web-based, tailored decision aid on women at high risk for breast cancer

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ABSTRACT

Objective: To assess the impact of Guide to Decide (GtD), a web-based, personally-tailored decision aid designed to inform women's decisions about prophylactic tamoxifen and raloxifene use.

Methods: Postmenopausal women, age 40-74, with BCRAT 5-year risk ≥1.66% and no prior history of breast cancer were randomized to one of three study arms: intervention (n=690), control 1 (n=160), or control 2 (n=162). Intervention participants viewed GtD prior to completing a post-test and 3 month follow-up assessment. Controls did not. We assessed the impact of GtD on women's' decisional conflict levels and treatment decision behavior at post-test and at 3 months.

Results: Intervention participants had significantly lower decisional conflict levels at post-test ($p<0.001$) and significantly higher odds of making a decision about whether or not to take prophylactic tamoxifen or raloxifene at 3-month follow-up ($p<0.001$) compared to control participants.

Conclusion: GtD lowered decisional conflict and helped women at high risk of breast cancer decide whether to take prophylactic tamoxifen or raloxifene to reduce their cancer risk.

Practice Implications: Web-based, tailored decision aids should be used more routinely to facilitate informed medical decisions, reduce patients' decisional conflict, and empower patients to choose the treatment strategy that best reflects their own values.

INTRODUCTION

Recent evidence suggests that approximately 15% of women aged 30-84 in the United States (US), more than 11.5 million women, may be at high risk of breast cancer (26), based on the National Cancer Institute Breast Cancer Risk Assessment Tool (BCRAT) 5-year absolute risk estimate (21, 50). For women who meet the high risk threshold of BCRAT 5-year risk ≥1.66%, the American Society of Clinical Oncology (ASCO) and National Comprehensive Cancer Network (NCCN) recommend that patients consider prophylactic treatment with tamoxifen or raloxifene to reduce the risk of invasive breast cancer in the future, although the latter is only recommended for postmenopausal women (27, 28). However, the decision to use prophylactic chemoprevention can be overwhelming to women, especially since there is not a clear right or wrong decision. The best decision for each woman must take into account the balance of potential risks and benefits, as well as one's own values and preferences. Thus, it is considered a preference-sensitive decision (51).

Decision aids are designed to help individuals make specific and deliberate choices about their care by providing accurate, balanced information on the options and outcomes to prepare individuals for decision making (31). Ideally, the decision aid should also help individuals clarify their own values and to better inform their personal choices (52). Decision aids have been shown to increase individual's knowledge of their options, provide evidence-based information about a health condition and the associated uncertainties, help patients recognize the value-sensitive nature of decisions, guide patients to consider which benefits and harms are most important to them, increase individuals' comfort with their personal choice, improve patient-provider communication about options, provide guidance in the steps of decision making and communication of their values, and enable patients to be active, informed participants (30, 31).

The purpose of this study was to assess the impact of Guide to Decide (GtD) a web-based, personally-tailored decision aid developed to inform women at high risk of breast cancer about the risks and benefits of prophylactic tamoxifen and raloxifene use (34). The International Patient Decision Aid Standards (IPDAS) Collaboration suggests that the primary measure for evaluating patient decision aids should be decision quality, defined as the extent to which a patient's decision is informed and based on personal values; furthermore, IPDAS recommended the need to assess patients' recognition that a decision needs to be made, appreciation of one's goals and values, and the importance of values in the decision(53). Subsequently, to assess these key concepts of the patient decision making process, we aimed to evaluate the impact of the Guide to Decide on women's decisional conflict and treatment decision behavior, as well as the association between these outcomes with patient satisfaction with the decision aid and preparation for decision making.

METHODS

Study Design and Intervention

Information about the study design, recruitment, study population and intervention has been previously described in detail (34). In brief, women at high risk of breast cancer (based on the National Cancer Institute Breast Cancer Risk Assessment Tool (BCRAT) 5-year risk ≥ 1.66%) were recruited from Group Health Cooperative (Seattle, WA) and the Henry Ford Health System (Detroit, MI). Potential participants were identified from automated medical records, mailed a study invitation letter, and directed how to log into the study website using a unique username and password to learn more about the study, be screened for eligibility, and enroll. Women were eligible if they were age 40-74, postmenopausal, not pregnant or nursing, had a BCRAT 5-year risk ≥ 1.66%, no prior history of breast cancer or chemoprevention, no contraindications for

tamoxifen or raloxifene use, no terminal illness, and did not participate in the Study of Tamoxifen and Raloxifene (STAR) trial (54).

Upon completing the eligibility and baseline questions, eligible participants were randomized to one of three study arms: intervention (n = 690), control 1 (n = 160), or control 2 (n = 162). Intervention participants received the personalized GtD decision aid at baseline, followed immediately by a post-test survey and a 3-month follow-up survey. Control 1 participants completed the same 'post-test' questionnaire at baseline as the intervention group (excluding items assessing satisfaction with the decision aid) and the 3-month follow-up survey. After completion of the last survey, they received access to their tailored GtD decision aid. Participants in control 2 completed an abbreviated 'post-test' survey (personality measures only) followed by the 3-month follow-up survey and access to the decision aid. The latter control group was used to address threats to internal validity, due to our concern that participants in control 1 would search the internet for information about tamoxifen and raloxifene after answering questions about these drugs in the post-test survey, potentially impacting their answers at the 3-month follow up. The inclusion of control 2 allowed us to have a control group truly blinded to the concept of chemoprevention and who we could compare the intervention group to at 3 months.

The original aim of the GtD trial was to examine the impact of 5 different content and presentation factors on participant knowledge and decision making: Comparative risk – a graph that showed how the woman's risk compared to the risk of the average US women of the same age and race; Personalization and Testimonials – information presented using 2nd person voice (vs. 3rd person) and inclusion of testimonials; Summary table – presentation of risks and benefits of the breast cancer treatments in a summary table; Binary versus trinary option presentation – presentation of information in the form of a 2 treatment option (chemoprevention vs. no

chemoprevention) or 3 treatment option (tamoxifen vs. raloxifene vs. no chemoprevention); and Order – presentation of risk information or benefit information first. Each factor was examined within the context of an online, personalized decision aid for breast cancer chemoprevention. Intervention participants also received information about breast cancer, their BCRAT 5-year risk score, and information on tamoxifen and raloxifene. These 5 factors were not the focus of the present report. However, analyses were conducted to assess the impact of the factors on our outcomes of interest and it was determined that excluding these covariates does not affect the analysis. Information on the risks of both drugs was tailored to each woman's age and race/ethnicity, while the benefits of the drugs were tailored based on the BCRAT risk score. All content was written in English at an 8th grade reading level.

Key Measures

Decisional Conflict

Decisional conflict was measured at post-test survey using the 16-item Decisional Conflict Scale (DCS) (55). This measure is used to assess patients' uncertainty in making health-related decisions, the factors that contribute to this uncertainty, and perceived effective decision making. It is composed of five subscales: informed, values clarity, support, uncertainty, and effective decision. In the present study, both total DCS and individual subscale scores were calculated as specified by O'Connor et al (56). Previously reported findings from the Guide to Decide study calculated decisional conflict such that higher scores corresponded to lower decisional conflict levels (34).

Participant Satisfaction and Identification with Decision Aid

Participant satisfaction with the GtD decision aid was measured at post-test using seven items. Four of the items were rated on a 7-point Likert scale ranging from 'completely disagree (1) to "completely agree (7): 1) "I felt that the risk/benefit numbers I received were "my numbers" (not

other people's)", 2) "I found the decision guide to be written personally for me", 3) "I felt that the information in this decision guide was relevant to me", and 4) "I felt that the information in this decision guide was designed specifically for me". The question "How trustworthy was the decision guide?" was measured on an 11-point Likert scale ranging from ("not at all trustworthy" (0) to "extremely trustworthy" (10)). The remaining two items: "The program included some numerical information about how likely a women would be to experience side effects of tamoxifen or raloxifene. How easy or difficult was it to understand?" ("very difficult to understand" (1) to "very easy to understand" (4)); and "Would you recommend this program to a close friend or family member?" ("definitely would not recommend" (1) to "definitely would recommend" (5)).

Preparation for Decision Making

The Preparation for Decision Making (PrepDM) Scale (57, 58) was used to evaluate participants' perceived preparation to make a decision about taking a chemopreventive agent to reduce their risk of future breast cancer. The PrepDM has been previously validated and shown to have good reliability (58) (59). PrepDM scores were calculated as specified by the scale's authors (57).

Stage of Decision Making

Participants' decision making behavior was measured in the 3-month follow-up survey using two items. First, participants were asked, "Have you made a decision about whether or not to take a breast cancer prevention drug as a way to prevent breast cancer?" For this analysis, we collapsed responses into two categories: "made a decision" (i.e. decided to not take either tamoxifen or raloxifene/decided to take tamoxifen/decided to take raloxifene) or "not made a decision." Individuals who reported that they had not made a decision whether or not to take a breast cancer drug were subsequently asked, "How close are you to making a decision about

whether to take a breast cancer prevention drug as a way to prevent breast cancer?" Response options for the latter question were categorized as ranging from Stage 1 "Not at all close to making a decision" to Stage 5 "Extremely close to making a decision."

