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Authors

Nelson, Heidi D
O'Meara, Ellen S
Kerlikowske, Karla
et al.

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Factors Associated with Rates of False-positive and False-negative Results from Digital Mammography Screening: An Analysis of Registry Data

Heidi D. Nelson, MD, MPH^{1,2}, Ellen S. O'Meara, PhD³, Karla Kerlikowske, MD, MPH⁴, Steven Balch³, and Diana Miglioretti, PhD^{3,5}

¹Pacific Northwest Evidence-based Practice Center, Department of Medical Informatics and Clinical Epidemiology, Oregon Health & Science University; Portland, OR

²Providence Cancer Center, Providence Health & Services; Portland, OR

³Group Health Research Institute, Group Health Cooperative, Seattle, WA

⁴General Internal Medicine Section, University of California; San Francisco, CA

⁵Department of Public Health Sciences, University of California, Davis, CA

Abstract

Background—Women screened with digital mammography may experience false-positive and false-negative results and subsequent additional imaging and biopsies. It is unclear how these outcomes vary by age, time since last screening, and individual risk factors.

Objective—To determine factors associated with false-positive and false-negative digital mammography results, additional imaging, and biopsies among a general population of women screened for breast cancer.

Design—Analysis of registry data.

Setting—Participating facilities at five U.S. Breast Cancer Surveillance Consortium breast imaging registries with linkages to pathology databases and tumor registries.

Patients—405,191 women aged 40–89 years screened with digital mammography between 2003–2011; 2,963 were diagnosed with invasive cancer or ductal carcinoma in situ within 12 months of screening.

Measurements—Rates of false-positive and false-negative results and recommendations for additional imaging and biopsies from a single screening round, and comparisons by age, time since last screening, and risk factors.

Results—Rates of false-positive results (121.2/1,000 women; 95% CI 105.6 to 138.7) and recommendations for additional imaging (124.9/1,000; 95% CI 109.3 to 142.3) were highest

Author Contact: Heidi D. Nelson; nelsonh@ohsu.edu; telephone: 503-494-1566.

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among women aged 40–49 years and decreased with age; rates of false-negative results (1.0 to 1.5/1,000) and recommendations for biopsy (5.6 to 17.5/1,000) did not differ greatly by age. Results did not differ by time since last screening. All rates were higher for women with risk factors, particularly family history of breast cancer, previous benign breast biopsy, high breast density, and low body mass index for younger women.

Limitations—Additional factors were not examined, including numbers of first- and second-degree relatives with breast cancer and diagnoses of previous benign biopsies.

Conclusions—False-positive results and additional imaging are common, particularly for younger women and those with risk factors, while biopsies occur less often. Rates of false-negative results are low.

Keywords

screening; digital mammography; adverse effects; false-positive result

INTRODUCTION

Clinical guidelines recommend a personalized approach to mammography screening that considers potential benefits and harms (1). Important harms include adverse effects of the screening process including false-positive and false-negative mammography results and subsequent additional imaging and biopsies. While procedures are often necessary to evaluate findings on screening mammography, most result in benign diagnoses. Minimizing these adverse effects could improve the benefit—harm screening equation for many women.

A personalized approach to screening includes identifying individual risk factors for breast cancer. Several risk factors have been associated with breast cancer in epidemiologic studies; however, most relationships are modest or inconsistent (2). Factors associated with high risks for breast cancer include specific mutations of breast cancer susceptibility genes (3) and other hereditary genetic syndromes (4); previously diagnosed high-risk breast lesions (5, 6); previous high-dose radiation therapy to the chest (4, 7); and family history of breast cancer, particularly among first-degree relatives. The degree of risk from family history varies according to familial patterns of disease. Estimates of lifetime risk over 20% are considered high (8), although lower levels may also be clinically important (9).

Additional factors that modestly increase risk include older age; current use of menopausal hormone therapy using combined estrogen and progestin regimens (10); current use of oral contraceptives (2); high breast density (11); and high body mass index (BMI) for postmenopausal women (12). How these factors influence performance outcomes of digital mammography screening has not been extensively explored.

The purpose of this study is to estimate rates of false-positive and false-negative digital mammography results and subsequent additional imaging and biopsies among a general population of women undergoing screening, and how rates vary by age, time since last mammography screening, and individual risk factors. This analysis will be used to inform updated clinical practice recommendations in the United States (13).

METHODS

Design Overview

This study is an analysis of data collected between 2003 to 2011 from the Breast Cancer Surveillance Consortium (BCSC), a collaborative network of mammography registries across the United States, supported by the National Cancer Institute (NCI) (14, 15). Registries collected data at the time mammography was performed at participating community radiology facilities. Breast cancer diagnoses were obtained by linking BCSC data to pathology databases, regional Surveillance, Epidemiology, and End Results (SEER) programs, and state tumor registries. Data were pooled at a Statistical Coordinating Center. Registries and the Coordinating Center received institutional review board approval for active or passive consenting processes or a waiver of consent to enroll participants, link data, and perform analysis. All procedures were Health Insurance Portability and Accountability Act compliant, and registries and the Coordinating Center received a federal Certificate of Confidentiality and other protections for the identities of women, physicians, and facilities.

Setting and Participants

The analysis includes data for 405,191 women aged 40 to 89 years who had routine screening with digital mammography during 2003 to 2011 at participating facilities at five BCSC breast imaging registries (Carolina Mammography Registry, Group Health [Washington state], New Hampshire Mammography Network, San Francisco Mammography Registry, and Vermont Breast Cancer Surveillance System) (Figure 1). Prior to each mammography examination, women completed questionnaires that included demographic and medical history information, including time since last mammography screening. All women with an eligible screening mammogram who completed a questionnaire providing permission to use their information for research were included.

Screening mammography examinations were designated by the radiologist or radiology technologist as performed for screening, and occurring more than 9 months after a previous imaging examination in women without histories of breast cancer, breast augmentations, or mastectomies. Each study-eligible routine screening required at least one mammography examination within the previous 30 months. Initial and unilateral examinations were excluded. Mammography information included Breast Imaging Reporting and Data System (BI-RADS) breast density, assessment, and recommendations for further work-up. For women with more than one mammography examination during the time period of the study, one observation was randomly selected to be included in the calculations to reduce potential bias, such as preferentially choosing women with shorter or longer screening histories. These data comprise a defined subset of BCSC data intended to represent the experience of a cohort of regularly screened women without histories of breast cancer or current breast symptoms.

Outcome and Risk Factor Measures

Outcome measures included rates of false-positive and false-negative mammography results and recommendations for additional imaging and biopsies from a single screening round. False-positive and false-negative mammography results were based on follow-up data within

one year of mammography screening and before the next screening examination. Positive versus negative initial and final results were defined according to BCSC standard definitions (16) which utilized standardized terminology and assessments of the American College of Radiology BI-RADS 4th edition atlas (17). Each screening mammography examination was given an initial BI-RADS assessment based on the screening views only. Positive initial results included four assessment categories: needs additional imaging evaluation (category 0), probably benign (category 3) with a recommendation for immediate work-up (these were treated as a category 0 based on the recommendation), suspicious abnormality (category 4), or highly suggestive of malignancy (category 5) (18). Negative results included assessments of negative (category 1) or benign findings (category 2), or category 3 without a recommendation for immediate work-up.

Recommendation for biopsy was defined as a positive final result after all imaging including work-up of an abnormal screening examination. Positive final results included BI-RADS assessments of 4 or 5 or 0 with a recommendation for biopsy (18). Negative final results included an assessment of 1, 2, or 3 or 0 with a recommendation for normal or short-interval follow-up or clinical exam.

We examined associations with common risk factors for breast cancer (2). These included first-degree relatives with breast cancer (none, 1); breast density (almost entirely fat, scattered fibroglandular densities, heterogeneously dense, extremely dense); benign breast biopsy (none, previous); race/ethnicity (white, black, Asian, Hispanic, other); menopausal status (pre, peri, postmenopausal); menopausal hormone therapy use (none, combination [estrogen with progestin], estrogen only); oral contraceptive use (no current use, current use), and body mass index (BMI) (<25, 25 to <30, 30 kg/m²). Since the BCSC data do not include information on types of menopausal hormone therapy, the analysis assumes that a woman with a uterus uses combination therapy, while a woman without a uterus uses estrogen-only therapy, as previously described (19, 20).

The main analysis analyzed three categories of breast density, combining almost entirely fat and scattered fibroglandular densities into one group. As a sensitivity analysis, we also analyzed density three additional ways: (1) three categories, combining heterogeneously dense and extremely dense into one group; (2) four separate BI-RADS categories; and (3) two categories that combine almost entirely fat and scattered fibroglandular densities into one group and heterogeneously dense and extremely dense into another group.

