Prospective Approach to Breast Cancer Risk Prediction in African American Women: The Black Women's Health Study Model

Deborah A. Boggs, Lynn Rosenberg, Lucile L. Adams-Campbell, and Julie R. Palmer

ABSTRACT

Purpose

Breast cancer risk prediction models have underestimated risk for African American women, contributing to lower recruitment rates in prevention trials. A model previously developed for African American women was found to underestimate risk in the Black Women's Health Study (BWHS).

Methods

We developed a breast cancer risk model for African American women using relative risks derived from 10 years of follow-up of BWHS participants age 30 to 69 years at baseline. Using the subsequent 5 years of follow-up data, we evaluated calibration as the ratio of expected to observed number of breast cancers and assessed discriminatory accuracy using the concordance statistic.

Results

The BWHS model included family history, previous biopsy, body mass index at age 18 years, age at menarche, age at first birth, oral contraceptive use, bilateral oophorectomy, estrogen plus progestin use, and height. There was good agreement between predicted and observed number of breast cancers overall (expected-to-observed ratio, 0.96; 95% CI, 0.88 to 1.05) and in most risk factor categories. Discriminatory accuracy was higher for women younger than age 50 years (area under the curve [AUC], 0.62; 95% CI, 0.58 to 0.65) than for women age $\geq$ 50 years (AUC, 0.56; 95% CI, 0.53 to 0.59). Using a 5-year predicted risk of 1.66% or greater as a cut point, 2.8% of women younger than 50 years old and 32.2% of women $\geq$ 50 years old were classified as being at elevated risk of invasive breast cancer.

Conclusion

The BWHS model was well calibrated overall, and the predictive ability was best for younger women. The proportion of women predicted to meet the 1.66% cut point commonly used to determine eligibility for breast cancer prevention trials was greatly increased relative to previous models.

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INTRODUCTION

African American women are more likely than white women to develop breast cancer before age 40 years,¹ to be diagnosed with estrogen receptor (ER)–negative tumors,² and to have higher 5-year breast cancer mortality rates.³ The effectiveness of breast cancer prevention and early detection strategies depends in part on the ability to accurately identify individuals at increased risk of breast cancer. Models for predicting the absolute risk of breast cancer have been used for chemoprevention decision making and for determining eligibility for recruitment into prevention trials.

The Breast Cancer Risk Assessment Tool, commonly known as the Gail model,⁴ was validated in

white women.^{5,6} However, it was found to underestimate risk in African American women and was modified based on data from African American women in the Women's Contraceptive and Reproductive Experiences (CARE) study.⁷ The CARE model, which uses information on age, age at menarche, family history of breast cancer, and number of breast biopsies, was well calibrated among African American women age 50 to 79 years in the Women's Health Initiative⁷ but underestimated risk among women age 30 to 69 years in the Black Women's Health Study (BWHS), particularly among women with a later age at first birth.⁸ Discriminatory accuracy of the CARE model was limited in both studies.^{7,8} Underestimation of risk for African American women has contributed to the under-representation

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of African American women in breast cancer prevention trials. The aim of this study was to develop a breast cancer risk prediction model for African American women using prospective data from the BWHS in follow-up from 1995 to 2005 and to validate the model in subsequent follow-up from 2006 to 2010, overall and by age and ER status.

METHODS

Study Population

The BWHS, an ongoing follow-up study of African American women, was established in 1995 when 59,000 African American women from across the United States enrolled through mailed health questionnaires. Study participants, age 21 to 69 years at baseline, are followed through biennial mailed questionnaires to obtain updated information on exposures and identify incident disease. The follow-up rate of the baseline cohort was 80% through 2011. The present analysis was restricted to 55,879 women who were age 30 to 69 years at baseline or who reached age 30 years during follow-up, had no history of cancer at baseline, and had no missing data on variables in the final model. The Boston University Medical Campus Institutional Review Board approved the protocol.