Statistical Analyses

Descriptive statistics were used to assess participants' baseline sociodemographic characteristics and BCRAT 5-year risk score. To assess the impact of the GtD on participants' decisional conflict, we used multivariate linear regression to compare post-test DCS and decisional conflict subscale scores between intervention and control group 1 participants, adjusting for age, race (White/non-White), education (high school diploma/GED, some college/trade school, and bachelor's degree or higher), and BCRAT 5-year risk score. Baseline covariates were included in the multivariate linear regression to improve estimate precision (60). We ran separate models for the overall DCS and subscale scores. Similar multivariate linear regression models were used to examine the association between DCS (total and subscale scores) and the seven patient satisfaction measures adjusting for age, race, education and BCRAT risk score.

To examine whether the GtD had an impact on self-reported decision making, we used a two-step modeling approach. First, logistic regression was used to assess whether there was a difference between the intervention, control group 1, and control group 2 participants in having made a decision about whether or not to take tamoxifen or raloxifene at 3-month follow-up. Second, among those participants who had not made a decision at 3-month follow-up, ordered logistic regression was used to examine self-reported stage of decision making at 3-month follow-up between the intervention, control group 1, and control group 2 participants. We then examined whether the decision aid was more helpful to those participants who had not made a decision and, thus, were actively considering their options at 3-month follow-up. To accomplish

this, we assessed the association between post-test PrepDM scores and treatment decision making behavior among intervention participants, using the same two-step modeling approach; specifically, post-test PrepDM scores was used as the predictor in both the logistic and ordered logistic regression models.

In regard to the 5 different content and presentation factors, bivariate analyses were performed to assess the association between each factor and the main outcomes of interest. We found no statistically significant associations and, therefore, did not include these factors in the final multivariate regression analyses (results not shown).

RESULTS

Participants' baseline characteristics and response rates

Participants' baseline demographic characteristics are described in Table 3.1. Intervention and control group participants were similar in age, race/ethnicity, educational attainment and BCRAT 5-year risk score at baseline. In general, participants were predominately non-Hispanic White and well-educated (65% with a bachelor's degree or higher), with a mean age of 61.8 years (standard deviation (SD)=5.2) and mean BCRAT 5-year risk of 2.6% (SD=1.2).

All 1,012 participants completed the 'post-test' survey. However, only 55.5% of the intervention group, 63.7% of the control group, and 61.7% of the control 2 group completed the 3-month follow-up. Participants who competed the 3-month follow-up were similar to non-responders, with the exception that 3-month respondents were more likely to have a college degree (71.1% vs. 58.8%, respectively, $p<0.001$).

Decisional conflict scale and decisional conflict subscale scores

Table 3.2 describes the decisional conflict scale (DCS) total and subscale scores of intervention and control group participants at post-test, adjusting for age at enrollment, race, education and baseline BCRAT 5-year risk score. Intervention group participants had significantly lower total DCS scores ($p<0.001$), as well as significantly lower scores on the uncertainty ($p<0.001$), informed ($p<0.001$), values clarity ($p<0.001$), support ($p<0.001$), and effective decision ($p<0.001$) subscales compared to control group participants.

Patient satisfaction with the decision aid

Patient satisfaction with the Guide to Decide was measured at post-test among intervention group participants. Overall, participants' responses trended toward higher satisfaction on each measure: The risk/benefit numbers I received were "my numbers" (mean=5.3, s.e.=.06; 1-7 point scale); The GtD was written personally for me (mean=4.4, s.e.=.06; 1-7 point scale); The information in the GtD was relevant to me (mean=5.1, s.e.=.06; 1-7 point scale); The information in the GtD was designed specifically for me (mean=4.2, s.e.=.06; 1-7 point scale); How trustworthy was the GtD (mean=7.2, s.e.=.08; 0-10 point scale); How easy/difficult was it to understand numerical information in the GtD (mean=3.7, s.e.=.03; 1-4 point scale); Would you recommend the GtD to a close friend or family member? (mean=3.9, s.e.=.03; 1-5 point scale); results not shown.

Association between decisional conflict and patient satisfaction with the decision aid

Among intervention group participants, higher post-test DCS scores were associated with significantly lower satisfaction with the decision aid at post-test (Table 3.3). Specifically, on six of the seven satisfaction items, increased decisional conflict levels at post-test were associated with significantly lower satisfaction with the decision aid. No significant association was found between DCS and participants' willingness to recommend the decision aid to a family member

or close friend. The same trend was found with each of the decisional conflict subscale scores (Supplemental Table 3.1).

Stage of decision making and preparation for decision making

At 3-month follow-up, the odds of having made a decision about whether or not to take a breast cancer chemoprevention drug were lower for participants in both control groups compared to intervention group participants; control 1 (OR=0.42 [95% CI: 0.27-0.67]; p<0.001) and control 2 (OR=0.35, [95% CI: 0.22-0.56]; p<0.001) (Table 3.4). Among those participants who had not made a decision by 3-month follow-up, participants in the control 2 group had significantly lower odds of being closer to making a decision compared to intervention group participants (OR=0.33 [95% CI: 0.17-0.65]; p=0.001). There was no statistically significant difference in self-reported stage of decision making between control 1 and intervention group participants who had not made a decision by 3-month follow-up.

Among intervention group participants, higher post-test PrepDM scores were associated with significantly decreased odds of having made a decision about whether to take a breast cancer chemoprevention drug at 3-month follow-up (OR=0.99, [95% CI: 0.98-1.0], p=0.03; Table 3.5). Of those intervention participants still in the decision making process at 3-month follow-up, individuals with a higher PrepDM score at post-test had increased odds of being farther along in the decision making process (OR=1.04, [95% CI: 1.02-1.06}; p<0.001). Table 3.6 shows the mean post-test PrepDM scores among individuals in each stage of the decision making process, for those who had not made a decision at 3-month follow-up.

Post-hoc analyses to assess post-test PrepDM scores between intervention group participants who completed the 3-month follow-up test and those lost to follow-up found no significant differences between groups (results not shown).

DISCUSSION AND CONCLUSION

Discussion

We found that women who received the GtD decision aid had greater odds of making a decision, or were closer to making a decision, about whether to take prophylactic tamoxifen or raloxifene than women who did not receive the decision aid. Furthermore, women in the intervention group had significantly lower decisional conflict levels. In fact, mean decisional conflict scores among women receiving the decision aid were less than half that of control 1 participants (22.0 vs. 55.7, respectively), with women in latter group among those who did not receive information or knowledge about the chemoprevention drugs.

These findings expand upon previous studies showing the effectiveness of decision aids for patients in different stages of the decision making process (58) and support research on the benefit of decision aids among individuals facing complex health decisions (52). Evidence suggests increased decisional conflict is associated with a higher likelihood of delayed decisions and wavering between choices (61), with decisional conflict scores of less than 25 associated with implementing decisions, whereas scores higher than 37.5 are associated with decision delay or feelings of uncertainty about decision implementation (56). Our study supports this previous research, finding that women in control 1 had lower odds of having made a decision about taking prophylactic chemoprevention compared to intervention participants. Moreover, among women who had not made a decision, participants in the control 2 had lower odds of being close to making a decision compared to those in the intervention group.

We found that lower levels of decisional conflict were associated with significantly increased patient satisfaction with the decision aid. Intervention group participants with lower decisional conflict were more likely to report that they felt the GtD was written personally for them, designed specifically for them, relevant, trustworthy, and that the risk/benefit number presented were “my numbers” (not other people’s) and easy to understand. Consequently, these findings suggest that decisional conflict may be associated with the patients’ ability to identify with, understand, and relate to the information presented in the decision aid.

In addition, our results on the PrepDM scores of women who received the decision aid support previous findings suggesting decision aids may be more useful to individuals who are actively considering a decision (58). Subsequently, GtD may be more helpful to women who are still contemplating the decision about whether to take prophylactic chemoprevention compared to those who have already made a choice or are not at all close to making a decision. These results reiterate the point that the timing of a decision aid intervention in the care pathway may affect the usefulness of decisional support to a patient.

While our study adds to the current literature, there are also some pragmatic limitations to be considered. First, this study was conducted in an educated, predominately White, insured population; therefore, the results may not generalize to women who are uninsured, lower SES or from other racial/ethnic backgrounds. Second, the use of a web-based decision aid may create a selection bias, since individuals without computer access were not eligible for this trial and women not comfortable using computers or the Internet may have chosen not to pursue enrollment. As such, the results may not generalize who do not use the Internet or are not comfortable with this technology. Third, some experts contend that reducing decisional conflict should not necessarily be an explicit goal of decision aids, because sometimes increased

awareness of tradeoffs may cause patients to feel more conflicted (62). These experts argue that the goal of decision aids is to inform people about their choices regardless of whether that increases or decreases conflict. Nevertheless, our study shows that the GtD informs patients about tradeoffs while, at the same time, reducing decisional conflict. Finally, the results may be specific to the GtD tool and not generalize to other decision aids. Despite these limitations, we believe the results do generalize to the intended audience (insured post-menopausal women at risk elevated risk for breast cancer who are comfortable using the Internet and eligible for breast cancer chemoprevention). Moreover, the results provide important insight into the value that decision aids can have in helping women make informed decisions regarding their care.