Two measures of time since last mammography screening were evaluated to represent broad and narrow estimates of one versus two years (9 to 18 versus 19 to 30 months; 11 to 14 versus 23 to 26 months).

Missing data for outcomes and risk factors are summarized in Appendix Table 1.

Statistical Analysis

From these data, we calculated age-specific rates by decade (numbers per 1,000 women per single screening round) for false-positive and false-negative mammography results, recommendations for additional imaging, and recommendations for biopsies, and

determined whether outcomes differed by age, time since last mammography screening, and risk factors. To account for correlation among mammograms interpreted at the same radiology facility, we estimated robust standard errors from logistic regression using generalized estimating equations with an independence working correlation matrix (21). We then constructed 95% confidence intervals (CIs) and, to assess differences between groups, 2-sided P-values. This method provides population-averaged estimates of effects, which are not necessarily causal relationships. Analyses were performed using SAS software, version 9.3 (SAS Institute Inc., Cary NC).

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RESULTS

Outcomes by Age

Data for regularly screened women based on results from a single screening round using digital mammography indicated that false-positive mammography results were common in all age groups (Table 1). The rate was highest among women aged 40 to 49 years (121.2 per 1,000 women; 95% CI 105.6 to 138.7) and declined with age ($p<0.001$). Rates of false-negative mammography results tended to increase with age, but were not statistically significantly different across age groups, and ranged from 1.0 to 1.5 per 1,000 women.

For women with initially positive mammography results, rates of recommendations for additional imaging were highest among women aged 40 to 49 years (124.9 per 1,000 women; 95% CI 109.3 to 142.3) and decreased with age ($p<0.001$). Rates of recommendations for biopsy were not statistically significantly different across age groups, and ranged from 15.6 to 17.5 per 1,000 women.

Rates of invasive breast cancer were lowest among women aged 40 to 49 years (2.2 per 1,000 women; 95% CI 1.8 to 2.6) and increased across age groups ($p<0.001$). Rates of DCIS were also lowest among women aged 40 to 49 years (1.6 per 1,000 women; 95% CI 1.3 to 1.9) and increased with age ($p=0.05$). Women aged 70 to 79 had the highest rates of invasive cancer (7.2 per 1,000 women; 95% CI 6.4 to 8.1) and DCIS (2.3 per 1,000 women; 95% CI 1.7 to 3.0), and the yield of screening was more favorable for older women. For every case of invasive breast cancer detected by mammography screening in women aged 40 to 49 years, 464 women had mammography, 58 were recommended for additional imaging, and 10 were recommended for biopsies. In comparison, for women aged 70 to 79, for every case of invasive breast cancer detected by screening, 139 women had mammography, 11 were recommended for additional imaging, and 3 were recommended for biopsies.

Outcomes by Time since Last Mammography Examination

Rates of false-positives, false-negatives, and recommendations for additional imaging did not differ in comparisons of times since last mammography regardless of interval durations (9 to 18 versus 19 to 30 months; 11 to 14 versus 23 to 26 months) (Appendix Table 2).

Biopsies were recommended at a higher rate for women aged 60 to 69 years who had their last mammogram 23 to 26 months previously compared to 11 to 14 months (18.8 versus 15.2 per 1,000 women; $p=0.03$).

Outcomes by Risk Factors

False-positive mammography results—Rates of false-positive mammography results were statistically significantly higher for women with specific risk factors compared with women without them (Table 2). These include women with first-degree relatives with breast cancer compared with no relatives for women aged 40 to 69 years. Women with heterogeneously dense breasts had higher false-positive rates than those with almost entirely fat and scattered fibroglandular densities, or extremely dense breasts, for all ages except 80 to 89 years. Rates were also higher among women with previous benign breast biopsies for ages 40 to 79 years. Comparisons based on race and ethnicity indicated the lowest rates among Asians for all age groups.

Premenopausal women had the highest false-positive rates for women aged 40 to 59 years compared with perimenopausal and postmenopausal women. Women using menopausal hormone therapy had the highest rates for ages 70 to 79 years, while comparisons for other age groups were not statistically significant. Women with lower body mass (BMI <30) had higher false positive rates for ages 40 to 59 years.

False-negative mammography results—Rates of false-negative results were higher for women with first-degree relatives with breast cancer for ages 40 to 79 years, although results were of borderline statistical significance for ages 50 to 69 years (Appendix Table 3). Women with almost entirely fat and scattered fibroglandular densities had lower rates than those with other types of breast density for ages 40 to 69 years. Rates were higher among women with previous benign breast biopsies for ages 50 to 89 years, and women with lower body mass (BMI <30) for ages 50 to 59 years. Other comparisons between groups were not statistically significant.

Recommendations for additional imaging—Risk factors associated with differences in rates of recommendations for additional imaging were similar to those for false positive mammography results (Appendix Table 4). Rates were highest among women with first-degree relatives with breast cancer for all ages, heterogeneously dense breasts (ages 40 to 79), previous benign breast biopsies (ages 40 to 79), premenopausal status (ages 40 to 50), use of menopausal hormone therapy (ages 70 to 79), and lower BMI (ages 40 to 49). Comparisons based on race and ethnicity indicated the lowest rates among Asians for all age groups.

Recommendations for biopsy—Rates of recommendations for biopsy were statistically significantly higher for women aged 40 to 69 years with first-degree relatives with breast

cancer, and for women aged 40 to 79 years with previous breast biopsies (Table 3). Women aged 40 to 59 years with heterogeneously dense or extremely dense breasts had higher rates than women with less dense breasts, while for women aged 60 to 79 years, rates were highest for women with heterogeneously dense breasts only. Higher rates were also associated with premenopausal status for ages 50 to 59 years; no current use of oral contraceptives for ages 40 to 49 years; lower BMI for ages 40 to 49, but higher BMI for ages 70 to 79. Other comparisons between groups were not statistically significant.

Breast density categories—Rates of false-positives, false-negatives, recommendations for additional imaging, and recommendations for biopsies were lowest for women with almost entirely fat breasts for all ages. False-negative rates were highest for women with extremely dense breasts for all ages, except those aged 60 to 69 years (Appendix Table 5). Rates of false-positives, recommendations for additional imaging, and recommendations for biopsies were highest for women with heterogeneously dense breasts or for the combined category of heterogeneously and extremely dense breasts, except for women aged 40 to 49 years where rates of recommendations for biopsies were highest among women with extremely dense breasts.

DISCUSSION

Our analysis of BCSC data on digital mammography screening indicated that false-positive rates and recommendations for additional imaging were highest among women aged 40 to 49 years and declined with age, while false-negative rates were low across all age groups. Rates of recommendations for biopsy did not differ between ages. Results did not differ by time since last mammography screening regardless of whether broad or narrow estimates of one versus two years were used.

Several risk factors were statistically significantly associated with higher rates of false-positive and false-negative results and recommendations for additional imaging and biopsy across most age groups. These included family history of breast cancer, high breast density, and previous benign breast biopsy. Premenopausal status, use of menopausal hormone therapy, and lower BMI were associated with some of the outcomes for specific age groups only. Comparisons based on race and ethnicity indicated the lowest rates of false-positive results and additional imaging among Asians. While some risk factors reflect high exposure to estrogen and related changes in breast tissue (premenopause, menopausal hormone therapy), others may serve primarily as markers of increased breast cancer risk (family history, previous benign biopsy).

Our analysis comparing different combinations of breast density categories indicated that rates for all outcomes were lowest for women with almost entirely fat breasts, and highest for women with heterogeneously dense breasts or for those in the combined category of heterogeneous and extreme density. Women with extremely dense breasts had the highest rates of false-negative results. The high rates for women with dense breasts are likely related to their particularly complex mammography images that are more difficult to interpret, limiting the discrimination of breast cancer from normal tissue and leading to more call backs and biopsies and higher false-negative rates in clinical practice (22–24).

This analysis indicates higher rates of false-positive results and recommendations for additional imaging, and lower rates of recommendations for biopsy, than our previous analysis of BCSC data that included 600,830 women screened between 2000 and 2005 using predominantly film mammography (25). The lower rates of recommendations for biopsy may suggest more selective use of procedures by radiologists because of improvements in image quality and interpretation for digital mammography and ultrasound over time.