Exposure Assessment

The baseline questionnaire collected information on age at menarche, height, weight at age 18 years, waist and hip circumference, educational attainment, and family history of breast cancer. Baseline and biennial follow-up questionnaires ascertained information on current weight, parity, age at first birth, duration of breastfeeding, oral contraceptive use, age at menopause, type of menopause, menopausal hormone use, previous diagnosis of benign breast disease and whether it was confirmed by biopsy, smoking history, alcohol intake, and vigorous physical activity. Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters.

Breast Cancer Ascertainment

Incident diagnoses of breast cancer were ascertained through self-report on biennial follow-up questionnaires and, for nonrespondents, through linkage with state cancer registries. Breast cancer deaths were identified through linkage with the National Death Index. We were able to obtain records for 94% of incident breast cancers identified from 1995 to 2010, of which more than 99% were confirmed by medical record or cancer registry data. Only patients with confirmed invasive breast cancer were included in the analysis.

Relative Risk Model

On the basis of follow-up data from 1995 to 2005, we used Cox proportional hazards models, stratified by age in years, to estimate relative risks (RRs) and 95% CIs for risk of invasive breast cancer associated with known and suspected risk factors. Women contributed person-years from baseline in 1995 or age 30 years (if younger than age 30 at baseline) until diagnosis of invasive breast cancer, death, or age 70 years, whichever occurred first. Women diagnosed with ductal carcinoma in situ were censored at diagnosis. Risk factors that changed over time were updated as time-varying variables at the start of each 2-year follow-up cycle.

The final model was selected by backward elimination using the Akaike information criterion and likelihood ratio tests at the significance level of $P < .10$. We also evaluated first-order interactions of all variables included in the final model with each other and with all other variables considered; there were no significant interactions.

We evaluated the following potential predictors, initially coded as follows: age at menarche (< 11 , 11, 12, 13, 14, or ≥ 15 years), BMI at age 18 years (< 20 , 20 to 22, 23 to 24, or ≥ 25 kg/m²), current BMI (< 25 , 25 to 29, 30 to 34, or ≥ 35 kg/m²), waist-to-hip ratio (< 0.74 , 0.74 to 0.78, 0.79 to 0.84, or ≥ 0.85), parity (none or one, two, or $\geq$ three births), age at first birth (< 20 , 20 to 24, 25 to 29, or ≥ 30 years), duration of breastfeeding (< 1 , 1 to 5, or ≥ 6

months), duration of oral contraceptive use (< 1 , 1 to 4, 5 to 9, or ≥ 10 years), recency of oral contraceptive use (never used or ≥ 15 , 10 to 14, 5 to 9, or < 5 years ago), type of menopause (premenopausal, natural menopause, bilateral oophorectomy, or hysterectomy), age at menopause (< 40 , 40 to 44, 45 to 49, or ≥ 50 years), duration of use of estrogen supplements (never used or < 2 , 2 to 3 to 4, or ≥ 5 years), recency of use of estrogen alone (never used or $\geq$ or < 5 years ago), duration of use of estrogen plus progestin supplements (never used or < 2 , 2 to 3 to 4, or ≥ 5 years), recency of use of estrogen plus progestin (never used or $\geq$ or < 5 years ago), history of benign breast disease or breast biopsy (no or yes), family history of breast cancer (none, first-degree relative diagnosed with breast cancer before age 50, first-degree relative diagnosed at age 50 or older, second-degree relative diagnosed before age 50, or second-degree relative diagnosed at age 50 or older), alcohol intake (< 1 , one to three, four to six, or ≥ 7 drinks per week), smoking history (never, former < 15 cigarettes a day, former ≥ 15 cigarettes a day, current < 15 cigarettes a day, or current ≥ 15 cigarettes a day), and vigorous physical activity (< 1 , 1 to 4, or ≥ 5 hours per week). We excluded women with missing values on any variable; the proportion of missing values was less than 1% for most variables.

