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Breast cancer incidence among women with a family history of breast cancer by relative's age at diagnosis

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AUTHOR CONTRIBUTIONS

Danielle D. Durham: Study concept and design, interpretation of the data, preparation of manuscript, and review and revision of the final manuscript. **Linn A. Abraham:** Study concept and design, analysis and interpretation of the data, preparation of the manuscript, and review and revision of the final manuscript. **Megan C. Roberts:** Study concept and design, interpretation of the data, and review and revision of the final manuscript. **Carly P. Khan:** Study concept and design and review and revision of the final manuscript. **Robert A. Smith:** Study concept and design, interpretation of the data, and review and revision of the final manuscript. **Karla Kerlikowske:** Data acquisition, study concept and design, interpretation of the data, and review and revision of the final manuscript. **Diana L. Miglioretti:** Data acquisition, study concept and design, interpretation of the data, and review and revision of the final manuscript.

Additional supporting information may be found in the online version of this article.

CONFLICT OF INTEREST

Robert A. Smith is employed by the American Cancer Society, which receives grants from private and corporate foundations, including foundations associated with companies in the health sector, for research outside the submitted work; his salary is funded solely through American Cancer Society funds. Carly Khan is a current employee of Patient-Centered Outcomes Research Institute. Karla Kerlikowske is a nonpaid consultant for GRAIL for the STRIVE study. Diana Miglioretti has received book royalties from Elsevier. The other authors made no disclosures.

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Abstract

BACKGROUND: Women with a first-degree family history of breast cancer are often advised to begin screening when they are 10 years younger than the age at which their relative was diagnosed. Evidence is lacking to determine how much earlier they should begin.

METHODS: Using Breast Cancer Surveillance Consortium data on screening mammograms from 1996 to 2016, the authors constructed a cohort of 306,147 women 30–59 years of age with information on first-degree family history of breast cancer and relative's age at diagnosis. The authors compared cumulative 5-year breast cancer incidence among women with and without a first-degree family history of breast by relative's age at diagnosis and by screening age.

RESULTS: Among 306,147 women included in the study, approximately 11% reported a first-degree family history of breast cancer with 3885 breast cancer cases identified. Women reporting a relative diagnosed between 40 and 49 years and undergoing screening between ages 30 and 39 or 40 and 49 had similar 5-year cumulative incidences of breast cancer (respectively, 18.6/1000; 95% confidence interval [CI], 12.1, 25.7; 18.4/1000; 95% CI, 13.7, 23.5) as women without a family history undergoing screening between 50–59 years of age (18.0/1000; 95% CI, 17.0, 19.1). For relative's diagnosis age from 35 to 45 years of age, initiating screening 5–8 years before diagnosis age resulted in a 5-year cumulative incidence of breast cancer of 15.2/1000, that of an average 50-year-old woman.

CONCLUSION: Women with a relative diagnosed at or before age 45 may wish to consider, in consultation with their provider, initiating screening 5–8 years earlier than their relative's diagnosis age.

Keywords

BCSC; breast cancer screening; Breast Cancer Surveillance Consortium; family history of breast cancer; mammography

INTRODUCTION

Family history is a strong risk factor for breast cancer and risk varies by the first-degree relative's age at breast cancer diagnosis.[1] The US Preventive Services Task Force (USPSTF) recommends initiating routine screening at 50 with personal choice from ages 40–49 years.[2] The American Cancer Society (ACS) recommends routinely initiating screening at age 45 and with personal choice from ages 40–44 years.[3] Decisions about initiation age are important for women with a family history of breast cancer because of their increased risk of developing the disease.[4] Women whose relatives were diagnosed before age 50 may wish to consider initiating screening earlier than average-risk women. Risk-stratified screening approaches, including some followed outside the United States,[5] recommend women with a first-degree family history initiate screening when their risk reaches that of an average-risk

50-year-old.[2,5] This personalized screening approach incorporates a woman's individual risk of developing breast cancer[6] with the timing of recommended screening initiation dependent on her risk status.