Our finding that results did not differ by time since last mammography screening differs from previous analyses from the BCSC that indicate higher rates for annual versus biennial screening (19, 26–30). However, our rates were based on digital mammography only and on a single round of screening that did not capture the longitudinal screening experiences of individual women that more accurately reflect clinical practice. A previous analysis of BCSC data that provided results of screening over a 10-year time period indicated that when screening began at age 40, cumulative rates of false-positive mammography and benign biopsy results were higher for annual than biennial screening (mammography 61% versus 41%; biopsy 7% versus 5%) (29).

The results of our analysis of associations with risk factors are generally consistent with previous BCSC analyses indicating that 10-year cumulative risks of false-positive results and benign biopsies were higher for women with heterogeneously dense or extremely dense breasts, family histories of breast cancer, and those who used combination menopausal hormone therapy (29, 31). While our analysis identified associations with additional risk factors, it differed from the study of 10-year cumulative risks because it was based on a single round of screening, did not adjust for other covariates, and included only digital mammography.

The strengths of this study include its use of digital mammography data and patient information from a large national collaborative of women screened in the United States, providing a comprehensive data source representing current clinical practice. This study uses the methods of the BCSC that have been standardized across the participating registries, allowing our analysis to build on prior work in this area (23, 32, 33).

To estimate screening outcomes applicable to clinical practice in the U.S., data sources must include information from U.S. practices because rates of false-positive and false-negative results and additional imaging and biopsies are substantially different elsewhere (34–36). These differences relate to how mammography screening and diagnosis are delivered and practiced in diverse areas.

This study has several limitations. The BCSC data reflect opportunistic screening in a fluctuating population of women in the U.S. whose information was collected by the participating registries. Findings may not be applicable to other populations. Limitations also include restrictions of registry data with pre-defined data elements and the inherent biases of observational data. Some outcomes, such as the effectiveness and harms of different screening intervals, would be more accurately determined by comparing outcomes between women who were randomly assigned to comparison groups. However, this question

has not yet been addressed by randomized trials of screening that used intervals ranging from 12 to 33 months (13).

Our goal was to provide overall rates of the outcome measures by time since last mammography screening and risk factors and thus, our estimates are derived from population-averaged models that provide variance estimates adjusted for correlation within facilities, but do not decompose within versus between facility effects or adjust for potential confounders. For example, it is possible that women with risk factors tend to seek care at facilities with different performance characteristics (e.g., academic medical centers) than women without risk factors, present for screening more often, or have other characteristics that explain the higher rates of screening harms, such as more complex breast tissue or increased risk of benign breast disease. Understanding the mechanisms through which risk factors affect performance or variation across facilities and radiologists is beyond the scope of this paper.

Our estimates are based on digital mammography performed without supplemental imaging. Digital breast tomosynthesis (37–42) and supplemental screening tests such as screening ultrasound (43) are becoming more widely used in the United States. A similar analysis of screening outcomes of these newer technologies using a large, generalizable cohort such as the BCSC is needed.

In conclusion, our analysis of outcomes from a single round of digital mammography screening in 405,191 women indicates that false-positive results and additional imaging are common, particularly for younger women and those with risk factors, while biopsies occur less often. Rates of false-negative results are low. The results of this study may be useful for women and clinicians considering the individual benefits and harms of screening, as well as health service administrators and planners determining the implications of screening on populations.

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Appendix

Appendix Table 1

Rates of missing data for outcome and risk factor measures for 405,191 women screened. Women with missing data were excluded from the specific analysis only.

	Women with missing data	
	Number	%
Outcome		
Invasive breast cancer cases, <i>n</i>	0	0%
DCIS cases, <i>n</i>	0	0%
False-positive mammography result	0	0%
False-negative mammography result	0	0%
Additional imaging recommended	0	0%
Biopsy recommended	9,633	2.4%
Screen-detected invasive cancer	0	0%
Screen-detected DCIS	0	0%
Risk factor		

Women with missing data		
	Number	%
First-degree relatives with breast cancer	3,943	1.0%
Breast density	65,919	16.3%
Benign breast biopsy	23,588	5.8%
Race/ethnicity	31,061	7.7%
Menopausal status	41,288	17.1% [*]
Menopausal hormone therapy	65,717	16.2%
Oral contraceptives	37,098	15.3% [*]
Body mass index, <i>kg/m²</i> [†]	190,560	47.0%
Time since last exam, <i>mo</i> [‡]	0	0%

^{*} % of 241,728 screened women aged 40–59; women ≥ 60 are postmenopausal.

[†] Most missing values are from facilities that do not collect this information.

[‡] No missing data for broad categories (9–18 vs. 19–30 months).

Appendix Table 2

Rates of false-positive and false-negative digital mammography results and recommendations for additional imaging and biopsies based on time since last mammography examination

Outcome	Time since last exam, <i>mo</i>	Age, <i>y</i>									
		40–49	50–59	60–69	70–79	80–89					
Comparing 9–18 vs. 19–30 months[*]											
Women screened, <i>n</i>	9–18	79,637	91,864	71,324	39,474	14,865					
	19–30	34,133	36,094	23,183	10,730	3,887					
Invasive breast cancer cases, <i>n</i>	9–18	240	391	474	322	119					
	19–30	109	183	177	105	35					
DCIS cases, <i>n</i>	9–18	126	185	156	94	32					
	19–30	65	61	52	26	11					
Outcomes, <i>n per 1,000 women screened (95% CI)</i>											
False-positive mammography result	9–18	122.1 (105.4, 141.0)	0.65	94.2 (83.3, 106.5)	0.37	80.6 (72.8, 89.2)	0.89	69.1 (61.9, 77.0)	0.55	66.5 (60.8, 72.8)	0.22
	19–30	119.0 (103.0, 137.1)		90.5 (80.4, 101.8)		81.1 (71.4, 92.1)		71.6 (62.2, 82.2)		60.2 (49.3, 73.3)	
False-negative mammography result	9–18	1.1 (0.9, 1.3)	0.14	1.2 (1.0, 1.4)	0.06	1.3 (1.0, 1.6)	0.26	1.6 (1.2, 2.1)	0.17	1.4 (0.9, 2.2)	0.27
	19–30	0.8 (0.6, 1.1)		0.9 (0.6, 1.2)		0.9 (0.6, 1.5)		1.0 (0.5, 2.0)		0.8 (0.3, 2.3)	
Additional imaging recommended [†]	9–18	125.6 (109.0, 144.3)	0.74	99.3 (88.2, 111.7)	0.47	88.2 (80.2, 96.9)	0.59	78.0 (70.7, 86.1)	0.30	75.3 (68.6, 82.6)	0.46
	19–30	123.3 (107.0, 141.7)		96.4 (85.9, 108.0)		90.1 (80.1, 101.2)		82.8 (72.5, 94.3)		71.3 (59.8, 84.8)	
Biopsy recommended [‡]	9–18	15.6 (12.8, 19.0)	0.11	15.7 (12.7, 19.3)	0.50	15.9 (14.0, 18.2)	0.10	17.3 (15.2, 19.6)	0.44	14.9 (12.4, 17.9)	0.25
	19–30	18.2 (13.7, 24.1)		16.4 (12.5, 21.4)		18.4 (14.7, 23.0)		18.5 (14.6, 23.5)		18.3 (13.9, 24.0)	
Screen-detected invasive cancer	9–18	2.0 (1.6, 2.5)	0.12	3.2 (2.7, 3.7)	0.009	5.5 (4.9, 6.2)	0.07	6.7 (5.8, 7.7)	0.04	6.8 (5.4, 8.5)	0.39
	19–30	2.5 (2.1, 3.0)		4.3 (3.7, 5.1)		6.8 (5.7, 8.1)		8.9 (7.4, 10.8)		8.2 (5.8, 11.6)	
Screen-detected DCIS	9–18	1.5 (1.2, 1.8)	0.18	1.9 (1.5, 2.4)	0.13	2.0 (1.8, 2.4)	0.79	2.3 (1.7, 3.0)	0.97	2.0 (1.2, 3.1)	0.42
	19–30	1.8 (1.4, 2.3)		1.6 (1.2, 2.0)		2.2 (1.4, 3.3)		2.2 (1.4, 3.6)		2.8 (1.5, 5.3)	
Comparing 11–14 vs. 23–26 months[*]											
Women screened, <i>n</i>	11–14	55,278	65,219	53,419	30,497	11,299					