Absolute Risk

To estimate absolute risk, we used RRs and attributable risks from the BWHS model, age-specific Surveillance, Epidemiology, and End Results breast cancer rates for African American women (1994 to 1998), and age-specific competing mortality rates for African American women (1996 to 2000; rates are listed in [Appendix Table A1](#), online only), using the methods described by Gail et al.⁷ For women at risk of incident breast cancer in 2006, we estimated the 5-year predicted risk from 2006 to 2010. We calculated the expected number of breast cancers by summing the predicted absolute risk for each participant. To assess calibration of the model, we compared the expected with the observed number of breast cancers (E/O ratio). The 95% CIs for the E/O ratio were calculated using the Poisson distribution. An E/O ratio greater than 1.0 indicates that the model overestimates risk of breast cancer, whereas an E/O ratio less than 1.0 indicates underestimation. We compared the expected and observed numbers of breast cancers by age group and other risk factor strata. To evaluate the model across levels of risk, we stratified the data by 5-year age groups and created age-adjusted quintiles of 5-year predicted risk to assess the model as a function of risk factors apart from age.

To assess the discriminatory accuracy of the model, we used the concordance statistic (c-statistic), or area under the receiver operating characteristic curve (AUC), which corresponds to the probability that a randomly selected woman with breast cancer has a higher predicted risk than a randomly selected unaffected woman. Random classification of women with breast cancer and women without breast cancer results in a c-statistic of 0.5, whereas perfect discrimination provides a c-statistic of 1. To assess the discriminatory accuracy for women of a given age, we estimated age-specific c-statistics in 5-year intervals and calculated the weighted average of these estimates with weights equal to the inverse variance of the age-specific estimates. Statistical analyses were performed using SAS version 9.3 (SAS Institute, Cary, NC).

RESULTS

Among 55,093 women age 30 to 69 years observed from 1995 through 2005, 896 incident invasive breast cancers were identified. The median age at diagnosis was 50 years. [Table 1](#) lists the RR estimates for variables included in the final model. The factor associated with the largest RR was a family history of breast cancer in a first-degree relative diagnosed before age 50 years (RR, 2.24; 95% CI, 1.76 to 2.84). A history of benign breast disease or biopsy, lower BMI at age 18 years, earlier age at menarche, later age at first birth, longer duration or more recent use of oral contraceptives, no history of bilateral oophorectomy, longer duration of estrogen plus progestin use, and greater height were also associated with increased risk of breast cancer in the final model.

Table 1. Relative Risk Estimates for Breast Cancer in the Black Women's Health Study, 1995 to 2005

Risk Factor	No. of Breast Cancers	No. of Person-Years	RR*	95% CI
Family history				
None	598	362,263	1.00	Reference
First-degree relative diagnosed at age < 50 years	77	19,288	2.24	1.76 to 2.84
First-degree relative diagnosed at age ≥ 50 years	76	24,421	1.53	1.20 to 1.94
Second-degree relative	145	66,008	1.35	1.12 to 1.62
Benign breast disease/biopsy				
No	598	372,449	1.00	Reference
Yes	298	99,530	1.45	1.25 to 1.67
Body mass index at age 18 years, kg/m ²				
< 20	442	197,739	1.50	1.17 to 1.92
20-24	378	210,802	1.31	1.02 to 1.68
≥ 25	76	63,438	1.00	Reference
Age at menarche, years				
< 12	273	132,548	1.42	1.16 to 1.73
12-13	472	246,749	1.24	1.03 to 1.50
≥ 14	151	92,683	1.00	Reference
Age at first birth, years				
Nulliparous or < 25	635	356,859	1.00	Reference
≥ 25	261	115,120	1.32	1.14 to 1.53
Oral contraceptive use				
< 10 years in duration and ≥ 10 years ago	663	312,506	1.00	Reference
≥ 10 years in duration or < 10 years ago	233	159,474	1.19	1.01 to 1.41
Bilateral oophorectomy				
No	793	422,531	1.46	1.18 to 1.80
Yes	103	49,449	1.00	Reference
Estrogen plus progestin use, years				
< 3	838	459,197	1.00	Reference
≥ 3	58	12,782	1.33	1.01 to 1.76
Height				
< 5 feet, 5 inches	384	213,182	1.00	Reference
≥ 5 feet, 5 inches	512	258,798	1.15	1.01 to 1.32

Abbreviation: RR, relative risk.

*Adjusted for age and all risk factors in the table.

