

Background

Results

- The National Cancer Institute's (NCI) Breast Cancer Risk Assessment Tool (BCRAT), also known as the "Gail model", predicts a woman's risk of developing invasive breast cancer over time
- While BCRAT risk projections have been extensively validated for White women, little is known about the performance of the BCRAT for U.S. Hispanic women
- Well-calibrated projections of risk may be used in clinical decisions, educating women about breast cancer treatment and prevention, and determining eligibility for clinical trials
- Understanding the performance of the BCRAT for U.S. Hispanics will allow for accurate assessment of breast cancer risk among Hispanic women and the ability to identify those women at high risk of developing breast cancer

Objective

Assess the relative risk feature, calibration, and discriminatory accuracy of the NCI BCRAT and an updated version of the BCRAT in 6,248 Hispanic and 127,426 Non-Hispanic White (NHW) postmenopausal Women's Health Initiative (WHI) participants aged 50 years and older.

Methods

Study population

- We used data on 6,353 Hispanic and 128,976 NHW women who entered the WHI Main Study, including 96,026 participants who enrolled in the Extension Study

Eligibility criteria

- Women 50-79 years of age
- Postmenopausal
- Entered the WHI study without a history of breast cancer or mastectomy (bilateral or unilateral) at baseline

Breast Cancer Risk Assessment Tool (BCRAT)

- The BCRAT 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
 - number of breast biopsies – presence of atypical hyperplasia
- Effect of number of biopsies modified by age (<50 or ≥50 years)
- Presence of atypical hyperplasia unavailable in WHI
- White women: BCRAT calibrated to 1983-1987 SEER rates
- Hispanic women: BCRAT combines relative risk and attributable risk estimates from White women with 1990-1996 SEER Hispanic rates
- The Updated BCRAT is calibrated to 1993-2007 SEER breast cancer rates and competing mortality rates, separately for NHW and Hispanic women

Statistical Analysis

Relative Risk Feature

- BCRAT relative risks estimates compared to those estimated from Cox proportional hazards models for NHWs and Hispanics separately

Calibration

- For BCRAT and Updated BCRAT, absolute risk of developing invasive breast cancer computed over two time periods:
 - from age at enrollment to the hypothetical age at end of the main study
 - from age at the beginning of the extension study to the hypothetical age at August 15, 2009
- Absolute risks summed over all women in each risk factor category and overall, to calculate the expected count (E)
- Expected count (E_e) compared to observed number of invasive breast cancers (O_e)
- For each category, an observed/expected (O/E) ratio and 95% confidence interval (CI) calculated

Discriminatory Accuracy

- Calculated the concordance statistic, or area-under-the-curve (AUC) statistic, for NHWs and Hispanics separately

Table 1. Distribution of BCRAT risk factors and breast cancer outcomes

Characteristic	Hispanic (n=6,353)		Non-Hispanic White (n=128,976)		p
	Mean [95% CI]	%	Mean [95% CI]	%	
BCRAT risk factors	60.20 [60.04, 60.37]		63.51 [63.47, 63.55]		<.001
Age at baseline, years					
Age at menarche, years					
< 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 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	

Breast Cancer Outcomes and Follow-up Time

	Hispanic	Non-Hispanic White	p
Invasive breast cancers	157	6,084	
Age at diagnosis, years	64.8 [63.7, 65.9]	69.4 [69.2, 69.6]	<.001
Follow-up time, years	9.54 [9.46, 9.62]	10.93 [10.91, 10.94]	<.001

Note: CI = confidence interval; OS = observational study; HT = hormone therapy; True 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.