Outcome	Time since last exam, mo	Age, y									
		40-49	50-59	60-69	70-79	80-89					
	23-26	13,584	14,407	9,907	4,291	1,504					
Invasive breast cancer cases, <i>n</i>	11-14	163	274	348	247	78					
	23-26	42	70	76	41	15					
DCIS cases, <i>n</i>	11-14	83	127	111	71	20					
	23-26	26	22	23	12	3					
Outcomes, <i>n</i> per 1,000 women screened (95% CI)											
False-positive mammography result	11-14	119.1 (103.5, 136.8)	0.69	93.3 (82.8, 105.0)	0.46	79.2 (72.2, 86.8)	0.91	67.6 (60.7, 75.2)	0.70	63.8 (58.2, 69.9)	0.71
	23-26	115.8 (98.7, 135.4)		89.9 (78.8, 102.4)		79.6 (70.3, 90.2)		65.7 (56.7, 76.0)		61.2 (47.3, 78.7)	
False-negative mammography result	11-14	1.2 (1.0, 1.5)	0.20	1.2 (1.0, 1.5)	0.11	1.2 (0.9, 1.6)	0.32	1.4 (1.1, 2.0)	0.95	1.2 (0.7, 1.8)	0.44
	23-26	0.9 (0.5, 1.5)		0.8 (0.4, 1.4)		0.8 (0.4, 1.8)		1.4 (0.6, 3.4)		2.0 (0.7, 6.0)	
Additional imaging recommended †	11-14	122.4 (106.7, 139.9)	0.77	98.3 (87.7, 109.9)	0.57	86.6 (79.5, 94.3)	0.55	76.6 (69.3, 84.5)	0.98	71.3 (65.4, 77.7)	0.98
	23-26	119.9 (102.6, 139.7)		95.5 (83.9, 108.5)		88.8 (79.2, 99.5)		76.7 (66.5, 88.2)		71.1 (57.1, 88.3)	
Biopsy recommended †	11-14	14.7 (12.2, 17.8)	0.31	15.1 (12.2, 18.6)	0.66	15.2 (13.5, 17.2)	0.03	16.6 (14.5, 18.9)	0.85	13.2 (10.8, 16.0)	0.33
	23-26	16.9 (11.9, 24.0)		15.8 (11.7, 21.3)		18.8 (15.2, 23.2)		17.0 (12.6, 23.0)		16.6 (11.2, 24.7)	
Screen-detected invasive cancer	11-14	1.8 (1.5, 2.3)	0.31	3.1 (2.6, 3.7)	0.05	5.5 (4.9, 6.2)	0.07	6.8 (5.8, 7.9)	0.35	5.9 (4.5, 7.8)	0.33
	23-26	2.3 (1.6, 3.2)		4.2 (3.3, 5.4)		7.0 (5.7, 8.5)		8.4 (5.7, 12.4)		8.0 (4.9, 13.1)	
Screen-detected DCIS	11-14	1.4 (1.1, 1.8)	0.20	1.9 (1.4, 2.4)	0.22	1.9 (1.6, 2.3)	0.59	2.2 (1.6, 3.0)	0.69	1.6 (0.9, 2.8)	0.75
	23-26	1.8 (1.3, 2.7)		1.4 (0.9, 2.1)		2.2 (1.3, 3.7)		2.6 (1.3, 5.1)		2.0 (0.6, 6.1)	

* 2-sided P-values and 95% confidence intervals from a logistic regression model that accounts for clustering by radiology facility using generalized estimating equations.

† After positive mammography result.

Abbreviations: CI=confidence interval; DCIS=ductal carcinoma in situ.

Appendix Table 3

Rates of false-negative results after screening with digital mammography by risk factors*

Factor		Age, y									
		40-49	50-59	60-69	70-79	80-89					
Women screened, <i>n</i>		113,770	127,958	94,507	50,204	18,752					
False-negative mammography result, <i>n</i>		115	139	112	73	24					
Number per 1,000 women screened per round (95% CI)											
First-degree relatives with breast cancer	None	0.9 (0.8, 1.1)	0.02*	1.0 (0.8, 1.2)	0.09	1.1 (0.8, 1.4)	0.10	1.2 (0.9, 1.6)	0.01	1.2 (0.8, 1.9)	0.49
	One or more	1.8 (1.3, 2.5)		1.6 (1.1, 2.4)		1.7 (1.1, 2.7)		2.4 (1.6, 3.7)		1.6 (0.8, 3.1)	
Breast density	Fat-Scattered	0.4 (0.3, 0.6)	<0.001	0.6 (0.4, 0.8)	0.002	0.8 (0.5, 1.1)	0.006	1.0 (0.6, 1.5)	0.01	0.9 (0.5, 1.6)	0.25
	Heterogeneous	1.3 (1.0, 1.7)		1.4 (1.0, 2.0)		1.7 (1.3, 2.3)		2.3 (1.6, 3.4)		1.1 (0.5, 2.4)	
	Extreme	1.7 (1.2, 2.5)		1.6 (0.9, 2.8)		1.2 (0.6, 2.7)		5.6 (2.4, 12.9)		6.9 (2.5, 18.5)	
Benign breast biopsy †	None	0.9 (0.8, 1.1)	0.53	0.8 (0.7, 1.1)	0.002	0.8 (0.6, 1.1)	0.001	0.9 (0.6, 1.3)	0.004	0.9 (0.5, 1.6)	0.02
	Previous	1.1 (0.7, 1.7)		1.7 (1.3, 2.3)		2.1 (1.6, 2.8)		2.6 (1.8, 3.9)		2.6 (1.6, 4.2)	
Race/ethnicity	White	1.2 (1.0, 1.4)	0.31	1.2 (0.9, 1.4)	0.04	1.3 (1.0, 1.6)	0.36	1.7 (1.2, 2.4)	0.29	1.4 (0.9, 2.3)	0.77
	Black	0.7 (0.3, 1.4)		1.2 (0.6, 2.2)		1.5 (0.8, 2.9)		0.9 (0.3, 2.3)		1.0 (0.2, 6.4)	
	Asian	0.8 (0.5, 1.3)		1.1 (0.7, 1.7)		0.6 (0.3, 1.2)		0.8 (0.4, 1.6)		0.4†	
	Hispanic	0.5 (0.2, 1.6)		0.2 (0.0, 1.1)		0.7 (0.2, 2.4)		0.8 (0.1, 4.6)		3.3 (0.4, 23.9)	
	Other	1.1 (0.4, 3.2)		1.6 (0.6, 4.1)		1.2 (0.2, 7.1)		1.5 (0.3, 8.5)		5.4 (1.0, 27.8)	
Menopausal status	Pre	1.2 (1.0, 1.4)	0.17	1.3 (0.9, 1.9)	0.53	NA	NA	NA	NA	NA	
	Peri	0.8 (0.2, 2.5)		1.0 (0.5, 2.1)							

Factor		Age, y									
		40-49	50-59	60-69	70-79	80-89					
Menopausal hormone therapy	Post	0.7 (0.4, 1.3)		1.0 (0.8, 1.3)							
	None	1.0 (0.9, 1.2)	0.76	1.0 (0.8, 1.2)	0.37	1.0 (0.8, 1.3)	0.33	1.3 (0.9, 1.8)	0.58	1.2 (0.8, 2.0)	0.62
	Combination	0 [‡]		1.9 (0.9, 3.7)		2.3 (1.0, 5.6)		0 [‡]		3.1 (1.5, 6.6)	
Oral contraceptives	Estrogen only	1.5 (0.2, 10.1)		0.4 (0.1, 2.6)		1.2 (0.4, 3.1)		0.8 (0.1, 5.6)		2.5 (0.4, 13.7)	
	No current	1.0 (0.8, 1.2)	0.77	1.1 (0.9, 1.3)	0.54	NA		NA		NA	
	Current use	1.1 (0.6, 2.1)		1.4 (0.6, 3.5)							
Body mass index, kg/m ²	<25	1.4 (1.2, 1.7)	0.06	1.3 (1.0, 1.6)	0.008	1.3 (0.9, 1.8)	0.66	2.4 (1.6, 3.6)	0.09	1.7 (0.7, 3.8)	0.96
	25 to <30	0.8 (0.6, 1.3)		1.0 (0.7, 1.6)		1.2 (0.7, 2.1)		1.0 (0.5, 1.8)		1.6 (0.7, 3.7)	
	30	0.7 (0.3, 1.4)		0.4 (0.2, 0.8)		1.0 (0.6, 1.8)		1.0 (0.4, 2.4)		0 [‡]	

* 2-sided P-value and 95% confidence intervals from logistic regression model that accounts for clustering by radiology facility using generalized estimating equations.

[†] Categories include: almost entirely fat=fat; scattered fibroglandular densities=scattered; heterogeneously dense=heterogeneous; and extremely dense=extreme.

[‡] No false-negative outcomes. Category omitted from model used to obtain CI and P-value.

Abbreviations: kg=kilogram; m=meter; NA=not applicable; peri=perimenopausal; pre=premenopausal; post=postmenopausal.