Current BMI, waist-to-hip ratio, parity, breastfeeding, age at menopause, alcohol intake, smoking history, and vigorous physical activity were not associated with risk of invasive breast cancer at the significance level of $P < .10$ and are not included in the prediction model (data not shown). On the basis of RRs from the BWHS model, the estimated attributable risks necessary for calculation of absolute risk were 0.73 for women age 30 to 49 years and 0.70 for women age 50 to 69 years.

During 5 years of follow-up from 2006 through 2010 of 48,193 women who had not developed breast cancer before 2006, 506 invasive breast cancers were identified, with a median age at diagnosis of 54 years. The 48,193 women observed from 2006 to 2010 were older at the beginning of follow-up in 2006 than the 55,093 women for whom follow-up began in 1995 and had a higher prevalence of late age at first birth, long-term use of estrogen plus progestin, and history of benign breast disease, as expected as a result of the age difference (Appendix Table A2, online only). The two groups were similar with regard to the other risk factors included in the prediction model. Data on ER status were available for 469 breast cancers, with 305 (65%) classified as ER positive and 164 (35%) classified as ER negative. The model predicted 485.8 breast cancers overall, yielding an E/O ratio of 0.96 (95% CI, 0.88 to 1.05; Table 2). The model significantly underestimated risk among women without a family history of breast cancer (E/O ratio, 0.90; 95%

CI, 0.81 to 0.99), nulliparous women (E/O ratio, 0.83; 95% CI, 0.70 to 0.99), and women who used oral contraceptives within the previous 10 years (E/O ratio, 0.75; 95% CI, 0.63 to 0.89). There was also a significant underestimation of risk in the second lowest age-adjusted quintile of risk (E/O ratio, 0.75; 95% CI, 0.61 to 0.91). There was good agreement between the predicted and observed number of breast cancers across categories of other risk factors.

We compared the RR estimates derived in the first 10 years of follow-up with estimates based on data from subsequent follow-up (data not shown). RRs for a family history of breast cancer were lower in later follow-up, which could explain the underestimation of risk among women without a family history. Conversely, the RR for long duration or recent use of oral contraceptives was higher in later follow-up, which could explain the underestimation of risk among women with recent use.

The discriminatory accuracy of the model, as measured by age-specific c-statistics, is presented in Table 3. The age-adjusted AUC was 0.59 (95% CI, 0.56 to 0.61) overall and was significantly higher ($P = .03$) for women younger than 50 years old (AUC, 0.62; 95% CI, 0.58 to 0.65) than for women ≥ 50 years old (AUC, 0.56; 95% CI, 0.53 to 0.59). The AUC was higher for ER-negative breast cancer than for ER-positive breast cancer (AUC, 0.62 and 0.58, respectively), but the difference was not statistically significant ($P = .10$).

Breast Cancer Risk Prediction for African American Women

Table 2. Comparison of Number of Breast Cancers Predicted by the Model With the Number Observed in the Black Women's Health Study, 2006 to 2010