Conclusion

Overall, our findings indicate that receiving an online decision aid may help women at high risk for breast cancer make a decision, or be further along in the decision making process, as well as reduce decisional conflict about future prophylactic tamoxifen or raloxifene use to reduce their cancer risk.

Practice Implications

Patient involvement in decisions about their health has become increasingly important, with patient-centered care recognized as a primary domain of quality health care (63, 64). Engaging patients in their own decision has the greatest potential to help guide medical decisions that incorporate individuals' preferences, needs, and values, as well as lead to increased satisfaction with one's health care and better quality of life (65, 66). However, patients must understand the facts relevant to their medical decision in order to be effective advocates and make informed decisions (29). Accordingly, for women at high risk of developing breast cancer, the decision to use tamoxifen or raloxifene as a prophylaxis is a preference-sensitive decision; that is, it involves weighing trade-offs between the risks (inconvenience, health care costs, and a number

of potential side effects) and benefits of the treatment (the chance that the drug will reduce one's risk of developing breast cancer). Further, each woman must weigh these relative risks and benefits for herself and make a decision that is aligned with her own values and preferences; there is no single right or wrong answer.

Personalized decision aids should be used more routinely to facilitate such informed medical decisions, reduce patients' decisional conflict, improve communication, and empower patients to choose the treatment strategy that best reflects their own values. GtD was developed as a decisional support tool that uses web-technology to provide useful information to women at high risk of developing breast cancer that can be accessed in the comfort of their own home, alone or with key members of their social support system, where patients are likely to be less distressed, and which may further improve understanding (35).

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Table 3.1 Baseline characteristics of participants

Characteristic	Intervention (n=690)	Control 1 (n=160)	Control 2 (n=162)	*p*
	Mean [95% CI]	Mean [95% CI]	Mean [95% CI]	
Age, years	61.7 [61.3, 62.1]	62.0 [61.2, 62.9]	61.5 [60.6, 62.4]	0.63
	n (%)	n (%)	n (%)	
Race/Ethnicity				
Non-Hispanic White	660 (95.7)	152 (95.0)	156 (96.3)	0.82
Educational attainment				
High School Diploma/GED	50 (7.3)	9 (5.6)	14 (8.7)	0.77
Some College/Trade School	179 (26.1)	45 (28.1)	46 (28.6)	
Bachelors Degree or higher	456 (66.6)	106 (66.3)	101 (62.7)	
	Mean [95% CI]	Mean [95% CI]	Mean [95% CI]	
5-Year BCRAT Risk Score	2.67 [2.58, 2.76]	2.60 [2.43, 2.76]	2.81 [2.52, 3.10]	0.32

Notes. 95% CI = 95% Confidence Interval. All estimates are based on participants who have a valid (non-missing) response to each variable.

Table 3.2 Participants' Decisional Conflict Scale and Subscale scores*

Characteristic	**Intervention** (n=690)	**Control 1** (n=160)	*p*
	Mean [95% CI]	Mean [95% CI]	
Total Decisional Conflict Score	22.0 [18.8, 25.1]	55.7 [38.9, 72.5]	<0.001
Uncertainty Subscore	37.4 [32.7, 42.0]	73.2 [48.5, 98.0]	<0.001
Informed Subscore	8.69 [5.46, 11.9]	57.4 [40.3, 74.6]	<0.001
Values Clarity Subscore	12.6 [8.9, 16.4]	47.7 [27.8, 67.6]	<0.001
Support Subscore	18.1 [14.6, 21.6]	43.3 [24.8, 61.8]	<0.001
Effective Decision Subscore	30.0 [26.1, 33.9]	55.5 [34.8, 76.3]	<0.001

Notes. Abbreviation: 95% CI = 95% Confidence Interval. * Total decisional conflict and subscale scores based on participants' responses to the Decisional Conflict Scale at post-test. Estimates derived from multivariate linear regression, adjusting for age, race, education, and baseline BCRAT 5-year risk score.

Table 3.3 Association between decisional conflict and satisfaction with the decision aid*

	Total DCS score (n=690)	
Participant Satisfaction Item	β (SE)	*p*
The risk/benefit numbers I received were "my numbers"	-0.02 (0.004)	<0.001
The GtD was written personally for me	-0.01 (0.004)	<0.001
The information in the GtD was relevant to me	-0.01 (0.003)	0.007
The information in the GtD was designed specifically for me	-0.01 (0.004)	0.001
How trustworthy was the GtD	-0.01 (0.005)	0.002
How easy/difficult was it to understand numerical information in the GtD	-0.004 (0.001)	0.003
Would you recommend the GtD to a close friend or family member	-0.002 [0.002)	0.291

Notes. Abbreviations: β=beta estimate; SE=standard error. *Estimates presented were obtained by multivariate linear regression analyses of total DCS score (predictor of interest) and patient satisfaction measures (modeled separately), adjusting for age, race, education, and BCRAT risk score as covariates; analyses among intervention group participants only.

Table 3.4 Impact of the Guide to Decide on treatment decision behavior

	Made a decision about whether to take breast cancer prevention drug*		
Treatment Arm	OR	95% CI	p-value
Intervention (n=382)	Ref	–	–
Control 1 (n=102)	0.42	0.27-0.67	<0.001
Control 2 (n=100)	0.35	0.22-0.56	<0.001
	Had not made a decision about whether to take breast cancer prevention drug Self-reported Stage of Decision Making (I-IV)***		
	OR	95% CI	p-value
Intervention (n=171)	Ref	–	–
Control 1 (n=67)	0.65	0.36-1.16	0.146
Control 2 (n=70)	0.33	0.17-0.65	0.001

Notes. Abbreviation: 95% CI = 95% Confidence Interval. *Estimates obtained from logistic regression analysis of having made a decision about whether or not to take a breast cancer prevention drug at 3-month follow-up between intervention arms; analyses based on those participants with a valid (non-missing) response **Estimates obtained from ordered logistic regression analyses, among participants who had not made a decision about whether to take a breast cancer prevention drug at 3-month follow-up, with self-reported Stage of Decision Making (I-IV) as the outcome and intervention arm as predictor.

Table 3.5 Association between preparation for decision making and treatment decision behavior

	Made a decision about whether to take breast cancer prevention drug*		
	OR	95% CI	p-value
PrepDM Score†	0.99	0.98-1.00	0.03
	Had not made a decision about whether to take breast cancer prevention drug Self-reported Stage of Decision Making_(I-IV)**		
	OR	95% CI	p-value
PrepDM Score†	1.04	1.02-1.06	<0.001

Abbreviations. OR=odds ratio; 95% CI = 95% Confidence Interval. *Estimates obtained from logistic regression analyses, with having made a decision about whether to take a breast cancer prevention drug at 3-month follow-up as the outcome and post-test PrepDM score as predictor. **Estimates obtained from ordered logistic regression analyses, among participants who had not made a decision about whether to take a breast cancer prevention drug at 3-month follow-up, with self-reported Stage of Decision Making (I-IV) as the outcome and post-test PrepDM score as predictor. †Among intervention group participants only who had not made a decision about whether or not to take a breast cancer chemoprevention drug at 3-month follow-up survey (n=171).

Table 3.6 Stage of decision making and preparation for decision making among intervention group participants in the decision making process*

		Post-test PrepDM Score		
Stage of decision making	**n**	Mean (SE)	F	p-value
I	103	64.8 (1.8)	6.54	<0.001
II	26	69.8 (2.7)		
III	29	73.8 (2.8)		
IV	11	86.6 (4.5)		

Abbreviations. PrepDM=Preparation for Decision Making; SE=standard error; F=F-statistic. *Among intervention group participants who had not made a decision about whether or not to take a breast cancer chemoprevention drug at 3-month follow-up survey, with a valid (non-missing) post-test PrepDM score (n=169).

Risk of developing invasive breast cancer in Hispanic women: A look across Hispanic subgroups

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ABSTRACT

Background: Breast cancer is a significant public health threat to Hispanic women in the United States. While evidence on the burden of breast cancer among Hispanic women is available, it is important to assess the heterogeneity in breast cancer risk among Hispanic women of different origins.

Methods: Using data from the 2000 and 2005 National Health Interview Survey (NHIS) Cancer Control Modules, we assessed the BCRAT 5-year and lifetime risk of developing invasive breast cancer among US Hispanic women (n=3,386) from six key subgroups. Multivariate linear and logistic regression methods were used to assess the distribution of both the five-year and lifetime absolute breast cancer risk, based on the BCRAT.

Results: Hispanic women had a significantly lower mean BCRAT 5-year risk and lifetime risk compared to non-Hispanic whites ($p<0.001$). Cuban/Cuban-American women had a significantly higher BCRAT 5-year risk ($p<0.05$), while Dominican women had a higher lifetime risk, compared Mexican/Mexican-American women ($p<0.001$). A greater proportion of Central/South American women were at high-risk of breast cancer, BCRAT 5-year risk ≥1.67, compared to Mexican/Mexican-American women ($p<0.001$).

Discussion: Our findings indicate that, based on the BCRAT, Hispanic women have a significantly lower risk of developing invasive breast cancer, compared to non-Hispanic white women, and that differences in breast cancer risk may differ between certain Hispanic subgroups. These findings suggest that the proportion of Hispanic women who may be eligible for, and potentially benefit from, breast cancer risk reduction strategies such as prophylactic tamoxifen and raloxifene ranges from about 1% of Central/South American women to 4% of Puerto Rican women.