Appendix Table 4

Rates of recommendations for additional imaging after screening with digital mammography by risk factors*

Characteristic		Age, y									
		40-49	50-59	60-69	70-79	80-89					
Women screened, n		113,770	127,958	94,507	50,204	18,752					
Additional imaging recommended, n		14,209	12,604	8,380	3,968	1,396					
Number per 1,000 women screened per round (95% CI)											
First-degree relatives with breast cancer	None	122.1 (107.7, 138.1)	0.02	95.2 (85.8, 105.6)	0.003	86.7 (79.0, 95.1)	0.002	77.5 (69.9, 85.7)	0.02	71.7 (64.6, 79.5)	0.01
	One or more	145.6 (119.6, 176.2)		117.1 (99.7, 137.0)		98.3 (87.9, 109.8)		86.9 (79.1, 95.4)		86.0 (75.5, 97.7)	
Breast density	Fat-Scattered	110.8 (97.9, 125.2)	0.001	84.4 (74.8, 95.1)	<0.001	81.0 (73.1, 89.6)	<0.001	75.6 (68.5, 83.4)	0.003	68.9 (61.7, 76.9)	0.002
	Heterogeneous	146.0 (123.9, 171.3)		121.6 (105.8, 139.3)		110.6 (99.7, 122.6)		99.0 (87.9, 111.4)		93.6 (82.4, 106.2)	
	Extreme	116.5 (98.4, 137.4)		98.4 (83.1, 116.2)		81.0 (70.3, 93.2)		63.3 (49.7, 80.1)		92.0 (66.6, 125.7)	
Benign breast biopsy	None	117.8 (103.4, 134.0)	0.001	90.9 (81.7, 101.0)	<0.001	81.9 (74.1, 90.6)	<0.001	72.2 (65.1, 79.9)	<0.001	72.1 (64.3, 80.7)	0.07
	Previous	172.5 (145.9, 202.8)		129.3 (112.8, 147.8)		108.2 (98.2, 118.9)		100.5 (90.0, 112.1)		82.7 (72.9, 93.7)	
Race/ethnicity	White	131.1 (119.4, 143.8)	0.001	103.2 (94.8, 112.3)	0.01	92.4 (85.7, 99.4)	0.005	83.3 (77.1, 90.1)	0.004	78.0 (71.1, 85.5)	0.11
	Black	95.9 (85.0, 108.0)		82.6 (68.4, 99.4)		70.8 (59.3, 84.3)		66.3 (59.1, 74.4)		60.3 (49.1, 74.0)	
	Asian	89.1 (76.0, 104.2)		73.5 (62.1, 86.8)		64.6 (54.0, 77.0)		52.6 (44.9, 61.4)		40.5 (33.4, 48.9)	
	Hispanic	127.8 (109.2, 149.0)		84.6 (71.9, 99.3)		76.9 (64.1, 92.0)		72.1 (61.6, 84.3)		62.3 (38.7, 98.9)	
	Other	131.6 (109.8, 157.1)		109.8 (97.1, 123.8)		98.8 (82.5, 117.8)		84.7 (64.0, 111.3)		65.2 (39.4, 106.2)	
Menopausal status	Pre	135.4 (117.4, 155.6)	0.01	124.6 (113.6, 136.4)	<0.001	NA		NA		NA	
	Peri	109.0 (92.8, 127.7)		101.4 (78.7, 129.8)							
	Post	114.2 (103.1, 126.4)		92.7 (84.0, 102.1)							
Menopausal hormone therapy	None	127.0 (111.2, 144.8)	0.63	97.0 (86.7, 108.5)	0.28	83.8 (76.5, 91.7)	0.18	76.5 (69.8, 83.9)	0.01	71.5 (64.2, 79.6)	0.20
	Combination	125.8 (83.6, 185.0)		137.4 (105.5, 177.1)		129.5 (96.3, 172.0)		120.7 (94.9, 152.4)		106.6 (79.4, 141.6)	
	Estrogen only	110.1 (85.6, 140.7)		105.4 (90.9, 121.8)		106.1 (86.0, 130.3)		125.1 (106.4, 146.6)		106.4 (82.6, 136.1)	
Oral contraceptives	No current	126.6 (110.9, 144.2)	0.05	99.0 (88.3, 110.7)	0.85	NA		NA		NA	
	Current use	110.4 (90.9, 133.6)		100.3 (84.4, 118.9)							
Body mass index, kg/m ²	<25	133.9 (118.1, 151.3)	0.006	105.9 (95.6, 117.2)	0.05	93.4 (85.4, 102.1)	0.31	79.5 (70.5, 89.5)	0.28	83.4 (69.8, 99.5)	0.20
	25 to <30	129.2 (114.7, 145.2)		99.3 (90.4, 108.9)		88.7 (79.1, 99.4)		84.1 (75.5, 93.6)		69.5 (58.5, 82.3)	
	30	110.7 (99.4, 123.2)		93.1 (84.2, 102.8)		89.2 (82.1, 96.8)		89.3 (78.5, 101.5)		88.4 (71.5, 108.8)	

* 2-sided P-values and 95% confidence intervals from a logistic regression model that accounts for clustering by radiology facility using generalized estimating equations.

† Categories include: almost entirely fat=fat; scattered fibroglandular densities=scattered; heterogeneously dense=heterogeneous; and extremely dense=extreme.

Abbreviations: kg=kilogram; m=meter; NA=not applicable; peri=perimenopausal; pre=premenopausal; post=postmenopausal.

Appendix Table 5

Rates of false-positive and false-negative digital mammography results and recommendations for additional imaging and biopsies by different breast density categories*