Factor	Women		Predicted No. of Breast Cancers	Observed No. of Breast Cancers	E/O Ratio	95% CI
	No.	%				
Overall	48,193		485.8	506	0.96	0.88 to 1.05
Age, years						
30-39	12,341	26	46.2	58	0.80	0.62 to 1.03
40-49	16,572	34	144.4	152	0.95	0.81 to 1.11
50-59	13,546	28	196.0	198	0.99	0.86 to 1.14
60-69	5,734	12	99.2	98	1.01	0.83 to 1.23
Family history of breast cancer						
None	37,274	77	326.4	364	0.90	0.81 to 0.99
First-degree relative age < 50 years	1,848	4	40.0	36	1.11	0.80 to 1.54
First-degree relative age ≥ 50 years	2,271	5	37.8	33	1.14	0.81 to 1.61
Second-degree relative	6,800	14	81.6	73	1.12	0.89 to 1.41
Benign breast disease/biopsy						
No	36,994	77	311.7	345	0.90	0.81 to 1.00
Yes	11,199	23	174.1	161	1.08	0.93 to 1.26
Body mass index at age 18, kg/m ²						
< 20	19,390	40	233.1	226	1.03	0.91 to 1.17
20-24	21,772	45	207.9	227	0.92	0.80 to 1.04
≥ 25	7,031	15	44.8	53	0.85	0.65 to 1.11
Age at menarche, years						
< 12	13,858	29	149.8	160	0.94	0.80 to 1.09
12-13	25,270	52	256.4	276	0.93	0.83 to 1.05
≥ 14	9,065	19	79.5	70	1.14	0.90 to 1.44
Parity, No. of births						
0	13,832	29	105.2	127	0.83	0.70 to 0.99
1-2	24,396	50	266.8	270	0.99	0.88 to 1.11
≥ 3	9,965	21	113.7	109	1.04	0.86 to 1.26
Age at first birth, years*						
< 20	10,361	21	111.2	103	1.08	0.89 to 1.31
20-24	11,089	23	116.6	133	0.88	0.74 to 1.04
≥ 25	12,911	27	152.7	143	1.07	0.91 to 1.26
Lactation*						
Never	18,910	39	215.8	206	1.05	0.91 to 1.20
Ever	15,451	32	164.7	173	0.95	0.82 to 1.10
Duration of oral contraceptive use, years						
< 1	16,480	34	176.9	175	1.01	0.87 to 1.17
1-9	23,368	49	218.5	229	0.95	0.84 to 1.09
≥ 10	8,345	17	90.4	102	0.89	0.73 to 1.08
Recency of oral contraceptive use†						
≥ 10 years ago	18,030	37	213.9	204	1.05	0.91 to 1.20
< 10 years ago	13,683	28	95.0	127	0.75	0.63 to 0.89
Type of menopause						
Premenopausal	27,133	56	190.4	214	0.89	0.78 to 1.02
Natural	8,502	18	141.3	128	1.10	0.93 to 1.31
Bilateral oophorectomy	5,512	11	56.6	68	0.83	0.66 to 1.06
Hysterectomy	7,046	15	97.4	95	1.03	0.84 to 1.25
Estrogen plus progestin use						
Never	44,543	92	421.6	441	0.96	0.87 to 1.05
< 3 years	1,892	4	27.2	33	0.83	0.59 to 1.16
≥ 3 years	1,758	4	36.9	32	1.15	0.82 to 1.63
Height						
< 5 feet, 5 inches	21,441	44	204.1	219	0.93	0.82 to 1.06
≥ 5 feet, 5 inches	26,752	55	281.7	287	0.98	0.87 to 1.10
Current body mass index, kg/m ²						
< 25	11,875	25	114.3	108	1.06	0.88 to 1.28
25-29	15,722	33	171.4	177	0.97	0.84 to 1.12
≥ 30	20,586	43	200.0	221	0.90	0.79 to 1.03

(continued on following page)

Table 2. Comparison of Number of Breast Cancers Predicted by the Model With the Number Observed in the Black Women's Health Study, 2006 to 2010 (continued)

Factor	Women		Predicted No. of Breast Cancers	Observed No. of Breast Cancers	E/O Ratio	95% CI
	No.	%				
Alcohol intake, No. of drinks per week						
< 1	36,283	75	359.0	368	0.98	0.88 to 1.08
1-6	9,302	19	98.1	113	0.87	0.72 to 1.04
≥ 7	2,608	5	28.7	25	1.15	0.77 to 1.70
Smoking status						
Never smoked	31,524	65	291.6	297	0.98	0.88 to 1.10
Past smoker	10,449	22	131.1	143	0.92	0.78 to 1.08
Current smoker	6,220	13	63.0	66	0.95	0.75 to 1.21
Age-adjusted quintile of risk						
1 (low)	9,656	20	53.6	59	0.91	0.70 to 1.17
2	9,591	20	71.7	96	0.75	0.61 to 0.91
3	9,690	20	88.3	94	0.94	0.77 to 1.15
4	9,628	20	108.6	108	1.01	0.83 to 1.21
5 (high)	9,628	20	163.6	149	1.10	0.93 to 1.29

Abbreviation: E/O, expected/observed.

*Parous women.

†Women with ≥ 1 year of oral contraceptive use.