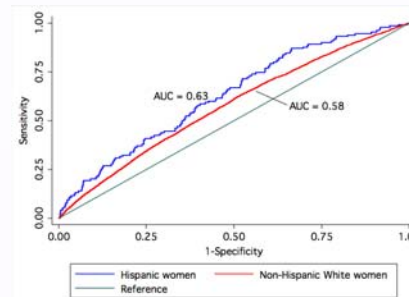


Figure 1. Area Under the Receiver Operating Characteristic (ROC) Curve

Table 2. Comparison of RR Estimates from the BCRAT and the WHI*

BCRAT Risk Category	BCRAT RR	WHI Hispanic		WHI non-Hispanic White	
		RR	95% CI	RR	95% CI
Age at menarche	1.10	1.08 [0.85, 1.37]	0.90	1.07 [1.03, 1.11]	0.23
Number of breast biopsies	1.27	1.71 [1.31, 2.24]	0.03	1.27 [1.22, 1.33]	0.99
Age at first live birth (AFB)	1.24	0.97 [0.78, 1.20]	0.02	1.13 [1.09, 1.18]	<.0001
Number of first-degree relatives with breast cancer (FDR)	2.61	2.16 [1.13, 4.13]	0.57	1.31 [1.15, 1.49]	<.001
AFB*FDR interaction	0.83	0.84 [0.55, 1.29]	0.92	1.01 [0.94, 1.09]	<.0001

* Parameter estimates are Relative Risks (RRs), based on follow-up through the end of WHI Main study only; † Test of difference between WHI Hispanic parameter estimates and the fixed parameter values in the BCRAT; ‡ Test of difference between WHI non-Hispanic White parameter estimates and the fixed parameter values in the BCRAT.

Table 3. BCRAT and Updated BCRAT Observed/Expected Ratios*

Hispanics	Observed cancers	BCRAT		Updated BCRAT*	
		Expected cancers†	O/E ratio	Expected cancers†	O/E ratio
Main Study (n = 6,353)	130	110	1.18 [0.99, 1.40]	120	1.08 [0.91, 1.28]
Extension Study (n = 3,253)	27	34	0.79 [0.54, 1.15]	37	0.73 [0.50, 1.06]

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]
Extension Study (n = 92,773)	1,371	1,657	0.83 [0.78, 0.87]	1,941	0.71 [0.67, 0.74]

*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.

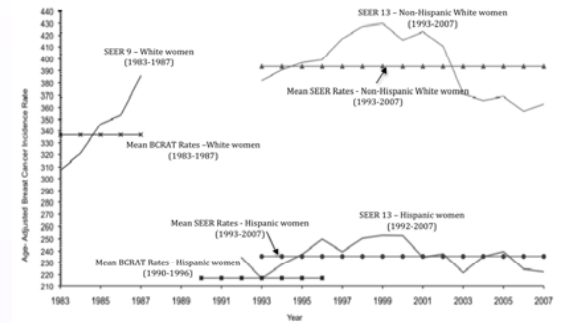


Figure 2. Age-adjusted SEER Invasive Breast Cancer Incidence Rates over the BCRAT and WHI time periods. Solid lines: SEER invasive breast cancer incidence rates used for BCRAT (White women – 1983 to 1987 and Hispanic women – 1990 to 1996), Updated BCRAT (1993-2007). Dotted lines: mean incidence rates over the time periods used in models

Discussion

- This is among the first, if not only, studies evaluating BCRAT performance, the most widely used breast cancer risk prediction model, for U.S. Hispanics
- WHI main study period, BCRAT underestimated invasive breast cancers in Hispanic and NHW women; underestimation corrected with Updated BCRAT
 - More frequent recalibration of models like BCRAT to SEER rates can improve performance
- BCRAT overestimated invasive breast cancers in the extension study
 - Overestimation may be due to trends in breast cancer incidence from 1993-2007 and lower screening frequency
- Relative risks for Hispanics in WHI agreed well with BCRAT, though RRs for number of biopsies and age at first live birth were significantly different
- Effect of positive family history among NHWs in WHI was smaller than in BCRAT, as seen in other cohorts
- Discriminatory accuracy of BCRAT for Hispanic women is modest and slightly better than for NHWs; differences may reflect lack of strong common risk factors in BCRAT
- Ultimately, a more comprehensive model based on sufficient data from U.S. Hispanic women is necessary to account for breast cancer risk factors distinct to this population