Personalized screening approaches offer recommendations based on risk and personal choice. For example, in the United States, women with a genetic predisposition are commonly advised to begin screening between ages 25 and 30.[7] However, women need evidence to make choices based on recommendations and advice. The benefit-to-harm ratio for breast cancer screening may be higher for high-risk women,[8] such as those with a family history of breast cancer, who are more likely to initiate screening mammography at a younger age (under 45–50 years) than women at average risk for breast cancer.[9] Women with a family history of breast cancer are more likely to attend mammography screening[10,11] and may be encouraged to initiate annual screening at earlier ages than recommended for average-risk women, typically 10 years earlier than the age at which their relative was diagnosed.[12,13] However, evidence to support this recommendation is lacking, and we cannot find a citation for the origin for this advice. The objective of this study was to calculate and compare 5-year cumulative incidence of breast cancer by age at screening mammography for women with and without a first-degree family history of breast cancer and by their family member's age at breast cancer diagnosis.

MATERIALS AND METHODS

Data source

We used data collected prospectively by the Breast Cancer Surveillance Consortium (BCSC), a population-based network of mammography registries.[14] BCSC data include radiologic, demographic, and breast cancer risk factor information for women undergoing breast imaging.[15] Breast cancer diagnoses and vital status information are obtained through linkage with state cancer and vital statistics registries. Completeness of capture by the registries is estimated at greater than 94%.[16] This study used data collected by three US breast imaging registries in the BCSC that collected relative's age at breast cancer diagnosis: Carolina Mammography Registry, San Francisco Mammography Registry, and Vermont Breast Cancer Surveillance System. Each BCSC registry and the Statistical Coordinating Center (SCC) received institutional review board approval for all study procedures, including passive consenting processes (the three participating registries) or a waiver of consent (SCC) to enroll participants, link data, and perform analytic studies. All procedures are Health Insurance Portability and Accountability Act (HIPAA) compliant. All registries and the SCC have received a Federal Certificate of Confidentiality and other protections for the identities of women, physicians, and facilities who are participants of this research.

Study sample, definitions, and outcomes

We constructed a retrospective cohort of women 30–59 years of age who had at least one screening mammogram on record in the BCSC between 1996 and 2016. Screening mammograms were defined using the BCSC strict definition of bilateral mammograms for women who had no mammogram in the prior 9 months and no personal history of breast

cancer, mastectomy, or breast augmentation.[17] Among women with more than one screening mammogram on record, we selected the first that met inclusion criteria. Within the BCSC, 72% of women have at least two mammograms and 28% of women have one.[18] We included breast cancer cases diagnosed on or following the first mammogram but women with a history of breast cancer before screening mammogram were excluded.

In the BCSC, women complete a self-administered questionnaire at the time of each screening mammogram. From this questionnaire, self-reported age, race and ethnicity, education, breast symptoms, menopausal status and use of post-menopausal hormone therapy, and family history are obtained. Women were considered to have a first-degree family history of breast cancer if this item was not missing and they self-reported a first-degree female relative (mother, sister, or daughter) diagnosed with breast cancer. If multiple relatives' ages at breast cancer diagnosis were reported, we selected the youngest age. If relative's age at diagnosis was reported as under 18 or as a range (e.g., 50+ years), then this item was considered unknown. Rural/urban classification used the zip code of patient residence and rural–urban commuting area codes.[19]

Statistical analysis

We used descriptive statistics to characterize demographic and breast cancer risk factors within three categories of first-degree family history status (Yes, age of relative at diagnosis is known; Yes, age of relative at diagnosis is unknown; and No family history of breast cancer). The Fine and Gray method[20] was used to estimate the 5-year cumulative incidence for breast cancer while accounting for competing risks. Women were followed from their first screening mammogram that fit study inclusion criteria until the earliest of the following events: 1) first diagnosis of invasive breast cancer or ductal carcinoma in situ, 2) mastectomy, 3) death, 4) end of complete cancer or vital status follow-up, or 5) 5 years after the screening mammogram. The models included a categorical variable that was a combination of family history of breast cancer status and relative's age at diagnosis (No; Yes, relative's age < 40, 40–49, 50–59, or 60+ years; Relative's age unknown), age group at screening mammogram (categorical, 10-year groups), and interaction of these covariates. We additionally adjusted for age at screening mammogram (continuous), race and ethnicity, and BCSC registry, and accounted for competing risks of mastectomy and death. Predicted cumulative incidences for each combination of covariates included in the model were weighted and summed based on the distribution of the adjusting covariates to obtain marginally adjusted cumulative incidence estimates for combinations of family history of breast cancer/relative's age at diagnosis and age group at screening mammogram. Confidence intervals (CIs) were calculated based on the 2.5th and 97.5th percentiles from 1000 random bootstrap samples. We repeated the analysis after subdividing two of the 10-year categories of age at screening mammogram into 5-year categories (40–44, 45–49, 50–54, and 55–59 years).