Compared with the lowest age-adjusted quintile of 5-year predicted risk, the RR for the highest quintile of predicted risk was 2.56 (95% CI, 1.89 to 3.46) for breast cancer overall (Table 4). Results were similar for ER-positive and ER-negative breast cancer. The RR for comparison of extreme quintiles was particularly high among younger women (RR, 4.11; 95% CI, 2.42 to 7.00), but there were only 17 breast cancers in the lowest quintile.

Among participants at risk of breast cancer in 2006, mean 5-year risks predicted by the BWHS model were 0.57% (range, 0.07% to 4.60%) for women younger than 50 years old and 1.37% (range, 0.35% to 7.48%) for women ≥ 50 years old; 2.8% of women younger than 50 years old and 32.2% of women ≥ 50 years old had a predicted risk of 1.66% or greater, the cut point typically used for enrollment in prevention trials (Table 5). In contrast, on the basis of the CARE model, mean predicted 5-year risks were 0.50% (range, 0.09% to 2.45%) and 1.16% (range, 0.71% to 3.83%) for younger and older

women, respectively, and only 0.1% of younger women and 7.3% of older women were predicted to have a 5-year risk of at least 1.66%.

DISCUSSION

We developed a risk prediction model for invasive breast cancer for African American women age 30 to 69 years based on 10 years of follow-up in the BWHS. The model includes family history, previous benign breast disease, BMI at age 18 years, age at menarche, age at first birth, oral contraceptive use, bilateral oophorectomy, estrogen plus progestin use, and height. In an internal validation during the subsequent 5 years of follow-up, the model was well calibrated in that it predicted 486 breast cancers in comparison to the 506 breast cancers that occurred (E/O ratio, 0.96). The model fit well in most risk factor strata but underestimated risk among women who had no family history of breast cancer, were nulliparous, had recently used oral

Table 3. Discriminatory Accuracy of the Black Women's Health Study Model, 2006 to 2010

Group	Overall		Estrogen Receptor Positive		Estrogen Receptor Negative	
	Concordance Statistic	95% CI	Concordance Statistic	95% CI	Concordance Statistic	95% CI
Age specific, years						
30-34	0.57	0.41 to 0.73	0.51	0.22 to 0.79	0.66	0.45 to 0.87
35-39	0.60	0.52 to 0.67	0.54	0.44 to 0.64	0.70	0.57 to 0.82
40-44	0.65	0.59 to 0.71	0.63	0.55 to 0.70	0.67	0.56 to 0.78
45-49	0.60	0.53 to 0.66	0.62	0.52 to 0.71	0.59	0.50 to 0.69
50-54	0.56	0.51 to 0.62	0.54	0.47 to 0.62	0.60	0.51 to 0.68
55-59	0.56	0.50 to 0.62	0.54	0.47 to 0.62	0.59	0.46 to 0.72
60-64	0.56	0.49 to 0.64	0.57	0.48 to 0.66	0.57	0.42 to 0.72
65-69	0.56	0.46 to 0.65	0.64	0.53 to 0.75	0.59	0.40 to 0.79
Weighted average						
Age < 50 years	0.62	0.58 to 0.65	0.60	0.55 to 0.65	0.65	0.59 to 0.71
Age ≥ 50 years	0.56	0.53 to 0.59	0.56	0.52 to 0.61	0.59	0.53 to 0.65
Overall	0.59	0.56 to 0.61	0.58	0.55 to 0.61	0.62	0.58 to 0.66

Table 4. RRs Comparing Age-Adjusted Quintiles of Predicted Risk in the Black Women's Health Study, 2006 to 2010

Quintile	Overall			ER-Positive Breast Cancer			ER-Negative Breast Cancer			Age < 50 Years			Age ≥ 50 Years		
	No. of Cancers	RR	95% CI	No. of Cancers	RR	95% CI	No. of Cancers	RR	95% CI	No. of Cancers	RR	95% CI	No. of Cancers	RR	95% CI
1 (low risk)	59	1.00	Reference	34	1.00	Reference	22	1.00	Reference	17	1.00	Reference	42	1.00	Reference
2	96	1.64	1.19 to 2.28	66	1.96	1.30 to 2.97	23	1.06	0.59 to 1.90	40	2.37	1.34 to 4.19	56	1.35	0.90 to 2.02
3	94	1.59	1.15 to 2.21	56	1.65	1.07 to 2.53	30	1.36	0.79 to 2.37	37	2.18	1.23 to 3.88	57	1.35	0.91 to 2.02
4	108	1.84	1.34 to 2.54	62	1.84	1.21 to 2.80	36	1.65	0.97 to 2.81	47	2.79	1.60 to 4.86	61	1.46	0.99 to 2.17
5 (high risk)	149	2.56	1.89 to 3.46	87	2.59	1.74 to 3.86	53	2.44	1.48 to 4.01	69	4.11	2.42 to 7.00	80	1.93	1.32 to 2.81