INTRODUCTION

Breast cancer is a significant public health threat to Hispanic women in the United States (US), as it represents the most frequently diagnosed cancer and leading cause of cancer-related death in this population (5). Although recent trends show declining incidence of breast cancer among US women, breast cancer incidence has declined at a slower rate for US Hispanic women (2); furthermore, these findings are consistent across stages of diagnosis, as the rate at which large breast cancer tumors are diagnosed among Hispanic women has not significantly declined (25). Despite having a low incidence rate of breast cancer, Hispanic women are more likely to present with advanced breast cancer at diagnosis (3, 4) and are 20% more likely to die from breast cancer compared non-Hispanic white women (6).

Although these data reflect the burden of breast cancer among Hispanic women as a whole, it is also important to understand the diversity of this population and the extent to which the risk of breast cancer varies between Hispanic women of different national origins and backgrounds. US Hispanics women are characterized by differences in genetic ancestry, environmental exposures, behavioral and lifestyle practices, which may lead to differences in the risk of developing breast cancer (2). However, the heterogeneity in breast cancer risk among women in different Hispanic subgroups has not been well-defined.

To address this gap, our objective was to assess the distribution of breast cancer risk among Hispanic women from six subgroups: Mexican/Mexican-American, Puerto Rican, Cuban/Cuban-American, Dominican (Republic), Central/South American, and Other Hispanic. Using data from the 2000 and 2005 National Health Interview Survey (NHIS) Cancer Control Modules, we assessed the 5-year and lifetime risk of developing invasive breast cancer among US Hispanic (n=3,386) and non-Hispanic white (n=16,131) women, based on the National Cancer Institute

(NCI) Breast Cancer Risk Assessment Tool (BCRAT). Evaluating breast cancer risk among different Hispanic subgroups has the potential to improve our understanding of the impact of breast cancer in this diverse population, and to identify those women from specific Hispanic subgroup who could benefit from breast cancer risk reduction strategies.

METHODS

Information about the study design, data source, and study population has been previously described in detail (26). In brief, the NHIS is an annual, cross-sectional household survey that obtains information on the health of the civilian, non-institutionalized population residing in the United States (67). The NHIS is a multistage cluster probability sample survey design, and oversamples both Hispanic and Black persons. Further, the NHIS core questionnaire is comprised of four components: household, family, sample adult, and sample child, with additional supplement questionnaires on specific topics, including: cancer control. The Cancer Control Module (CCM), designed and funded by the National Cancer Institute (NCI), is administered every five years and collects information on diet and nutrition, physical activity, tobacco usage, cancer screening, genetic testing, family history and other risk factors related to cancer. The CCM collects data from one randomly sampled adult 18 years and older, from each sampled family and household.

The 2000 and 2005 NHIS CCM surveys collected data on 32,374 and 31,321 sampled adults, respectively. For this study, we analyzed data on Hispanic (n=3,386**)** and non-Hispanic white females (n=16,131) aged 35-84 years, with no history of breast cancer or mastectomy (unilateral or bilateral), who completed the CCM module.

Key Measures

Absolute risk of developing breast cancer

The NCI BCRAT (17, 21) estimates a woman's absolute risk of developing invasive breast cancer based on age, age at first live birth, age at menarche, number of first-degree relatives with breast cancer, number of breast biopsies, and presence of atypical hyperplasia. Information on atypical hyperplasia was unavailable in the NHIS. When information on a particular risk factor is missing, BCRAT imputes the lowest category of risk. We used the BCRAT to estimate participants' absolute risk of invasive breast cancer over two time periods: i) 5-year risk: from age at interview to the hypothetical age that a woman would attain if she survived 5 years from the date of the interview; and ii) lifetime risk: from age at interview to the hypothetical age that a woman would attain if she survived to age 90 years.

Hispanic origin

The 2000 and 2005 NHIS collected self-reported data on race and Hispanic origin (based on country of origin and ancestry), which we used to categorize women as non-Hispanic white or Hispanic. Hispanic women were further divided into six distinct subgroups: Mexican/Mexican-American, Cuban/Cuban-American, Puerto Rican, Dominican (Republic), Central or South American, Other Latin American/Other Spanish/Multiple Hispanic (referred to as "Other Hispanic").

Explanatory variables

We included several variables in the analyses that previous research indicates may be associated with the risk of developing breast cancer (14, 15, 68-74). Sociodemographic variables included marital status (married/living with intimate partner, other), education (less than high school graduate, high school graduate/GED, more than high school), and federal poverty level (<100%, 100-200%, ≥200%). Two variables were included as proxies for access to

health care: usual source of care (yes, no) and insurance status (private, public, uninsured). We also included information on county of birth (US born, foreign born), years in the US (<5 years, 5-9 years, ≥10 years) and language most often spoken (mostly/only Spanish, Spanish/English about the same, mostly/only English), and body mass index (BMI<25 “normal”, BMI 25-30 “overweight”, BMI>30 “obese”).

Statistical Analyses

Data from the 2000 and 2005 NHIS were be pooled for this analysis. To obtain U.S. population estimates, the observations were weighted by the sample weights for each year, which were summed and divided by two (75). The complex design of the NHIS was accounted for when calculating standard error (SE) and 95% confidence intervals (CIs) (75).

Descriptive statistics were used to assess participants’ baseline BCRAT, sociodemographic, access, acculturation and BMI characteristics. We estimated participants’ BCRAT five-year and lifetime risk estimates, and corresponding 95% CIs (17, 21).

Bivariate linear regression analyses were conducted to compare differences in both five-year and lifetime absolute breast cancer risk between Hispanics and non-Hispanic White women, as well as between Hispanic subgroups. Multivariate linear regression models were then estimated for both the five-year and lifetime absolute breast cancer risk estimates, separately, controlling for the explanatory variables. For each risk estimate, two different comparisons were made: 1) between Hispanic vs. non-Hispanic Whites and 2) among Hispanic subgroups. A three step multiple imputation method was used to impute poverty level, as previously described (76), since about 24% of the observations were missing these values. First, we estimated an ordinal logistic regression model for poverty level using marital status, education and Hispanic subgroup combined with country of birth/time in the US. Second, for each individual with

missing poverty level data, we generated probability cut-points for each category of poverty level, based on regression model coefficients. Third, we drew a random number between zero and one from a uniform distribution and compared it to the probability cut-points in order to assign each individual to one category.

Additionally, a stepwise approach to the multivariate models was employed, using four different models. Model 1 adjusted for marital status, age, education, federal poverty level; Model 2 adjusted for model 1 covariates plus usual source of care and insurance; Model 3 adjusted for model 2 covariates plus BMI; and Model 4 adjusted for model 3 covariates plus country of origin and years in the US. For the acculturation, a composite variable was generated that combined county of birth (US born, foreign born) and years in the US (<5 years, 5-9 years, ≥10 years). Bivariate analyses indicated that language most often spoken was not predictive of breast cancer risk and, accordingly, was dropped from the final regression analyses. All computations were conducted using SAS software version 9.2 (SAS Institute Inc, Cary, North Carolina) and SAS callable SUDAAN version 9.0 (RTI, Research Triangle Park, North Carolina).

RESULTS

Sociodemographic and breast cancer risk factors

Non-Hispanic white women had a significantly higher mean age compared to Hispanic women (54.3 years vs. 50.3 years, respectively, $p<0.001$) (Table 4.1). Overall, a significantly greater proportion of Hispanics were younger at initiation of menarche, younger at first live birth, had no family history of breast cancer, and had never received a breast biopsy compared to non-Hispanic white women. Hispanic women, overall, had a significantly higher proportion with less than a high school education (46.0%) and had a household income that was less than 100% of

the federal poverty level (21.7%) compared to non-Hispanic whites (11.9% and 6.8%, respectively).

Among Hispanic subgroups, Cuban/Cuban-American women had the highest mean age, 56.5 years. A greater proportion of Mexican/Mexican-American (48.3%) and Other Hispanic women (86.5%) were born in the US, while Puerto Rican women had the greatest proportion that spoke only/mostly Spanish (27.4%). Puerto Rican (91.4%) and Other Hispanic (93.8%) women had the greatest proportion with a usual source of care, and Central/South American had the greatest proportion of uninsured women (52.8%). Mexican/Mexican-American (36.4%) and Puerto Ricans (36.7%) had the greatest proportion of obese women among Hispanic subgroups.

Risk of developing breast cancer

Hispanic women had a significantly lower mean BCRAT 5-year risk (0.6%) and lifetime risk (5.9%) compared to non-Hispanic whites (1.2% and 8.6%, respectively, $p<0.001$) (Table 4.2). Among Hispanic women, Cuban/Cuban-American and Other Hispanic women had a significantly higher mean BCRAT 5-year risk compared to Mexican/Mexican-American women ($p<0.001$). Dominican and Central/South American women had a significantly higher mean BCRAT lifetime risk compared to Mexican/Mexican-American women ($p<0.001$).