To display the cumulative incidence for specific values of relative's age at breast cancer diagnosis and age at screening mammogram, we fit a similar model that included family history of breast cancer and age at screening mammogram as continuous variables instead of categorical variables. Based on this model, which parameterized age at mammogram and

relative's age at diagnosis as continuous variables, we computed the predicted cumulative incidence of breast cancer for women who were age 50 at the time of their screening mammogram (reference line, Figure 1). Analyses were conducted using SAS version 9.4 (SAS Institute Inc, Cary, North Carolina).

RESULTS

The study cohort included 306,147 women. Nearly 82% were non-Hispanic White and 9% were non-Hispanic Black. Almost 52% had a screening mammogram between the ages of 40 and 49 years, 11% reported a first-degree family history of breast cancer, and 8% reported a first-degree relative's age at breast cancer diagnosis. Among women reporting a first-degree family history of breast cancer, 44% knew and 41% did not know the age at which their relative was diagnosed. Women reporting a relative's age at breast cancer diagnosis were more likely than women without a family history of breast cancer to be younger than 40 years at the time of their screening mammogram (19% vs. 10%, $p < .001$). Among women who reported their relative's age at breast cancer diagnosis, for nearly 38%, the age was 49 years or younger (Table 1).

The estimated cumulative 5-year incidences of breast cancer were 13.8 per 1000 (95% CI, 13.2, 14.4) for the entire study sample, 13.0 per 1000 (95% CI, 12.4, 13.6) for those without a first-degree family history of breast cancer, and 19.9 per 1000 (95% CI, 18.3, 21.7) for those with a family history. As expected, for the entire sample, the estimated 5-year cumulative incidence increased with age at screening mammogram (Table 2). Among women who reported a relative's age at diagnosis, the 5-year estimated cumulative incidence of breast cancer increased as relative's diagnosis age decreased. Women reporting a first-degree family history of breast cancer who underwent screening mammography between 30 and 39 years had a 5-year cumulative incidence of breast cancer (10.9 per 1000; 95% CI, 8.1, 14.0) similar to women without a first-degree family history who underwent screening mammography between 40 and 49 years (11.0 per 1000; 95% CI, 10.3, 11.6). Women reporting a relative diagnosed between 40 and 49 years and who underwent screening mammography between ages 30 and 39 or 40 and 49 years had 5-year cumulative incidences of breast cancer (18.6 per 1000; 95% CI, 12.1, 25.7 and 18.4 per 1000; 95% CI, 13.7, 23.5, respectively) that were similar to women without a first-degree family history who underwent screening mammography between 50 and 59 years (18.0 per1000; 95% CI, 17.0, 19.1) (Table 2).

We also assessed 5-year cumulative incidence within 5-year age at screening mammography groups for the 40–49 and 50–59 age groups. Within the group that received screening mammography at age 40–44, among those reporting a first-degree family history of breast cancer, 5-year cumulative incidence increased as relative's age decreased (12.2 per 1000 if relatives diagnosed at 60+ years to 23.9 per 1000 if relatives diagnosed at <40 years). The cumulative incidences for women without a first-degree family history of breast cancer in the 40–44 and 45–49 age groups were 9.8 per 1000 (95% CI, 9.0, 10.5) and 12.6 per 1000 (95% CI, 11.6, 13.7), respectively. Within categories of relative's age, younger women (30–39 years at screening mammography) with a relative diagnosed younger than 50 years

had a 5-year cumulative incidence that exceeded that of women without a family history who received screening mammography at age 45–49 or 50–54 years (Table S1).

Figure 1 displays the estimated 5-year cumulative incidence of breast cancer by age at screening mammography and family history status including relative's age at breast cancer diagnosis. When age at screening mammogram was greater than 45 years, differences in cumulative incidence of breast cancer across relative's age of diagnosis decreased with increasing age at screening mammogram. When relative's age at breast cancer diagnosis was 40 years, the age at screening mammogram at which cumulative incidence was closest to the average incidence for a 50-year-old receiving screening mammography was 34 years (Figure 1, inset); for a relative's diagnosis age of 55 years, the screening mammogram age was 42 years. For women with relatives diagnosed at age 35, 40, and 45 years, the ages at screening mammogram at which 5-year cumulative incidence of breast cancer per 1000 equaled 15.2 were 30, 34, and 37 years, respectively, with differences of 5, 6, and 8 years, respectively. Women reporting no first-degree family history of breast cancer had a lower cumulative incidence than women reporting a family history regardless of whether the relative's age at diagnosis was known (black dashed line vs. red dashed line).