Abbreviations: ER, estrogen receptor; RR, relative risk.

contraceptives, or had low predicted risk. Previously, we evaluated the CARE model in the BWHS and found that it underestimated risk overall (E/O ratio, 0.88) and particularly among women with an older age at first birth.⁸ The CARE model included only the following three predictors: age at menarche, family history, and an interaction between number of breast biopsies and age.

The discriminatory accuracy for breast cancer overall was previously estimated to be 0.57 based on the CARE model,⁸ compared with 0.59 based on the BWHS model in the current analysis. Previously, discriminatory accuracy of the CARE model was higher for ER-positive breast cancer (AUC, 0.59) than for ER-negative breast cancer (AUC, 0.54).⁸ In contrast, the discrimination of the BWHS model was higher for ER-negative than for ER-positive breast cancer, although the difference was not statistically significant ($P = .10$). Reasons for the apparently greater discriminatory accuracy of the BWHS model for ER-negative breast cancer are unclear. Future work in the BWHS after accrual of more breast cancer diagnoses will include developing breast cancer risk prediction models separately by ER status.

Discriminatory accuracy was significantly better for younger women in the present analysis (AUC, 0.62 for age < 50 years and 0.56 for age ≥ 50 years). In 2009, the US Preventive Services Task Force recommended against routine mammography in women younger than age 50 years.⁹ However, African American women are more likely than other racial or ethnic groups to be diagnosed with breast cancer at a young age,¹ and the BWHS model could be a clinically

useful tool to identify women who may benefit from targeted screening recommendations before age 50 years. Women age ≥ 70 years were not included in the analysis because of limited numbers. In addition, discrimination has been found to be lower for women older than age 70 years, possibly as a result of weaker associations between risk factors and breast cancer incidence at older ages.¹⁰

Enrollment in breast cancer prevention trials has traditionally been restricted to women with a 5-year predicted risk of at least 1.66%. Because breast cancer risk prediction models have underestimated risk for African American women, recruitment has been disproportionately low. Two studies have demonstrated that a greater proportion of African American women would meet trial eligibility criteria for elevated risk by using the CARE model rather than the original Gail model.^{7,11} However, the CARE model underestimates risk for certain subgroups of African American women, as we previously found in the BWHS.⁸ In this study, we show that 14.6% of women age 30 to 69 years were predicted to have a 5-year risk of at least 1.66% using the BWHS model, compared with only 3.0% using the CARE model. Therefore, use of the BWHS model could result in increased eligibility of African Americans for prevention trials. It should be noted, however, that the model overestimated risk by approximately 10% (not statistically significant) in the highest quintile of risk, which could account for some of the discrepancy between the BWHS and CARE models in terms of the proportion of women predicted to have a 5-year risk of at least 1.66%.

Table 5. Comparison of the BWHS and CARE Models for Prediction of 5-Year Risk Less Than or ≥ the Cut Point of 1.66%

BWHS Model	CARE Model					
	< 1.66%		≥ 1.66%		Total	
	No. of Participants	%	No. of Participants	%	No. of Participants	%
Overall						
< 1.66%	40,979	85.0	197	0.4	41,176	85.4
≥ 1.66%	5,780	12.0	1,237	2.6	7,017	14.6
Total	46,759	97.0	1,434	3.0		
Age < 50 years						
< 1.66%	28,102	97.2	7	< 0.1	28,109	97.2
≥ 1.66%	787	2.7	17	0.1	804	2.8
Total	28,889	99.9	24	0.1		
Age ≥ 50 years						
< 1.66%	12,877	66.8	190	1.0	13,067	67.8
≥ 1.66%	4,933	25.9	1,220	6.3	6,213	32.2
Total	17,870	92.7	1,410	7.3		

Abbreviations: BWHS, Black Women's Health Study; CARE, Women's Contraceptive and Reproductive Experiences.