A significantly lower proportion of Hispanic women, overall, were at high risk of breast cancer, based on both the BCRAT 5-year and lifetime risk estimates, compared to non-Hispanic white women ($p<0.001$) (Table 4.3). Approximately 2.6% of all Hispanic women had BCRAT 5-year risk ≥1.67% and only 0.2% had a lifetime risk ≥20.0%. Central/South American women had a significantly lower proportion of women at high risk of breast cancer (1.0%) compared to Mexican/Mexican-American women (2.7%, $p<0.001$). Among Hispanic subgroups, few women

had a BCRAT lifetime risk ≥20.0%, with only 0.4% of Other Hispanic women and 0.3% of Mexican/Mexican-American women meeting this high-risk threshold.

Multivariate regression analyses

Table 4.4 summarizes the results of the multivariate regression models, indicating that Hispanic women had a significantly lower BCRAT 5-year and lifetime risk of developing breast cancer, compared to non-Hispanic whites, even after controlling for all covariates ($p<0.001$). Specifically, Hispanics' 5-year risk of breast cancer was consistently about 0.4% lower than non-Hispanic white women ($p<0.001$), while the lifetime risk of breast cancer for Hispanics was approximately 2.8% lower than the lifetime risk of non-Hispanic white women ($p<0.001$).

In regard to Hispanics, Cuban/Cuban-American women's 5-year risk of breast cancer was nearly 5% higher than risk for Mexican/Mexican-American women ($p<0.05$). No other differences in 5-year BCRAT risk were observed among Hispanic subgroups, when compared to Mexican/Mexican-American women. In assessing lifetime risk of breast cancer, Dominican women's risk was significantly higher than the risk for Mexican/Mexican-American women, and remained significant after controlling for all covariates ($p<0.001$). There were no other differences observed in lifetime risk when comparing other Hispanic subgroups to Mexican/Mexican-American women.

Comparing all Hispanics to non-Hispanic whites, age, education, poverty level, insurance status and BMI were all significantly associated with women's 5-year risk of breast cancer Table S.4.1). In particular, increased age, having public health insurance and being overweight/obese were all associated with significant increases in 5-year risk. Similar trends were observed for lifetime risk of breast cancer, although increased age was associated with a significantly lower lifetime risk of breast cancer. For comparisons among Hispanic subgroups (Table S.4.2), age,

marital status, education, poverty level, insurance status and years in the US were significantly associated with 5-year risk of breast cancer. Specifically, women of the same Hispanic subgroup who had lived in the US for less than 5 years, had a significantly lower 5-year risk of breast cancer compared to those women born in the US ($p<0.05$), controlling for all other covariates. This association was not observed for lifetime risk of breast cancer.

DISCUSSION

Building on current literature, the present study was a broad assessment of breast cancer risk among different subgroups of Hispanic women. Our findings indicate that, overall, Hispanic women's 5-year and lifetime risk of developing invasive breast cancer, based on the BCRAT, was significantly lower compared to non-Hispanic white women. Among Hispanic subgroups, Cuban/Cuban-American women had a greater BCRAT 5-year risk of developing breast cancer, while Dominican women had a greater BCRAT lifetime risk of breast cancer. Factors including age, education, health insurance, usual source of care, poverty level, and length of residence in the US were associated with differences in breast cancer risk among Hispanic subgroups. Furthermore, the proportion of Hispanic women who may be eligible for breast cancer risk reduction strategies such as prophylactic tamoxifen and raloxifene use, based on the American Society of Clinical Oncology (ASCO) and National Comprehensive Cancer Network (NCCN) guidelines, ranges from about 1% of Central/South American women to 4% of Puerto Rican women.

Consistent with previous findings (77), we found that Hispanic women have a significantly lower 5-year and lifetime risk of developing invasive breast cancer, based on the BCRAT. Further, the magnitude by which Hispanic women's breast cancer risk was lower than non-Hispanic whites remained significant, and relatively constant, even after multivariate adjustment for key risk

factors. These findings suggest other factors, either unidentified and/or unmeasured in this analysis, may help explain the differences observed in BCRAT risk estimates between Hispanic and non-Hispanic white women.

Evidence on the risk of developing breast cancer risk among Hispanics has highlighted differences between US and foreign-born women (14), with results from the San Francisco Bay Area Women's Breast Cancer Study showing that foreign-born Hispanic post-menopausal women had a significantly lower risk of breast cancer compared to their US-born counterparts. Our study expands on this by evaluating differences in risk by Hispanic subgroup, finding that, compared to Mexican/Mexican-American women, Cuban/Cuban-Americans had a significantly higher 5-year risk of breast cancer, whereas Dominicans had a significantly higher lifetime risk of breast cancer. Consequently, while BCRAT risk among other Hispanic subgroups did not differ, the increased risk among Cuban/Cuban-American and Dominican women may reflect other important underlying factors, such as genetic ancestry (78), that accounts for differences in the BCRAT estimates of the risk of developing invasive breast cancer among these Hispanic subgroups.

Our finding of lower breast cancer risk in foreign-born Hispanic women, with less than five years of residence in the US, further strengthens the importance of birthplace, migration and length of residence in the US as factors associated with breast cancer risk among Hispanic women (14, 79). Therefore, migration-related changes experienced by Hispanic women who move to the US, such as those to hormonal and lifestyle factors (i.e. weight gain or changes in diet), may have important ramifications on the risk of developing breast cancer.

Noteworthy, our study is among the first, if not only, to provide an estimate of the proportion and number of women from different Hispanic subgroups who may be eligible for prophylactic

tamoxifen and raloxifene use. Both ASCO and NCCN recommend that patients who meet the high risk threshold of BCRAT 5-year risk ≥1.67%, consider counseling and/or treatment with tamoxifen or raloxifene to reduce the risk of developing invasive breast cancer in the future (27, 28). Thus, as indicated by our findings, up to 2.7% of Mexican-American women (approximately 99,000) or 3.7% of Puerto Rican women (approximately 30,000), among others, may benefit from risk-reduction counseling to consider these options to prevent the onset of breast cancer.

In interpreting the results of this study it is important to acknowledge its strengths and limitations. The NHIS is a large, population-based study, which allowed us to explore US Hispanic women; however, our study was limited by small samples of women from certain Hispanic subgroups. Nevertheless, these findings build upon those studies of breast cancer risk among different subgroups of Hispanic women, adding considerably to the sparse literature documenting the heterogeneity of the Hispanic population. A possible limitation of this study is that the NHIS is a cross-sectional study and, therefore, we are not able to draw any causal inference on the relationship between breast cancer risk and the risk factors included in our analysis. Another limitation is the use of the NCI BCRAT to estimate breast cancer risk, which has been shown to underestimate risk among US Hispanic women (80). Despite such underestimation, our findings represent a conservative estimate of breast cancer risk among Hispanic women and the number of women in each subgroup who could benefit from risk-reduction strategies.

In summary, our findings indicate that, based on the BCRAT, Hispanic women have a significantly lower risk of developing invasive breast cancer, compared to non-Hispanic white women; furthermore, we highlight differences in the BCRAT risk among women in different Hispanic subgroups. While country of origin and length of residence were significantly associated with BCRAT risk estimates in our study sample, it is imperative to further investigate

how Hispanic ancestry and migration impact women's risk of developing breast cancer. Lastly, we provide national estimates of the number of Hispanic women from six key subgroups, who would be eligible for prophylactic breast cancer chemoprevention as recommended by ASCO and NCCN. Future studies are warranted that further investigate the impact of breast cancer among Hispanics of different ancestry, as well as other important breast cancer risk factors, such as history of cancer in second and higher-degree relatives in this population.

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Table 4.1 Distribution of BCRAT risk factors and breast cancer outcomes

Characteristic	Non-Hispanic Whites (n=16,131)	Hispanics Total (n=3,386)	Hispanic Subgroups: Mexican/ Mexican American (n=1,932)	Puerto Rican (n=385)	Cuban/ Cuban American (n=274)	Dominican (Republic) (n=123)	Central/ South American (n=468)	Other Hispanic (n=204)
BCRAT risk factors								
Mean Age, years	54.3	50.3†	49.8*	51.0	56.5	48.0	48.0	52.8
[95% CI}	[54.1, 54.3]	[49.7, 50.9]	[48.9, 50.6]	[49.5, 52.4]	[54.5, 58.4]	[45.7, 50.3]	[46.7, 49.3]	[50.2, 55.5]
Age at menarche, yrs	%	%	%	%	%	%	%	%
< 12	17.7	23.2†	22.0*	29.8	26.8	18.1	24.1	16.9
12-13	55.3	50.0	49.0	53.3	46.5	69.2	44.7	61.5
≥ 14	26.9	26.8	29.0	16.9	26.7	12.75	31.2	21.6
Age at first live birth, yrs								
Nulliparous	16.1	10.8†	8.5*	11.9	22.5	10.9	12.7	9.5
< 20	18.8	29.8	32.1	37.3	17.1	18.5	21.2	33.7
20-24	33.7	33.1	36.1	31.7	24.2	23.8	29.9	31.9
25-29	19.7	17.1	15.8	10.8	25.7	33.8	19.8	14.7
≥ 30	11.6	9.5	7.5	8.2	10.5	13.0	16.4	10.1
No. of 1st degree relatives w/ breast cancer								
0	88.5	93.9†	93.5*	91.7	94.7	91.2	98.1	91.6
≥ 1	11.5	6.1	6.5	8.3	5.3	8.8	1.9	8.4
No. of previous breast biopsies								
0	82.3	90.6†	90.8*	88.5	94.1	94.1	90.3	87.5
≥1	17.72	9.4	9.2	11.5	5.9	5.9	9.7	12.5
Acculturation								
Years in US[a]								
US Born	95.4	37.2†	48.3*	28.8	9.2	2.1	5.3	86.5
<5	0.3	4.1	3.4	3.1	5.2	2.5	8.6	----
5-9	0.4	7.8	6.1	3.1	9.9	14.2	18.3	0.3
≥10	3.9	51.0	42.2	65.0	75.6	81.2	67.7	13.2
Language Spoken								
Only/Mostly Eng.	99.1	49.0†	48.3*	40.7	61.9	78.6	61.5	6.1
Equal Eng./Span.	0.2	28.0	28.1	31.9	21.0	10.5	15.1	73.1
Only/Mostly Span.	0.7	23.0	23.6	27.4	17.1	10.9	23.4	20.8