DISCUSSION

In this study sample of women undergoing screening mammography, we observed differences in 5-year cumulative incidence of breast cancer by family history of breast cancer status and relative's age at diagnosis. Consistent with prior research,[21,22] women reporting a first-degree family history of breast cancer had a higher 5-year cumulative incidence of breast cancer than women without (19.9 per 1000 vs. 13.0 per 1000). The 5-year cumulative incidence of breast cancer increased as relative's diagnosis age decreased. When relative's diagnosis age ranged from 35 to 45 years, initiating screening 5–8 years before relative's diagnosis age resulted in 5-year cumulative incidence of breast cancer of an average risk 50-year-old woman (15.2 per 1000). Among women reporting a first-degree family history of breast cancer, the age at which the 5-year cumulative incidence of breast cancer equaled 15.2 per 1000 was 43 years, which is 2–7 years younger than the ACS and USPSTF guideline-recommended ages (45^2 and 50^3 years, respectively) to routinely initiate screening mammography for average-risk women. Depending on their relative's age at breast cancer diagnosis, women with a family history of breast cancer may wish to consider initiating screening 5–8 years earlier than their youngest relative with breast cancer if that relative was diagnosed between 35 and 45 years. Women with relatives diagnosed at age 50 or older should consider screening in their 40s.

Risk-based personalized screening strategies for women ages 30–39 with a family history of breast cancer and relative diagnosed before 50 years should consider the benefits and harms of having women at above-average risk initiate screening mammography earlier than average-risk women. Women who are BRCA gene mutation carriers may benefit from initiating screening at an earlier age.[23,24] Therefore, women ages 30–39 with more than one first-degree relative diagnosed with breast cancer may wish to consider genetic counseling. However, harms of breast cancer screening include false–positive results that may lead to invasive procedures and increased radiation exposure.[25,26] Reducing screening

age may increase harms generally, as women will undergo more screening over their lifetimes. Furthermore, mammography may not perform as well in younger women,[27] because they are more likely to have dense breasts that increases difficulty in interpreting the examination.[28] Nonetheless, given their higher risk of breast cancer, including risk of an earlier diagnosis, women with a first-degree relative diagnosed before age 50 may judge the higher risk of harms as an acceptable trade-off. A recent study identified risk-based ages for breast cancer screening initiation using 10-year cumulative risk of developing invasive breast cancer and similarly concluded that the age at which a woman with a first-degree relative diagnosed with breast cancer attains the breast cancer risk of an average-risk 50-year-old woman varies by the number and type of affected relative.[21] Alternative strategies to breast cancer screening based on age may be better suited for some patients. Risk-based approaches that consider multiple risk factors, use of risk models, and the woman's family history to determine screening eligibility are receiving increased interest.[29–32]

The results of the current study may be used to inform breast cancer screening guidelines for women with a first-degree family history of breast cancer to help determine when women might wish to consider initiating screening earlier than recommended for average-risk women. To calculate predicted cumulative incidence, we selected 50 years because it is the most commonly recommended age for mammography initiation. Breast screening guidelines have moved toward including an age group for which screening is based on personal choice. Results from this study may be used as inputs in risk-prediction models or as additions to current risk-prediction tools for shared decision-making when women discuss breast cancer screening options with their physicians. These conversations might include the appropriateness of when to undergo genetic risk assessment based on family history and other risk factors. Future studies may wish to assess the impact of varying the initiation age and degrees of family history status in conjunction with other risk factors such as known genetic mutations, race and ethnicity, and balance of harms and benefits of screening among young women.