The BWHS model underestimated risk among women without a family history of breast cancer, possibly because information on family history had not been reported since 1999. Thus, some of the women may have been misclassified as not having a family history.

To our knowledge, this is the first study to use prospective data to develop a breast cancer risk prediction model for black women. A key strength was the inclusion of both younger and older African American women. A limitation is that the model was developed and validated in the same cohort, which may have resulted in optimistic model performance. Although we developed the model with data from one time period and evaluated it with subsequent follow-up data, our model may not perform as well in other study populations. We did not have data on mammographic density, which has modestly improved the Gail model in some studies.^{12,13} This measurement is not readily available for many women, which makes it less feasible to include in a risk model in large-scale studies. We also lacked information on benign breast disease subtypes including atypical hyperplasia.

In summary, we developed a breast cancer risk prediction model for African American women that was well calibrated across a wide age range and across strata of risk factors. The discriminatory accuracy of the model remains modest but was higher for breast cancer overall and for ER-negative breast cancer than the discriminatory accuracy of a previous model with fewer risk factors.⁷ The predictive ability was better for younger women, and the model may be a useful tool to

identify women who may benefit from screening before age 50 years. It is unclear how well the model will perform in study populations with different distributions of risk factors; the calibration and discrimination of the BWHS model should be evaluated in independent studies.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Disclosures provided by the authors are available with this article at www.jco.org.

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Prospective Approach to Breast Cancer Risk Prediction in African American Women: The Black Women's Health Study Model

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Appendix

Table A1. Rates Used to Estimate Absolute Risk of Breast Cancer in the BWHS (for African American women)

Age (years)	Breast Cancer Incidence Rates (per 100,000 person-years; SEER, 1994-1998)*	Competing Mortality Rates (per 100,000 person-years; NCHS, 1996-2000)†
30-34	31.1	145.9
35-39	67.6	215.9
40-44	119.4	315.1
45-49	187.4	448.8
50-54	241.5	632.3
55-59	291.1	963.0
60-64	310.1	1,471.8
65-69	365.6	2,116.3

Abbreviations: BWHS, Black Women's Health Study; NCHS, National Center for Health Statistics.

*SEER, 13 registries, 1994 to 1998.

†Competing mortality rates from causes other than breast cancer, obtained from the NCHS (1996 to 2000).

Breast Cancer Risk Prediction for African American Women

Table A2. Black Women's Health Study Cohort Characteristics in 1995 and 2006

Characteristic	% of Women	
	1995 (n = 55,093)	2006 (n = 48,193)
Age, years		
Mean	39.9	47.2
Standard deviation	9.3	9.5
Family history		
None	77.2	77.3
First-degree relative diagnosed at < 50 years	4.0	3.8
First-degree relative diagnosed at ≥ 50 years	4.9	4.7
Second-degree relative	13.9	14.1
Benign breast disease/biopsy		
No	81.4	76.8
Yes	18.6	23.2
Body mass index at age 18 years, kg/m ²		
< 20	40.9	40.2
20-24	45.0	45.2
≥ 25	14.1	14.6
Age at menarche, years		
< 12	28.4	28.8
12-13	52.3	52.4
≥ 14	19.3	18.8
Age at first birth, years		
Nulliparous or < 25	78.2	73.2
≥ 25	21.8	26.8
Oral contraceptive use		
< 10 years in duration and ≥ 10 years ago	62.4	64.2
≥ 10 years in duration or < 10 years ago	37.6	35.8
Bilateral oophorectomy		
No	92.2	88.6
Yes	7.8	11.4
Estrogen plus progestin use, years		
< 3	98.6	96.4
≥ 3	1.4	3.6
Height		
< 5 feet, 5 inches	45.0	44.5
≥ 5 feet, 5 inches	55.0	55.5