Table 4.1 continued Distribution of BCRAT risk factors and breast cancer outcomes

Characteristic	Non-Hispanic Whites (n=16,131)	Hispanics Total (n=3,386)	Hispanic Subgroups: Mexican/ Mexican American (n=1,932)	Puerto Rican (n=385)	Cuban/ Cuban American (n=274)	Dominican (Republic) (n=123)	Central/ South American (n=468)	Other Hispanic (n=204)
Sociodemographic								
Marital Status								
Married/Living with Int. Partner	68.8	66.1†	69.1*	55.3	63.4	51.3	68.7	64.9
Education								
<HS Graduate	11.9	46.0†	53.4*	43.0	34.3	57.6	35.5	19.9
HS Graduate/GED	33.7	23.5	23.3	20.2	21.7	18.6	22.7	26.7
>High School	54.4	30.5	23.3	30.9	43.9	23.8	41.7	53.3
Poverty Level								
<100%	6.8	21.7†	24.3*	26.4	13.4	34.8	13.3	14.7
100-199%	15.7	28.2	29.7	26.7	26.6	34.6	27.1	18.7
≥200%	77.4	50.1	46.0	46.9	60.0	30.5	59.7	66.6
Access								
Usual Source of Care								
Yes	93.6	83.6†	80.7*	91.4	87.3	89.7	81.0	93.8
Insurance								
Private	59.1	43.3†	42.4*	40.4	43.4	37.9	46.1	52.8
Public	29.0	27.0	23.8	41.9	37.1	31.1	19.4	30.9
Uninsured	11.9	29.7	33.8	17.7	19.3	31.0	34.5	16.3
Behavioral								
Body Mass Index								
Normal	46.9	32.9†	29.1*	31.9	35.1	39.1	39.6	47.0
Overweight	29.6	34.7	34.5	31.4	43.2	39.6	33.9	31.5
Obese	23.5	32.4	36.4	36.7	21.7	21.2	26.5	21.5

Notes: CI = confidence interval. Dash marks signify too few observations in a given cell to report. [a]Years in US presents the number of years residing in the US, among those participants who are foreign born †p<0.001 comparing All Hispanics to Non-Hispanic Whites; *p<0.001 for trend test comparing Hispanic subgroups.

Table 4.2 Mean BCRAT 5-year and lifetime absolute risk estimates by Hispanic subgroup

	Total no.	BCRAT 5-year risk	BCRAT Lifetime risk
		Mean [95% CI]	Mean [95% CI]
Non-Hispanic white	53,600,388	1.24 [1.23, 1.26]	8.63 [8.56, 8.70]
All Hispanic	6,616,996	0.64 [0.62, 0.66]†	5.88 [5.77, 5.99]†
Hispanic Subgroups			
Mexican/Mexican American	3,682,494	0.62 [0.60, 0.65]	5.83 [5.70, 5.95]
Puerto Rican	795,878	0.67 [0.60, 0.74]	5.82 [5.53, 6.10]
Cuban/Cuban American	523,990	0.83 [0.76, 0.89]*	5.47 [5.14, 5.80]
Dominican	198,432	0.62 [0.54, 0.70]	6.68 [6.17, 7.18]*
Central/South American	1,034,701	0.59 [0.55, 0.62]	6.23 [5.95, 6.51]*
Other Hispanic	381,500	0.70 [0.64, 0.75]*	5.71 [5.15, 6.27]

Notes: CI = confidence interval. Estimates of the total number (Total no.) of women are based on weighted data from the years 2000 and 2005 National Health Interview Survey Cancer Control Modules. †$p<0.001$ comparing All Hispanics to Non-Hispanic Whites; *$p<0.001$ comparing Hispanic subgroups to Mexican/Mexican American women

Table 4.3 Estimates of the total number of women at high risk of breast cancer based on BCRAT 5-year and lifetime absolute risk estimates

	5-year risk ≥ 1.67%		**Lifetime risk ≥ 20.0%**	
	No.	**% (s.e)**	**No.**	**% (s.e)**
		% (s.e.)		% (s.e)
Non-Hispanic white	10479744	19.5 (0.4)	730723	1.4 (0.1)
All Hispanic	171484	2.6 (0.3)†	11425	0.2 (0.1)†
Hispanic Subgroups				
Mexican/Mexican American	99227	2.7 (0.4)	10008	0.3 (0.1)
Puerto Rican	29801	3.7 (1.5)	---	---
Cuban/Cuban American	15874	3.0 (1.0)	---	---
Dominican	6210	3.1 (2.3)	---	---
Central/South American	10426	1.0 (0.3)**	---	---
Other Hispanic	9948	2.6 (1.0)	1417	0.4 (0.4)

Notes. No.=number, SE=standard error. Estimates of the total number of women based on weighted data from the years 2000 and 2005 National Health Interview Survey Cancer Control Modules. Dash marks signify too few observations in a given cell to report †p<0.001 comparing All Hispanics to Non-Hispanic Whites; *p<0.05 comparing Hispanic subgroups to Mexican/Mexican American women; **p<0.001 comparing Hispanic subgroups to Mexican/Mexican American women.

Table 4.4 Results of multivariate regression analyses of BCRAT 5-year and lifetime risk of breast cancer by Hispanic subgroup

	BCRAT 5-year risk			
	Model 1 β (s.e.)	**Model 2 β (s.e.)**	**Model 3 β (s.e.)**	**Model 4 β (s.e.)**
Non-Hispanic white	Ref.	Ref.	Ref.	Ref.
All Hispanic	-0.41 (0.01)‡	-0.41 (0.01)‡	-0.41 (0.01)‡	-0.42 (0.02)‡
Mexican/Mexican American	Ref.	Ref.	Ref.	Ref.
Puerto Rican	0.02 (0.03)	0.01 (0.03)	0.00 (0.03)	0.01 (0.03)
Cuban/Cuban American	0.05 (0.03)†	0.05 (0.03)†	0.04 (0.03)	0.05 (0.03)†
Dominican	0.02 (0.03)	0.01 (0.03)	0.02 (0.03)	0.03 (0.03)
Central/South American	-0.02 (0.02)	-0.01 (0.02)	-0.01 (0.02)	0.01 (0.02)
Other Hispanic	-0.00 (0.03)	-0.01 (0.03)	-0.01 (0.03)	-0.01 (0.03)

	BCRAT Lifetime risk			
	Model 1 β (s.e.)	**Model 2 β (s.e.)**	**Model 3 β (s.e.)**	**Model 4 β (s.e.)**
Non-Hispanic white	Ref.	Ref.	Ref.	Ref.
All Hispanic	-2.86 (0.07)‡	-2.81 (0.07)‡	-2.79 (0.07)‡	-2.77 (0.08)‡
Mexican/Mexican American	Ref.	Ref.	Ref.	Ref.
Puerto Rican	0.02 (0.14)	-0.00 (0.14)	-0.06 (0.14)	0.00 (0.14)
Cuban/Cuban American	0.18 (0.17)	0.16 (0.18)	0.11 (0.18)	0.15 (0.18)
Dominican	0.73 (0.21)‡	0.75 (0.23)†	0.82 (0.25)‡	0.85 (0.26)‡
Central/South American	0.04 (0.11)	0.05 (0.12)	0.07 (0.12)	0.12 (0.12)
Other Hispanic	-0.19 (0.21)	-0.20 (0.21)	-0.23 (0.22)	-0.23 (0.22)

Notes: β=beta estimate; SE=standard error; Ref=referent category. Estimates presented were obtained by multivariate linear regression analyses, Model 1 – adjusted for age, marital status, education, federal poverty level; Model 2 – adjusted for model 1 covariates + usual source of care, insurance; Model 3 – adjusted for model 2 covariates + BMI; and Model 4 – adjusted for model 3 covariates + US born (US vs. Foreign born), Years in US (US born, ≤5 years, >5 years).