Strengths and limitations

In addition to knowing if a woman had a relative diagnosed with breast cancer, we incorporated information on the relative's age at breast cancer diagnosis. Given the long follow-up of women in the BCSC, we were able to calculate 5-year cumulative incidence of breast cancer, which is clinically useful for shared decision-making and consideration of personalized screening options for women at above-average risk. This information allowed us to suggest the timing of initiating screening for women to consider if they have above-average risk of breast cancer due to family history. A limitation was that relatives' breast cancer status and age at diagnosis relied on self-report. A small proportion (3%) of women reported a relative diagnosed with breast cancer but not an age at diagnosis. However, among those reporting unknown age for a relative's diagnosis, we observed a higher 5-year cumulative incidence of breast cancer than women reporting no family history of breast cancer. Additionally, we excluded women with age at screening mammogram under 30 years and combined women with relative's age at diagnosis less than 30 with those having relatives 30–39 years of age due to few observations and the inability to reliably calculate cumulative incidence in those groups.

We did not have genetic testing results (i.e., presence of BRCA 1/2 mutation) for this study sample. Beyond family history of breast cancer, we did not have information on the reasons for initiating screening before the recommended age. We evaluated women who reported a first-degree relative and used the youngest age; however, the impact of more than one first-degree relative, second-degree relatives, and combinations of first- and second-degree relatives diagnosed with breast cancer may also be informative[21,22,33] for women and their physicians to evaluate risk of developing breast cancer and suitable options for genetic counseling and breast cancer screening. We included those with nonmissing family history status. Before exclusion, those missing information on family history of breast cancer comprised 6.4% of the sample. This information may not be missing at random and these women may initiate screening mammography at different ages.[7] Finally, although the BCSC data are population-based, this does not guarantee the sample was representative of the general US screening population.

In conclusion, our results do not support a standard recommendation for all women with a first-degree relative diagnosed with breast cancer to initiate screening 10 years earlier than the relative's diagnosis age. We did find empirical evidence that women with a first-degree relative diagnosed before age 50 are at higher risk of a diagnosis at a younger age and could consider initiating screening earlier based on the age of the first-degree relative's diagnosis. Rather than unsubstantiated advice to begin screening 10 years earlier than the age of breast cancer diagnosis of the youngest affected first-degree relative, our findings suggest women with a relative diagnosed at or before age 45 may consider initiating screening 5–8 years earlier than their relative's diagnosis age if they wish to initiate screening when their 5-year absolute risk is equivalent to that of an average risk 50-year-old woman. Ultimately, advice about beginning screening earlier should be grounded in an evidence-based guideline. Thus, results of this study and others may inform breast screening guidelines and precision screening for breast cancer among women at above-average risk due to a first-degree family history of breast cancer who are considering initiating breast cancer screening earlier than is routinely recommended for average-risk women.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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DATA AVAILABILITY STATEMENT

Data for this article were provided by the Breast Cancer Surveillance Consortium Research Resource (BCSC) Statistical Coordinating Center (see http://www.bcsc-research.org/).

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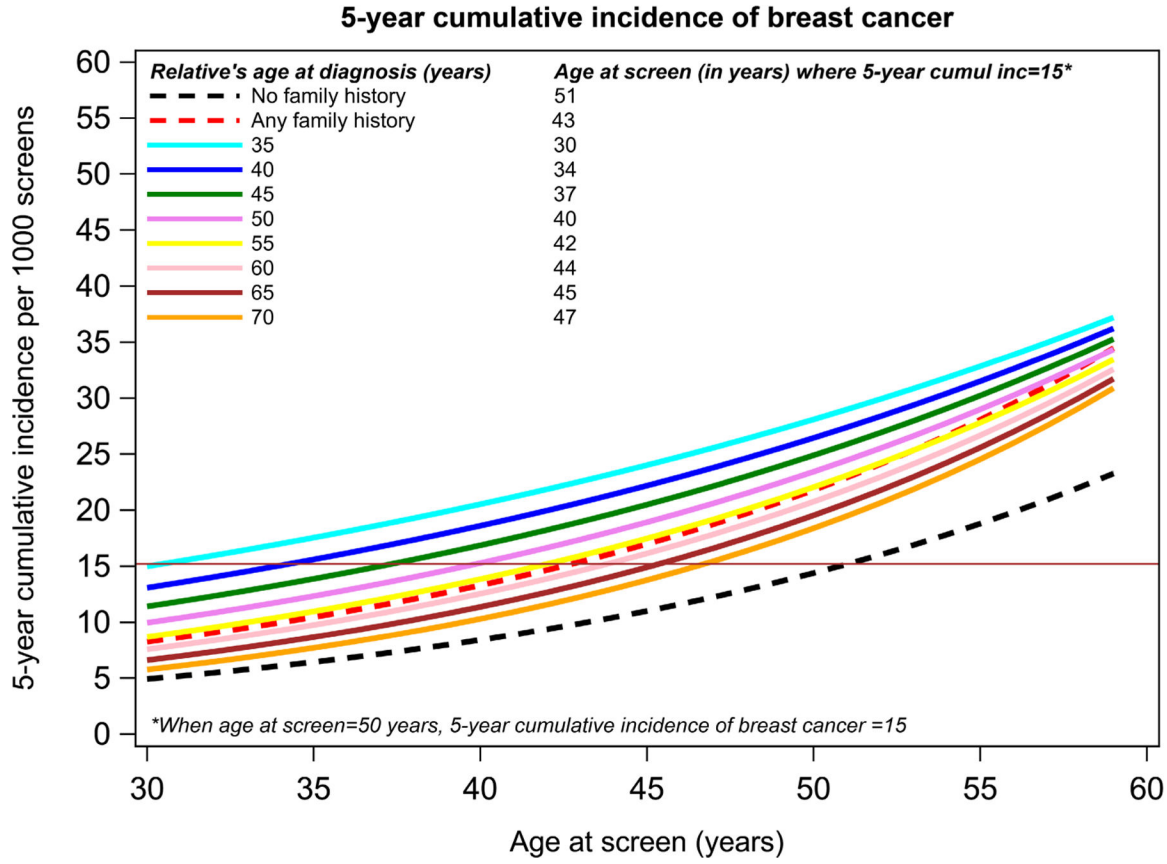