	Age, y									
	40-49		50-59		60-69		70-79		80-89	
Women screened, n	113,770		127,958		94,507		50,204		18,752	
False-positive mammography results										
Number per 1,000 women screened per round (95% CI)										
A Fat-Scattered	108.4 (95.5, 122.7)	<0.001	80.5 (71.1, 90.9)	<0.001	74.1 (66.4, 82.6)	<0.001	67.3 (60.4, 74.9)	0.003	60.3 (54.0, 67.4)	0.001
Heterogeneous	142.2 (120.2, 167.4)		115.8 (100.3, 133.2)		101.8 (91.0, 113.8)		88.7 (78.7, 99.9)		82.4 (72.6, 93.5)	
Extreme	112.1 (94.4, 132.7)		92.7 (77.5, 110.5)		75.2 (64.7, 87.1)		57.7 (43.9, 75.5)		85.1 (61.7, 116.2)	
B Fat	63.0 (51.2, 77.4)	<0.001	52.1 (44.9, 60.3)	<0.001	48.5 (43.1, 54.4)	<0.001	45.4 (39.7, 51.9)	<0.001	39.5 (32.1, 48.5)	<0.001
Scattered	116.8 (102.9, 132.3)		87.7 (77.1, 99.6)		81.6 (72.7, 91.4)		73.4 (65.4, 82.2)		65.8 (58.4, 73.9)	
Heterogeneous-Extreme	135.3 (113.9, 160.0)		112.0 (96.9, 129.2)		98.9 (88.4, 110.4)		86.2 (76.4, 97.1)		82.7 (72.6, 93.9)	
C Fat	63.0 (51.2, 77.4)	<0.001	52.1 (44.9, 60.3)	<0.001	48.5 (43.1, 54.4)	<0.001	45.4 (39.7, 51.9)	<0.001	39.5 (32.1, 48.5)	<0.001
Scattered	116.8 (102.9, 132.3)		87.7 (77.1, 99.6)		81.6 (72.7, 91.4)		73.4 (65.4, 82.2)		65.8 (58.4, 73.9)	
Heterogeneous	142.2 (120.2, 167.4)		115.8 (100.3, 133.2)		101.8 (91.0, 113.8)		88.7 (78.7, 99.9)		82.4 (72.6, 93.5)	
Extreme	112.1 (94.4, 132.7)		92.7 (77.5, 110.5)		75.2 (64.7, 87.1)		57.7 (43.9, 75.5)		85.1 (61.7, 116.2)	
D Fat-Scattered	108.4 (95.5, 122.7)	0.003	80.5 (71.1, 90.9)	<0.001	74.1 (66.4, 82.6)	<0.001	67.3 (60.4, 74.9)	<0.001	60.3 (54.0, 67.4)	<0.001
Heterogeneous-Extreme	135.3 (113.9, 160.0)		112.0 (96.9, 129.2)		98.9 (88.4, 110.4)		86.2 (76.4, 97.1)		82.7 (72.6, 93.9)	
False-negative mammography results										
Number per 1,000 women screened per round (95% CI)										
A Fat-Scattered	0.4 (0.3, 0.6)	<0.001	0.6 (0.4, 0.8)	0.002	0.8 (0.5, 1.1)	0.006	1.0 (0.6, 1.5)	0.01	0.9 (0.5, 1.6)	0.25
Heterogeneous	1.3 (1.0, 1.7)		1.4 (1.0, 2.0)		1.7 (1.3, 2.3)		2.3 (1.6, 3.4)		1.1 (0.5, 2.4)	
Extreme	1.7 (1.2, 2.5)		1.6 (0.9, 2.8)		1.2 (0.6, 2.7)		5.6 (2.4, 12.9)		6.9 (2.5, 18.5)	
B Fat	0.2 (0.0, 0.9)	<0.001	0.3 (0.1, 0.7)	<0.001	0.6 (0.2, 1.5)	0.007	0.3 (0.1, 1.1)	0.001	0.4 (0.1, 3.1)	0.14
Scattered	0.5 (0.3, 0.7)		0.7 (0.5, 0.9)		0.8 (0.6, 1.2)		1.2 (0.7, 1.9)		1.0 (0.6, 1.7)	
Heterogeneous-Extreme	1.4 (1.2, 1.8)		1.5 (1.1, 1.9)		1.6 (1.2, 2.2)		2.6 (1.8, 3.7)		1.7 (0.8, 3.3)	
C Fat	0.2 (0.0, 0.9)	<0.001	0.3 (0.1, 0.7)	<0.001	0.6 (0.2, 1.5)	0.02	0.3 (0.1, 1.1)	0.002	0.4 (0.1, 3.1)	0.17
Scattered	0.5 (0.3, 0.7)		0.7 (0.5, 0.9)		0.8 (0.6, 1.2)		1.2 (0.7, 1.9)		1.0 (0.6, 1.7)	
Heterogeneous	1.3 (1.0, 1.7)		1.4 (1.0, 2.0)		1.7 (1.3, 2.3)		2.3 (1.6, 3.4)		1.1 (0.5, 2.4)	
Extreme	1.7 (1.2, 2.5)		1.6 (0.9, 2.8)		1.2 (0.6, 2.7)		5.6 (2.4, 12.9)		6.9 (2.5, 18.5)	
D Fat-Scattered	0.4 (0.3, 0.6)	<0.001	0.6 (0.4, 0.8)	<0.001	0.8 (0.5, 1.1)	0.002	1.0 (0.6, 1.5)	0.003	0.9 (0.5, 1.6)	0.18
Heterogeneous-Extreme	1.4 (1.2, 1.8)		1.5 (1.1, 1.9)		1.6 (1.2, 2.2)		2.6 (1.8, 3.7)		1.7 (0.8, 3.3)	
Recommendations for additional imaging										
Number per 1,000 women screened per round (95% CI)										
A Fat-Scattered	110.8 (97.9, 125.2)	0.001	84.4 (74.8, 95.1)	<0.001	81.0 (73.1, 89.6)	<0.001	75.6 (68.5, 83.4)	0.003	68.9 (61.7, 76.9)	0.002
Heterogeneous	146.0 (123.9, 171.3)		121.6 (105.8, 139.3)		110.6 (99.7, 122.6)		99.0 (87.9, 111.4)		93.6 (82.4, 106.2)	
Extreme	116.5 (98.4, 137.4)		98.4 (83.1, 116.2)		81.0 (70.3, 93.2)		63.3 (49.7, 80.1)		92.0 (66.6, 125.7)	
B Fat	64.4 (52.3, 79.1)	<0.001	54.1 (46.5, 62.8)	<0.001	53.4 (47.9, 59.4)	<0.001	52.0 (46.5, 58.2)	<0.001	44.8 (36.6, 54.6)	<0.001
Scattered	119.4 (105.5, 135.0)		92.1 (81.2, 104.3)		89.0 (79.9, 99.1)		82.1 (73.9, 91.2)		75.2 (66.5, 84.8)	
Heterogeneous-Extreme	139.3 (117.7, 164.1)		117.8 (102.4, 135.3)		107.3 (96.7, 118.9)		96.1 (85.5, 107.9)		93.5 (82.1, 106.3)	
C Fat	64.4 (52.3, 79.1)	<0.001	54.1 (46.5, 62.8)	<0.001	53.4 (47.9, 59.4)	<0.001	52.0 (46.5, 58.2)	<0.001	44.8 (36.6, 54.6)	0.001
Scattered	119.4 (105.5, 135.0)		92.1 (81.2, 104.3)		89.0 (79.9, 99.1)		82.1 (73.9, 91.2)		75.2 (66.5, 84.8)	
Heterogeneous	146.0 (123.9, 171.3)		121.6 (105.8, 139.3)		110.6 (99.7, 122.6)		99.0 (87.9, 111.4)		93.6 (82.4, 106.2)	

		Age, y									
		40–49		50–59		60–69		70–79		80–89	
	Extreme	116.5 (98.4, 137.4)		98.4 (83.1, 116.2)		81.0 (70.3, 93.2)		63.3 (49.7, 80.1)		92.0 (66.6, 125.7)	
D	Fat-Scattered	110.8 (97.9, 125.2)	0.003	84.4 (74.8, 95.1)	<0.001	81.0 (73.1, 89.6)	<0.001	75.6 (68.5, 83.4)	0.001	68.9 (61.7, 76.9)	<0.001
	Heterogeneous-Extreme	139.3 (117.7, 164.1)		117.8 (102.4, 135.3)		107.3 (96.7, 118.9)		96.1 (85.5, 107.9)		93.5 (82.1, 106.3)	
Recommendations for biopsy											
Number per 1,000 women screened per round (95% CI)											
A	Fat-Scattered	12.2 (9.9, 15.0)	<0.001	11.8 (9.6, 14.5)	<0.001	15.6 (13.7, 17.7)	0.008	16.2 (14.2, 18.4)	0.007	14.2 (12.0, 16.8)	0.07
	Heterogeneous	18.9 (15.8, 22.5)		20.2 (17.3, 23.7)		19.3 (16.9, 22.2)		21.0 (18.0, 24.5)		19.0 (15.5, 23.2)	
	Extreme	20.2 (16.8, 24.3)		19.2 (14.3, 25.7)		13.8 (10.5, 18.2)		13.0 (7.2, 23.3)		16.1 (8.0, 32.1)	
B	Fat	7.5 (5.5, 10.1)	<0.001	8.4 (6.0, 11.7)	<0.001	11.7 (9.5, 14.6)	<0.001	12.8 (10.2, 16.1)	0.003	9.7 (5.8, 16.0)	0.04
	Scattered	13.1 (10.6, 16.1)		12.7 (10.3, 15.6)		16.7 (14.7, 19.0)		17.1 (14.9, 19.6)		15.4 (12.5, 18.8)	
	Heterogeneous-Extreme	19.2 (16.2, 22.7)		20.1 (16.9, 23.7)		18.7 (16.6, 21.2)		20.4 (17.4, 23.8)		18.7 (15.2, 23.0)	
C	Fat	7.5 (5.5, 10.1)	<0.001	8.4 (6.0, 11.7)	<0.001	11.7 (9.5, 14.6)	<0.001	12.8 (10.2, 16.1)	0.003	9.7 (5.8, 16.0)	0.06
	Scattered	13.1 (10.6, 16.1)		12.7 (10.3, 15.6)		16.7 (14.7, 19.0)		17.1 (14.9, 19.6)		15.4 (12.5, 18.8)	
	Heterogeneous	18.9 (15.8, 22.5)		20.2 (17.3, 23.7)		19.3 (16.9, 22.2)		21.0 (18.0, 24.5)		19.0 (15.5, 23.2)	
	Extreme	20.2 (16.8, 24.3)		19.2 (14.3, 25.7)		13.8 (10.5, 18.2)		13.0 (7.2, 23.3)		16.1 (8.0, 32.1)	
D	Fat-Scattered	12.2 (9.9, 15.0)	<0.001	11.8 (9.6, 14.5)	<0.001	15.6 (13.7, 17.7)	0.002	16.2 (14.2, 18.4)	0.008	14.2 (12.0, 16.8)	0.03
	Heterogeneous-Extreme	19.2 (16.2, 22.7)		20.1 (16.9, 23.7)		18.7 (16.6, 21.2)		20.4 (17.4, 23.8)		18.7 (15.2, 23.0)	

* 2-sided P-values and 95% confidence intervals from a logistic regression model that accounts for clustering by radiology facility using generalized estimating equations.

† Categories include: almost entirely fat=fat; scattered fibroglandular densities=scattered; heterogeneously dense=heterogeneous; and extremely dense=extreme.