Table S.4.1 Results of multivariate regression analyses of BCRAT 5-year risk of breast cancer among Hispanic and non-Hispanic white women

	BCRAT 5-year risk			
	Model 1 β **(s.e.)**	**Model 2** β **(s.e.)**	**Model 3** β **(s.e.)**	**Model 4** β **(s.e.)**
Non-Hispanic white	Ref.	Ref.	Ref.	Ref.
All Hispanic	-0.41 (0.01)‡	-0.41 (0.01)‡	-0.41 (0.01)‡	-0.42 (0.02)‡
Sociodemographic				
Age, years				
35-49	Ref.	Ref.	Ref.	Ref.
50-64	0.65 (0.01)‡	0.65 (0.01)‡	0.65 (0.01)‡	0.65 (0.01)‡
≥65	1.14 (0.02)‡	1.09 (0.02)‡	1.11 (0.02)‡	1.11 (0.02)‡
Marital Status				
Married/Living with Int. Partner	Ref.	Ref.	Ref.	Ref.
Not married/Living with Int. Partner	-0.01 (0.01)	-0.01 (0.01)	0.01 (0.01)	0.01 (0.01)
Education				
>High School	Ref.	Ref.	Ref.	Ref.
HS Graduate/GED	-0.06 (0.01)‡	-0.06 (0.01)‡	-0.07 (0.01)‡	-0.07 (0.01)‡
<HS Graduate	-0.14 (0.02)‡	-0.14 (0.02)‡	-0.16 (0.02)‡	-0.16 (0.02)‡
Poverty Level				
≥200%	Ref.	Ref.	Ref.	Ref.
100-199%	-0.04 (0.01)‡	-0.04 (0.02)†	-0.04 (0.02)†	-0.04 (0.02)†
<100%	-0.07 (0.02)‡	-0.08 (0.02)‡	-0.08 (0.02)‡	-0.08 (0.02)‡
Access				
Usual Source of Care				
Yes	-----	Ref.	Ref.	Ref.
No		-0.06 (0.01)‡	-0.05 (0.01)‡	-0.05 (0.02)‡
Insurance				
Uninsured	-----	Ref.	Ref.	Ref.
Public		0.07 (0.02)‡	0.07 (0.02)‡	0.07 (0.02)‡
Private		0.01 (0.01)	0.01 (0.01)	0.01 (0.01)
Behavioral				
Body Mass Index				
Normal	-----	-----.	Ref.	Ref.
Overweight/Obese			0.03 (0.01)†	0.03 (0.01)†
Years in US				
US Born	-----	-----	-----	Ref.
Foreign Born				
<5 years				-0.06 (0.04)
5-9 years				-0.00 (0.03)
≥10 years				0.01 (0.02)

Notes: β=beta estimate; SE=standard error; Ref=referent category. Estimates presented were obtained by multivariate linear regression analyses, Model 1 – adjusted for age, marital status, education, federal poverty level; Model 2 – adjusted for model 1 covariates + usual source of care, insurance; Model 3 – adjusted for model 2 covariates + BMI; and Model 4 – adjusted for model 3 covariates + US born (US vs. Foreign born), Years in US (US born, ≤5 years, >5 years).

Table S.4.1 continued Results of multivariate regression analyses of BCRAT lifetime risk of breast cancer among Hispanic and non-Hispanic white women

		BCRAT lifetime risk			
		Model 1 β (s.e.)	**Model 2 β (s.e.)**	**Model 3 β (s.e.)**	**Model 4 β (s.e.)**
Non-Hispanic white		Ref.	Ref.	Ref.	Ref.
All Hispanic		-2.86 (0.07)‡	-2.81 (0.07)‡	-2.79 (0.07)‡	-2.77 (0.08)‡
Sociodemographic					
Age, years	35-49	Ref.	Ref.	Ref.	Ref.
	50-64	-1.69 (0.07)‡	-1.69 (0.07)‡	-1.67 (0.08)‡	-1.69 (0.08)‡
	≥65	-5.41 (0.07)‡	-5.42 (0.10)‡	-5.40 (0.10)‡	-5.41 (0.10)‡
Marital Status					
Married/Living with Int. Partner		Ref.	Ref.	Ref.	Ref.
Not married/Living with Int. Partner		-0.25 (0.06)†	-0.25 (0.06)‡	-0.26 (0.06)‡	-0.26 (0.06)‡
Education					
>High School		Ref.	Ref.	Ref.	Ref.
HS Graduate/GED		0.90 (0.07)‡	-0.90 (0.07)‡	-0.93 (0.07)‡	-0.94 (0.07)‡
<HS Graduate		-1.23 (0.09)‡	-1.22 (0.09)‡	-1.29 (0.08)‡	-1.30 (0.09)‡
Poverty Level					
≥200%		Ref.	Ref.	Ref.	Ref.
100-199%		-0.35 (0.08)‡	-0.31(0.08)‡	-0.28 (0.08)‡	-0.27 (0.08)†
<100%		-0.42 (0.08)‡	-0.37 (0.09)‡	-0.34 (0.09)‡	-0.33 (0.09)‡
Access					
Usual Source of Care					
Yes		-----	Ref.	Ref.	Ref.
No			-0.16 (0.10)	-0.16 (0.10)	-0.15 (0.10)
Insurance					
Uninsured		-----	Ref.	Ref.	Ref.
Public			0.17 (0.12)	0.17 (0.12)	0.17 (0.12)
Private			0.22 (0.08)†	0.24 (0.09)†	0.24 (0.09)†
Behavioral					
Body Mass Index					
Normal		-----	-----.	Ref.	Ref.
Overweight/Obese				0.02 (0.06)	0.02 (0.06)
Years in US					
US Born		-----	-----	-----	Ref.
Foreign Born	<5 years				-0.40 (0.22)
	5-9 years				-0.12 (0.17)
	≥10 years				-0.03 (0.09)

Notes: β=beta estimate; SE=standard error; Ref=referent category. Estimates presented were obtained by multivariate linear regression analyses, Model 1 – adjusted for age, marital status, education, federal poverty level; Model 2 – adjusted for model 1 covariates + usual source of care, insurance; Model 3 – adjusted for model 2 covariates + BMI; and Model 4 – adjusted for model 3 covariates + US born (US vs. Foreign born), Years in US (US born, ≤5 years, >5 years).

Table S.4.2 Results of multivariate regression analyses of BCRAT lifetime risk of breast cancer by Hispanic subgroup

		BCRAT lifetime risk			
		Model 1 β **(s.e.)**	**Model 2** β **(s.e.)**	**Model 3** β **(s.e.)**	**Model 4** β **(s.e.)**
Mexican/Mexican American		Ref.	Ref.	Ref.	Ref.
Puerto Rican		0.02 (0.03)	0.01 (0.03)	0.00 (0.03)	0.01 (0.03)
Cuban/Cuban American		0.05 (0.03)†	0.05 (0.03)†	0.04 (0.03)	0.05 (0.03)†
Dominican		0.02 (0.03)	0.01 (0.03)	0.02 (0.03)	0.03 (0.03)
Central/South American		-0.02 (0.02)	-0.01 (0.02)	-0.01 (0.02)	0.01 (0.02)
Other Hispanic		-0.00 (0.03)	-0.01 (0.03)	-0.01 (0.03)	-0.01 (0.03)
Sociodemographic					
Age, years	35-49	Ref.	Ref.	Ref.	Ref.
	50-64	0.42 (0.02)‡	0.42 (0.02)‡	0.42 (0.02)‡	0.42 (0.02)‡
	≥65	0.66 (0.03)‡	0.62 (0.03)‡	0.63 (0.03)‡	0.62 (0.03)‡
Marital Status					
Married/Living with Int. Partner		Ref.	Ref.	Ref.	Ref.
Not married/Living with Int. Partner		0.04 (0.02)†	0.04 (0.02)†	0.04 (0.02)†	0.04 (0.02)†
Education					
>High School		Ref.	Ref.	Ref.	Ref.
HS Graduate/GED		-0.04 (0.02)†	-0.04 (0.02)†	-0.04 (0.02)†	-0.05 (0.02)†
<HS Graduate		-0.06 (0.02)‡	-0.06 (0.02)‡	-0.06 (0.02)‡	-0.06 (0.02)†
Poverty Level					
≥200%		Ref.	Ref.	Ref.	Ref.
100-199%		-0.04 (0.02)†	-0.03 (0.02)†	-0.04 (0.02)†	-0.03 (0.02)
<100%		-0.06 (0.02)†	-0.06 (0.02)†	-0.07 (0.02)†	-0.06 (0.02)†
Access					
Usual Source of Care					
Yes		-----	Ref.	Ref.	Ref.
No			-0.01 (0.02)	-0.01 (0.02)	-0.01 (0.02)
Insurance					
Uninsured		-----	Ref.	Ref.	Ref.
Public			0.07 (0.02)†	0.07 (0.02)†	0.07 (0.02)†
Private			0.03 (0.02)	0.02 (0.02)	0.02 (0.02)
Behavioral					
Body Mass Index					
Normal		-----	-----	Ref.	Ref.
Overweight/Obese				0.01 (0.02)	0.02 (0.01)
Years in US					
US Born		-----	-----	-----	Ref.
Foreign Born	<5 years				-0.06 (0.02)†
	5-9 years				-0.04 (0.03)
	≥10 years				-0.00 (0.02)

Notes: β=beta estimate; SE=standard error; Ref=referent category. Estimates presented were obtained by multivariate linear regression analyses, Model 1 – adjusted for age, marital status, education, federal poverty level; Model 2 – adjusted for model 1 covariates + usual source of care, insurance; Model 3 – adjusted for model 2 covariates + BMI; and Model 4 – adjusted for model 3 covariates + US born (US vs. Foreign born), Years in US (US born, ≤5 years, >5 years).