FIGURE 1.

Five-year cumulative breast cancer incidence per 1000 screening examinations by age at screen and first-degree family history of breast cancer. Horizontal line, reference showing the cumulative incidence (15.2 per 1000) for women age 50 years at screening mammogram with no family history of breast cancer. Models used for the figure included age at screening mammogram and relative's age at breast cancer diagnosis as continuous variables. Model adjusted for mammography registry, and race. For each 5-year group of relative's age at breast cancer diagnosis, we determined the age at screening mammography for which the cumulative incidence was closest to the reference of women without a family history who were age 50 at the time of screening mammogram.

TABLE 1.

Study cohort demographic distribution and breast cancer risk factors among women receiving screening mammography between 1996 and 2016 by first-degree family history of breast cancer status

		First-degree family history of breast cancer		
	Total	Yes, relative's age known[a]	Yes, relative's age unknown[b]	No
	N (column %)	*N* (column %)	*N* (column %)	*N* (column %)
Total	306,147	25,243	9179	271,725
Relative's age at diagnosis, (y)[c]				
<40	—	3265 (12.9)	—	—
40–49	—	6296 (24.9)	—	—
50–59	—	6663 (26.4)	—	—
60+	—	9019 (35.7)	—	—
Age at screen (y)				
30–39	32,598 (10.6)	4847 (19.2)	1183 (12.9)	26,568 (9.8)
40–49	159,509 (52.1)	11,162 (44.2)	3789 (41.3)	144,558 (53.2)
50–59	114,040 (37.3)	9234 (36.6)	4207 (45.8)	100,599 (37.0)
Race/ethnicity				
White, non-Hispanic	235,629 (81.8)	21,433 (88.5)	6582 (77.4)	207,614 (81.3)
Black, non-Hispanic	27,179 (9.4)	1384 (5.7)	1128 (13.3)	24,667 (9.7)
Hispanic	9049 (3.1)	546 (2.3)	256 (3.0)	8247 (3.2)
Asian, Pacific Islander	11,780 (4.1)	514 (2.1)	377 (4.4)	10,889 (4.3)
Other	4563 (1.6)	352 (1.5)	162 (1.9)	4049 (1.6)
Unknown	17,947 (5.9)	1014 (4.0)	674 (7.3)	16,259 (6.0)
Education				
<High school	13,358 (6.0)	913 (4.8)	607 (9.1)	11,838 (6.0)
High school/GED	58,070 (25.9)	4537 (23.6)	1616 (24.3)	51,917 (26.2)
Some college	56,974 (25.5)	4838 (25.2)	1550 (23.3)	50,586 (25.6)
College graduate	95,417 (42.6)	8898 (46.4)	2888 (43.4)	83,631 (42.2)
Unknown	82,328 (26.9)	6057 (24.0)	2518 (27.4)	73,753 (27.1)
Location of woman's residence				
Urban	173,082 (57.4)	13,825 (55.7)	5780 (64.0)	153,477 (57.3)