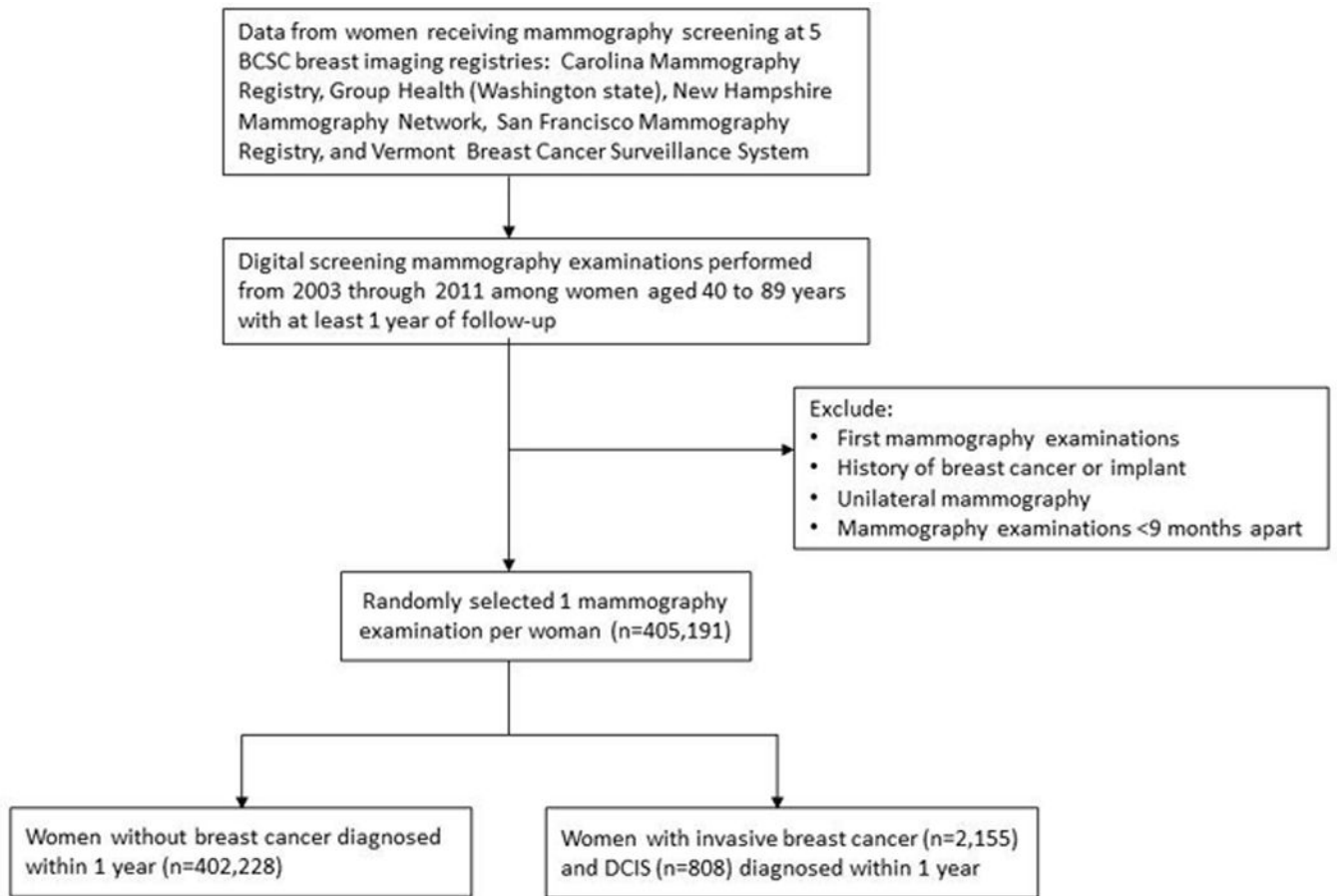


Figure 1.

Description of Breast Cancer Surveillance Consortium data sources for the study

Abbreviations: BCSC= Breast Cancer Surveillance Consortium; DCIS=ductal carcinoma in situ.

*Screening mammography examinations were those designated by the radiologist or radiology technologist as performed for screening and occurring more than 9 months after a previous imaging examination. Routine screening required at least one mammography examination within the previous 2 years (defined as 30 months).

Age-specific rates of false-positive and false-negative digital mammography results and recommendations for additional imaging and biopsies from a single screening round in the BCSC

Table 1

	Age, y					Difference (P-value)*
	40–49	50–59	60–69	70–79	80–89	
Women screened, <i>n</i>	113,770	127,958	94,507	50,204	18,752	
Invasive breast cancer cases, <i>n</i>	349	574	651	427	154	
DCIS cases, <i>n</i>	191	246	208	120	43	
Outcomes, <i>n</i> per 1,000 women screened (95% CI)						
False-positive mammography result	121.2 (105.6, 138.7)	93.2 (82.8, 104.7)	80.8 (72.9, 89.4)	69.6 (62.6, 77.3)	65.2 (58.8, 72.2)	<0.001
False-negative mammography result	1.0 (0.9, 1.2)	1.1 (0.9, 1.3)	1.2 (0.9, 1.5)	1.5 (1.1, 1.9)	1.3 (0.9, 1.9)	0.32
Additional imaging recommended [†]	124.9 (109.3, 142.3)	98.5 (88.0, 110.1)	88.7 (80.6, 97.4)	79.0 (71.9, 86.9)	74.4 (67.4, 82.2)	<0.001
Biopsy recommended [†]	16.4 (13.2, 20.3)	15.9 (12.7, 19.7)	16.5 (14.3, 19.1)	17.5 (15.2, 20.2)	15.6 (13.4, 18.2)	0.12
Screen-detected invasive cancer	2.2 (1.8, 2.6)	3.5 (3.1, 4.0)	5.8 (5.3, 6.4)	7.2 (6.4, 8.1)	7.1 (5.9, 8.5)	<0.001
Screen-detected DCIS	1.6 (1.3, 1.9)	1.8 (1.5, 2.2)	2.1 (1.7, 2.5)	2.3 (1.7, 3.0)	2.1 (1.5, 3.0)	0.05

* 2-sided P-values and 95% confidence intervals from a logistic regression model that accounts for clustering by radiology facility using generalized estimating equations.

[†] After positive mammography result.

Abbreviations: CI=confidence interval; DCIS=ductal carcinoma in situ.

Table 2

Rates of false-positive results after screening with digital mammography by risk factors*