Table S.4.2 continued Results of multivariate regression analyses of BCRAT lifetime risk of breast cancer by Hispanic subgroup

	BCRAT lifetime risk			
	Model 1 β (s.e.)	**Model 2** β (s.e.)	**Model 3** β (s.e.)	**Model 4** β (s.e.)
Mexican/Mexican American	Ref.	Ref.	Ref.	Ref.
Puerto Rican	0.02 (0.14)	-0.00 (0.14)	-0.06 (0.14)	-0.00 (0.14)
Cuban/Cuban American	0.18 (0.17)	0.16 (0.18)	0.11 (0.18)	0.15 (0.18)
Dominican	0.73 (0.21)‡	0.75 (0.23)†	0.82 (0.25)†	0.85 (0.26)‡
Central/South American	0.04 (0.11)	0.05 (0.12)	0.07 (0.12)	0.12 (0.12)
Other Hispanic	-0.19 (0.21)	-0.20 (0.21)	-0.23 (0.22)	-0.23 (0.22)
Sociodemographic				
Age, years 35-49	Ref.	Ref.	Ref.	Ref.
50-64	-1.07 (0.10)‡	-1.08 (0.11)‡	-1.09 (0.11)‡	-1.13 (0.10)‡
≥65	-3.56 (0.12)‡	-3.62 (0.15)‡	-3.64 (0.15)‡	-3.70 (0.15)‡
Marital Status				
Married/Living with Int. Partner	Ref.	Ref.	Ref.	Ref.
Not married/Living with Int. Partner	-0.04 (0.09)	-0.04 (0.09)	-0.05 (0.09)	-0.03 (0.09)
Education				
>High School	Ref.	Ref.	Ref.	Ref.
HS Graduate/GED	-0.92 (0.11)‡	-0.64 (0.12)‡	-0.63 (0.13)‡	-0.68 (0.13)‡
<HS Graduate	-0.64 (0.12)‡	-0.92 (0.11)‡	-0.94 (0.12)‡	-0.93 (0.12)‡
Poverty Level				
≥200%	Ref.	Ref.	Ref.	Ref.
100-199%	-0.29 (0.10)†	-0.25 (0.11)†	-0.26 (0.12)†	0.23 (0.12)†
<100%	-0.44 (0.10)‡	-0.38 (0.11)‡	-0.41 (0.11)‡	-0.40 (0.11)‡
Access				
Usual Source of Care				
Yes	-----	Ref.	Ref.	Ref.
No		0.01 (0.12)	0.03 (0.13)	0.03 (0.13)
Insurance				
Uninsured	-----	Ref.	Ref.	Ref.
Public		0.21 (0.12)	0.26 (0.12)†	0.29 (0.11)†
Private		0.23 (0.12)	0.22 (0.12)	0.28 (0.13)†
Behavioral				
Body Mass Index				
Normal	-----	-----	Ref.	Ref.
Overweight/Obese			0.04 (0.10)	0.09 (0.09)
Years in US				
US Born	-----	-----	-----	Ref.
Foreign Born <5 years				-0.14 (0.19)
5-9 years				0.05 (0.18)
≥10 years				-0.07 (0.10)

Notes: β=beta estimate; SE=standard error; Ref=referent category. Estimates presented were obtained by multivariate linear regression analyses, Model 1 – adjusted for age, marital status, education, federal poverty level; Model 2 – adjusted for model 1 covariates + usual source of care, insurance; Model 3 – adjusted for model 2 covariates + BMI; and Model 4 – adjusted for model 3 covariates + US born (US vs. Foreign born), Years in US (US born, ≤5 years, >5 years).

DISCUSSION

The surge in research and use of models to project personalized risk of breast cancer underscores the potential value of these tools for predicting breast cancer risk and potentially preventing onset of the disease (81). The Quality in the Continuum of Cancer Care outlines the importance of risk prediction as the first type of care across the spectrum of cancer care from prevention to end-of-life. Further, evidence on the efficacy of risk identification and primary prevention abounds (82), suggesting risk prediction can be used to apply effective and efficient prevention strategies. In accordance, BCRAT estimates have been used in several facets of public heath and health care, such as determining eligibility for prophylactic chemoprevention and counseling women in regard to breast cancer decisions (27, 38, 81).

However, the applicability and utility of breast cancer risk assessment tools are predicated on models that are well calibrated for different populations. Until now, there was great uncertainty about the performance of the BCRAT for Hispanic women (21, 24). Our validation of the BCRAT for US Hispanic women addresses this significant gap in the literature. Although the BCRAT was found to underestimate invasive breast cancer risk by 18% for Hispanic women in the WHI, we attribute the underestimation to secular changes in breast cancer incidence rates and highlight differences in the relative risk estimates for factors currently used in the BCRAT. These findings suggest the BCRAT may be improved for use in Hispanic women and call for a breast cancer risk prediction model based on risk factors specfic to Hispanic women.

Improving the performance of the BCRAT for Hispanic women, or adapting it for Hispanic women as has been done for African-American and Asian-American women, will greatly enhance the value of the tool in its different applications. Use of the BCRAT for determining participant eligibility in the STAR trials (54, 83), prior to knowledge on the performance of the

BCRAT for Hispanics and other racial/ethnic minority women, led to ineligibility and low participation in these early chemoprevention studies by these populations (7, 84). Freedman et al. found that the number of Hispanic women who would benefit from chemoprevention use could not be calculated, because only 2% of STAR participants were Hispanic women; additionally, these researchers pointed out that more accurate data on the precision of breast cancer risk prediction models for various racial/ethnic minority populations, including Hispanics, was necessary (85).

Accordingly, the results of our work contribute valuable information to this issue. Considering the BCRAT underestimates risk for Hispanic women, our findings present a conservative estimate of the number of Hispanic women, overall and by subgroup, that may be eligible for and potentially benefit from prophylactic tamoxifen and raloxifene. Specifically, we indicate that approximately 2.6% of all US Hispanic women, ranging from about 1% of Central/South American women to 3.7% of Puerto Rican women, meet the high risk threshold for breast cancer (BCRAT 5-year risk ≥1.67%) currently used to assess tamoxifen and raloxifene use eligibility. Thus, these estimates may help to identify the potential need for these breast cancer chemopreventive agents among Hispanic women and highlight the differences in potential need that may be present between women of different Hispanic subgroups.

Importantly though, identifying women who may be eligible for breast cancer chemoprevention is only the first step. Since, to achieve the intended benefits of chemoprevention, women will need to make well-informed decisions and decide to uptake the treatment. Our results from the Guide to Decide study illustrate how personalized decision aids can be used to facilitate such informed medical decisions, by communicating information about a woman's individualized risk of breast cancer and the risks and benefits of the prophylactic tamoxifen and raloxifene. Through engaging women at high risk for breast cancer in their own decision to embark in such

risk reduction strategies, we may increase the potential for both good care and positive outcomes, which depend upon the decisions of patients and health care professionals during the multiple process of care (32). However, to be maximally effective among Hispanic populations, future decision aids may need to be culturally tailored to these groups and rely on BCRAT rates that are also tailored to Hispanic women.

Overall, the use of breast cancer risk prediction models in research and health care has great potential, as strategies and interventions that incorporate personalized estimates of breast cancer risk may lead to improved quality of care and positive cancer outcomes. While much work is still needed to develop a tool that is well calibrated for estimating breast cancer risk in Hispanic women, the findings from our work lay the foundation on which a Hispanic-specific model can be created. Moreover, we indicate how the current BCRAT can be used to assess invasive breast cancer risk in Hispanic women and how decision aids may guide decisions on breast cancer primary prevention. Ultimately, we hope that this information will contribute to future efforts to reduce the burden of breast cancer in Hispanics and other women alike.

FUTURE DIRECTIONS

The work presented in this dissertation has provided the impetus for future research work. Currently, a group of investigators, including the primary author, has already begun working to develop a comprehensive breast cancer risk prediction model that will be based on breast cancer risk factors distinct to Hispanics and which will be well calibrated to project individualized estimates of breast cancer risk in Hispanic women. Additional research is ongoing to further uncover the diversity of breast cancer risk and risk factors across different Hispanic subgroups; this work will help us understand the impact of breast cancer under the large umbrella of Hispanics. Finally, as noted above, there is a need to develop culturally-relevant decision aids

that empower Hispanics to engage in and make well-informed decisions about their breast cancer care. These efforts will benefit from our ongoing and future work to better understand breast cancer risk among Hispanic women.

CONCLUSION

The findings from this body of work have important implications for the use of personalized estimates of breast cancer risk in research, clinical practice and public health. First, the current NCI BCRAT, the most widely used breast cancer risk prediction model, underestimates risk of developing invasive breast cancer in US Hispanic women. Second, personalized decision aids may be effective tools to provide useful information about a woman's individual risk of developing breast cancer, as well as to facilitate informed medical decisions, reduce patients' decisional conflict, and empower patients to choose a treatment strategy that best reflects their own values. Third, the risk of developing invasive breast cancer, based on the BCRAT, among Hispanic women is significantly lower compared to non-Hispanic white women, though, importantly, BCRAT risk may also differ between certain Hispanic subgroups. Together, these results improve our understanding of the prediction and distribution of breast cancer risk among US Hispanic women, and help identify ways in which breast cancer risk can be communicated to help inform women about specific breast cancer prevention options.

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