	Total	First-degree family history of breast cancer		
		Yes, relative's age known[a]	Yes, relative's age unknown[b]	No
	N (column %)	*N* (column %)	*N* (column %)	*N* (column %)
Rural	128,567 (42.6)	11,002 (44.3)	3256 (36.0)	114,309 (42.7)
Other/unknown	4498 (1.5)	416 (1.6)	143 (1.6)	3,939 (1.4)
Menopausal status				
Pre-menopausal	185,473 (61.6)	15,406 (61.8)	4965 (55.4)	165,102 (61.8)
Yes, natural	71,945 (23.9)	5930 (23.8)	2561 (28.6)	63,454 (23.7)
Yes, surgical	36,710 (12.2)	2976 (11.9)	1213 (13.5)	32,521 (12.2)
Yes, reason NOS	7106 (2.4)	598 (2.4)	230 (2.6)	6278 (2.3)
Unknown	4913 (1.6)	333 (1.3)	210 (2.3)	4370 (1.6)

Note: Percentages are column percentages based on nonmissing values. Comparisons of each characteristic between family history of breast cancer groups gave *p* values <.001 (based on χ^2 tests).

Abbreviations: GED, General Education Development; NOS, not otherwise specified.

[a]Includes women reporting a family history of breast cancer AND at least one exact age (≥18) of relative's (mother, sister, daughter) diagnosis.

[b]Includes women reporting a family history of breast cancer but relative's age at diagnosis is unknown or reported as a categorical variable.

[c]Based on minimum age (mother, sister, daughter) reported.

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TABLE 2.

Five-year estimated cumulative incidence and 95% CI of breast cancer per 1000 screening examinations by first-degree family history of breast cancer and age at screening mammography (10-year age groups)

		Age (y) of woman at screening mammography								
		30–39			40–49			50–59		
	Overall 5-year cumulative incidence per 1000 women	No. of women	No. of cancers	5-year cumulative incidence per 1000 (95% CI)	No. of women	No. of cancers	5-year cumulative incidence per 1000 (95% CI)	No. of women	No. of cancers	5-year cumulative incidence per 1000 (95% CI)
Overall	13.8 (13.2, 14.4)	32,598	216	6.0 (5.2, 7.0)	159,509	1723	11.7 (11.0, 12.3)	114,040	1946	18.9 (18.0, 20.0)
First-degree family history of breast cancer?										
No	13.0 (12.4, 13.6)	26,568	145	5.4 (4.5, 6.3)	144,558	1479	11.0 (10.3, 11.6)	100,599	1637	18.0 (17.0, 19.1)
Yes	19.9 (18.3, 21.7)	6030	71	10.9 (8.1, 14.0)	14,951	244	17.2 (14.9, 19.6)	13,441	309	26.3 (23.5, 29.4)
Relative's age at diagnosis (y)										
<40	26.2 (20.0, 32.9)	1055	16	17.1 (9.5, 26.0)	1304	36	28.5 (19.5, 37.5)	906	21	25.7 (14.6, 36.9)
40–49	24.3 (20.2, 28.6)	1555	27	18.6 (12.1, 25.7)	2769	50	18.4 (13.7, 23.5)	1972	62	34.2 (25.9, 43.3)
50–59	18.4 (15.1, 22.1)	1375	13	9.8 (4.6, 15.4)	2939	44	15.7 (11.1, 21.0)	2349	52	24.6 (18.3, 31.4)
60+	18.1 (15.2, 21.0)	862	6	6.9 (2.2, 12.9)	4150	72	17.6 (13.4, 22.0)	4007	82	21.9 (17.4, 26.4)
Unknown	17.6 (14.6, 20.5)	1183	9	8.1 (2.4, 14.8)	3789	42	13.0 (9.1, 17.0)	4207	92	26.7 (21.4, 32.3)

Note: The model includes categorical family history of breast cancer status, categorical age group at screening mammography, and their interaction. The model adjusts for continuous age, race, mammography registry, and competing risks (mastectomy, death). End of follow-up corresponds to the minimum of: first diagnosis of breast cancer, first evidence of mastectomy, date of death, end of complete cancer registry information, end of vital status data, 5 years after screening mammography.

Abbreviation: CI, confidence interval.