Factor	Age, y								
	40-49	50-59	60-69	70-79	80-89				
Women screened, <i>n</i>	113,770	127,958	94,507	50,204	18,752				
False-positive, <i>n</i>	13,784	11,923	7,633	3,494	1,223				
Number per 1,000 women screened per round (95% CI)									
First-degree relatives with breast cancer									
None	118.7 (104.3, 134.7)	90.4 (81.1, 100.7)	0.005	79.4 (71.8, 87.7)	0.02	68.6 (61.1, 76.8)	0.11	63.3 (56.8, 70.5)	0.05
One or more	139.8 (113.9, 170.5)	109.0 (92.3, 128.2)		87.2 (77.2, 98.4)		75.0 (67.6, 83.1)		73.1 (64.1, 83.3)	
Breast density [†]									
Fat-Scattered	108.4 (95.5, 122.7)	80.5 (71.1, 90.9)	<0.001	74.1 (66.4, 82.6)	<0.001	67.3 (60.4, 74.9)	0.003	60.3 (54.0, 67.4)	0.001
Heterogeneous	142.2 (120.2, 167.4)	115.8 (100.3, 133.2)		101.8 (91.0, 113.8)		88.7 (78.7, 99.9)		82.4 (72.6, 93.5)	
Extreme	112.1 (94.4, 132.7)	92.7 (77.5, 110.5)		75.2 (64.7, 87.1)		57.7 (43.9, 75.5)		85.1 (61.7, 116.2)	
Benign breast biopsy									
None	114.3 (99.8, 130.5)	85.9 (76.7, 96.0)	<0.001	74.6 (66.8, 83.1)	<0.001	63.4 (56.2, 71.3)	<0.001	63.0 (56.3, 70.6)	0.09
Previous	167.3 (140.6, 197.9)	122.5 (106.2, 140.7)		98.6 (88.8, 109.3)		88.6 (79.1, 99.2)		71.6 (62.3, 82.3)	
Race/ethnicity									
White	127.0 (115.5, 139.4)	97.6 (89.5, 106.4)	0.001	83.8 (77.4, 90.7)	0.006	73.5 (67.7, 79.8)	<0.001	68.9 (62.6, 75.7)	0.04
Black	92.6 (82.0, 104.5)	78.9 (65.2, 95.3)		64.5 (53.6, 77.3)		58.9 (51.7, 67.0)		52.4 (43.6, 63.0)	
Asian	85.2 (72.2, 100.4)	67.6 (56.5, 80.7)		58.0 (47.9, 70.2)		43.6 (36.9, 51.6)		35.8 (29.6, 43.4)	
Hispanic	125.4 (106.8, 146.7)	80.9 (69.1, 94.6)		72.9 (60.3, 87.8)		60.7 (50.6, 72.8)		55.7 (31.3, 97.2)	
Other	127.8 (105.8, 153.6)	102.3 (88.5, 117.8)		91.5 (76.2, 109.5)		72.6 (53.3, 98.2)		48.9 (29.3, 80.6)	
Menopausal status									
Pre	131.3 (113.3, 151.8)	118.3 (107.2, 130.5)	<0.001	NA		NA		NA	
Peri	103.9 (88.5, 121.7)	97.6 (75.7, 125.1)							
Post	111.3 (100.2, 123.4)	87.2 (78.8, 96.4)							
Menopausal hormone therapy									
None	123.3 (107.4, 141.2)	91.8 (81.6, 103.2)	0.27	76.2 (69.2, 84.0)	0.22	67.6 (61.1, 74.8)	0.01	62.2 (55.5, 69.8)	0.27
Combination	122.0 (78.8, 184.1)	131.1 (99.5, 170.7)		122.5 (87.3, 169.2)		105.9 (81.8, 136.0)		94.0 (74.0, 118.8)	
Estrogen	108.7 (84.4, 138.8)	101.3 (87.1, 117.6)		97.6 (77.3, 122.5)		114.0 (94.8, 136.5)		89.1 (68.5, 115.1)	
Oral contraceptives									
No current	122.9 (107.2, 140.6)	93.6 (83.1, 105.4)	0.63	NA		NA		NA	
Current use	106.2 (86.4, 130.0)	97.0 (81.3, 115.2)							
Body mass index, <i>kg/m²</i>									
<25	129.0 (113.8, 145.9)	99.5 (89.3, 110.8)	0.04	85.8 (77.9, 94.4)	0.14	70.5 (62.0, 80.0)	0.78	73.9 (60.6, 89.8)	0.33
25 to <30	124.8 (110.1, 141.2)	93.6 (85.0, 103.0)		78.6 (69.5, 88.9)		72.7 (64.8, 81.6)		62.2 (51.4, 75.1)	

	Age, y					
	40-49	50-59	60-69	70-79	80-89	
Factor	30	107.2 (96.0, 119.5)	86.1 (77.7, 95.2)	81.1 (74.1, 88.6)	74.2 (64.1, 85.7)	73.8 (59.1, 91.9)

* 2-sided P-values and 95% confidence intervals from a logistic regression model that accounts for clustering by radiology facility using generalized estimating equations.

† Categories include: almost entirely fat=fat; scattered fibroglandular densities=scattered; heterogeneously dense=heterogeneous; and extremely dense=extreme.

Abbreviations: kg=kilogram; m=meter; NA=not applicable; peri=perimenopausal; pre=premenopausal; post=postmenopausal.

Table 3
Rates of recommendations for biopsy after screening with digital mammography by risk factors*

Factor	Age, y									
	40–49	50–59	60–69	70–79	80–89					
Women screened, <i>n</i>	113,770	127,958	94,507	50,204	18,752					
Biopsy recommended, <i>n</i>	1,863	2,030	1,562	880	293					
Number per 1,000 women screened per round (95% CI)										
First-degree relatives with breast cancer										
None	15.7 (12.6, 19.4)	0.002	14.8 (11.8, 18.4)	<0.001	15.8 (13.7, 18.3)	0.002	17.0 (14.7, 19.6)	0.09	15.2 (12.8, 18.0)	0.24
One or more	21.1 (16.9, 26.3)	21.9 (17.5, 27.3)	20.1 (17.0, 23.7)		20.3 (16.7, 24.6)		20.3 (16.7, 24.6)		17.6 (14.1, 22.1)	
Breast density [†]										
Fat-Scattered	12.2 (9.9, 15.0)	<0.001	11.8 (9.6, 14.5)	<0.001	15.6 (13.7, 17.7)	0.008	16.2 (14.2, 18.4)	0.007	14.2 (12.0, 16.8)	0.07
Heterogeneous	18.9 (15.8, 22.5)	20.2 (17.3, 23.7)			19.3 (16.9, 22.2)		21.0 (18.0, 24.5)		19.0 (15.5, 23.2)	
Extreme	20.2 (16.8, 24.3)	19.2 (14.3, 25.7)			13.8 (10.5, 18.2)		13.0 (7.2, 23.3)		16.1 (8.0, 32.1)	
Benign breast biopsy										
None	14.8 (11.8, 18.7)	<0.001	13.9 (11.1, 17.3)	<0.002	15.0 (12.7, 17.8)	<0.001	15.3 (13.1, 17.7)	<0.001	15.8 (13.4, 18.7)	0.54
Previous	27.8 (22.8, 33.7)	25.1 (20.1, 31.2)			21.8 (19.1, 24.9)		25.2 (21.4, 29.7)		17.1 (13.7, 21.5)	
White	16.7 (13.7, 20.3)	0.21	16.6 (13.6, 20.2)	0.39	17.6 (15.6, 20.0)	0.05	18.7 (16.6, 21.2)	0.23	16.2 (13.5, 19.4)	0.12
Race/ethnicity										
Black	13.6 (10.4, 17.8)	14.7 (10.4, 20.6)			13.9 (10.6, 18.0)		14.9 (11.4, 19.5)		8.9 (4.4, 18.0)	
Asian	16.2 (10.6, 24.5)	14.8 (9.5, 22.9)			12.0 (6.9, 20.6)		11.8 (6.8, 20.3)		9.2 (5.6, 15.3)	
Hispanic	16.3 (10.3, 25.6)	11.9 (8.1, 17.5)			14.2 (11.4, 17.6)		15.9 (10.1, 25.1)		16.4 (8.5, 31.5)	
Other	19.8 (14.4, 27.3)	17.4 (10.5, 28.6)			16.4 (10.8, 24.8)		16.6 (10.0, 27.6)		5.4 (0.7, 39.2)	
Menopausal status										
Pre	17.6 (14.0, 22.1)	0.49	19.8 (15.7, 24.9)	0.02	NA		NA		NA	
Peri	17.8 (14.4, 22.0)		16.4 (10.6, 25.4)							
Post	15.8 (12.5, 20.0)		15.4 (12.1, 19.4)							
Menopausal hormone therapy										
None	16.3 (13.2, 20.2)	0.34	15.6 (12.6, 19.2)	0.50	15.9 (13.9, 18.3)	0.37	17.2 (15.1, 19.4)	0.14	15.2 (12.8, 17.9)	0.13
Combination	15.2 (8.2, 28.2)		18.3 (12.7, 26.3)		16.9 (12.6, 22.6)		33.0 (23.7, 45.9)		21.9 (14.0, 34.2)	
Estrogen only	26.4 (14.7, 47.2)		18.3 (12.3, 27.2)		21.0 (14.5, 30.2)		25.3 (17.7, 36.1)		32.2 (22.2, 46.4)	
Oral contraceptives										
No current	16.7 (13.6, 20.6)	0.007	16.0 (13.1, 19.5)	0.32	NA		NA		NA	
Current use	12.5 (9.5, 16.3)		13.0 (7.0, 24.3)							
Body mass index, kg/m ²										
<25	21.4 (17.0, 26.8)	0.02	19.3 (14.7, 25.1)	0.40	17.4 (14.4, 21.0)	0.12	16.5 (13.5, 20.1)	0.02	17.1 (13.8, 21.2)	0.26
25 to <30	17.6 (13.7, 22.6)		18.0 (13.3, 24.4)		18.9 (15.3, 23.4)		21.9 (18.2, 26.3)		16.6 (12.5, 21.9)	
30	15.3 (12.3, 19.2)		18.4 (14.5, 23.4)		22.2 (18.1, 27.2)		26.7 (21.9, 32.4)		26.6 (18.5, 38.1)	

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* 2-sided P-values and 95% confidence intervals from a logistic regression model that accounts for clustering by radiology facility using generalized estimating equations.

[†]Categories include: almost entirely fat=fat; scattered fibroglandular densities=scattered; heterogeneously dense=heterogeneous; and extremely dense=extreme.

Abbreviations: kg=kilogram; m=meter; NA=not applicable; peri=perimenopausal; pre=premenopausal; post=postmenopausal.