Age-based versus Risk-based Mammography Screening in Women 40–49 Years Old:
A Cross-sectional Study

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Background: Risk-based screening in women 40–49 years old has not been evaluated in routine screening mammography practice.

Purpose: To use a cross-sectional study design to compare the trade-offs of risk-based and age-based screening for women 45 years of age or older to determine short-term outcomes.

Materials and Methods: A retrospective cross-sectional study was performed by using a database of 20 539 prospectively interpreted consecutive digital screening mammograms in 10 280 average-risk women aged 40–49 years who were screened at an academic medical center between January 1, 2006, and December 31, 2013. Two hypothetical screening scenarios were compared: an age-based (≥45 years) scenario versus a risk-based (a 5-year risk of breast cancer greater than that of an average 50-year-old) scenario. Risk factors for risk-based screening included family history, race, age, prior breast biopsy, and breast density. Outcomes included breast cancers detected at mammography, false-positive mammograms, and benign biopsy findings. Short-term outcomes were compared by using the χ^2 test.

Results: The screening population included 71 148 screening mammograms in 24 928 women with a mean age of 55.5 years ± 8.9 (standard deviation) (age range, 40–74 years). In women 40–49 years old, usual care included 50 screening-detected cancers, 1787 false-positive mammograms, and 384 benign biopsy results. The age-based (≥45 years) screening strategy revealed more cancers than did the risk-based strategy (34 [68%] vs 13 [26%] of 50; $P < .001$), while prompting more false-positive mammograms (899 [50.3%] vs 216 [12.1%] of 1787; $P < .001$) and benign biopsy results (175 [45.6%] vs 49 [12.8%] of 384; $P < .001$). The risk-based strategy demonstrated low levels of eligibility (few screenings) in the 40–44-year age group. Differences in outcomes in the 45–49-year age group explained the overall hypothetical screening strategy differences.

Conclusion: Risk-based screening for women 40–49 years old includes few women in the 40–44-year age range. Significant trade-offs in the 45–49-year age group explain the overall difference between hypothetical screening scenarios, both of which reduce the benefits as well as the harms of mammography for women 40–49 years old.

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Breast cancer is the leading cause of death for women 35–49 years old (1,2). Mammography reduces mortality for women between the ages of 40 and 49 years, but the benefits-to-harms ratio described in the literature is less favorable compared with that in women in older age ranges (3–5). The United States Preventive Services Task Force recommends that women 40–49 years old forgo screening unless motivated by risk or values when weighing potential benefits and harms (5). The American Cancer Society (ACS) encourages the option to screen starting at age 40 years considering personal risk and recommends annual screening starting at age 45 (4).

Risk-based screening in women 40–49 years old aims to balance the benefits with harms: early cancer detection and mortality reduction with false-positive mammograms, benign biopsy results, overdiagnosis, and associated anxiety (6). However, risk-based protocols may eliminate the mortality benefits of screening (7). Risk-based screening policies promote the use of breast cancer risk to determine the

Abbreviations

ACS = American Cancer Society, AUC = area under the receiver operating characteristic curve, BCSC = Breast Cancer Surveillance Consortium, CI = confidence interval, DCIS = ductal carcinoma in situ

Summary

Hypothetical screening scenarios show that for women 40–49 years old, initiating age-based mammography screening starting at age 45 reveals more cancers and results in more false-positive mammograms and benign biopsy results than risk-based screening; however, short-term outcome differences depended on age range: 40–44-year-olds in both scenarios had similar outcomes, which resembled those of not screening, while 45–49-year-olds showed significant differences for all outcomes.

Key Points

- Age-based mammography screening beginning at age 45 detected more cancers than risk-based screening (34 vs 13 of 50; $P < .001$), while prompting more false-positive mammograms (899 vs 216 of 1787; $P < .001$) and benign biopsy results (175 vs 49 of 384; $P < .001$).

- Both of the hypothetical screening scenarios of age-based (≥45 years) screening and risk-based screening decreased the benefits as well as the harms of screening women 40–49 years old.

- Significant differences between hypothetical screening scenarios in terms of cancers detected, false-positive mammograms, and benign biopsy results were driven by outcome divergence in the 45–49-year age range because screening is comparably low in the 40–44-year age range.

age to start screening in women younger than 50 years (4,5) and to inform the screening interval in women in age groups starting at 50 years and older (8). In this study, we focus on the former.

Risk prediction models designed to personalize mammography screening include personal and familial risk factors (9–11), which have been validated in case-control data (12) but less frequently in screening populations (13). A substantial number of women diagnosed with breast cancer do not exhibit breast cancer risk factors (14).

Virtually all mammography screening trials use an age-based rather than a risk-based recruitment strategy, emphasizing the importance of studying the effectiveness of risk-based breast cancer screening strategies prior to implementation. Growing interest in risk-based screening creates an urgent mandate to determine effectiveness (4–6,15). The Women Informed to Screen Depending on Measures of Risk, or WISDOM, trial (NCT02620852) will examine the effectiveness of a personalized, risk-based approach to breast cancer screening (16), with the risk of a 50-year-old woman as a threshold. However, in light of the expense and long-term commitment of randomized trials, observational studies can also assess risk-based screening in diverse and real-world environments (17). We examined short-term outcomes, meaning the immediate sequelae of the screening examination, including benefits (namely, screening-detected cancer) and harms (namely, false-positive mammograms and benign biopsy results), and did not examine the long-term outcome of mortality. We hypothesized that risk-based screening in this age group will reduce both short-term benefits and harms compared with age-based (≥45 years) screening. Our purpose

was to compare the trade-offs of risk-based and age-based screening for women 45 years of age or older.

Materials and Methods

The University of Wisconsin Health Sciences Institutional Review Board waived the need to obtain written informed consent for this Health Insurance Portability and Accountability Act–compliant database. Our study population was a subpopulation of a larger radiologic-epidemiologic database (details of which have been previously published [18]).

We derived the following two hypothetical cohorts: (a) a risk-based screening cohort of women 40–49 years old and (b) an age-based (≥45 years) screening cohort from a screening program that allows screening mammography from age 40 years.

Definitions and Measures

We used the Breast Cancer Surveillance Consortium (BCSC) Risk Calculator (9,10,16,19) to identify women who were eligible for risk-based screening. The BCSC model (*https://tools. bcsc-scc.org/BC5yearRisk/intro.htm*) uses variables to calculate 5- and 10-year risks of invasive breast cancer. These variables include age, family history of breast cancer in a first-degree relative, race/ethnicity, history of prior breast biopsy, and the American College of Radiology Breast Imaging Reporting and Data System, or BI-RADS, density category. Risk factors included in the BCSC Risk Calculator model were either clinically available or were routinely collected in our practice at the time of mammography.

Family history of breast cancer in a first-degree relative (mother, daughter, sister), race/ethnicity, and number of breast biopsies were all obtained from each woman's self-report on a clinical intake form at the time of mammography. The breast biopsy variable in the BCSC calculator allows the following entries: none (no prior biopsy); prior biopsy, unknown diagnosis; nonproliferative; proliferative without atypia; proliferative with atypia; and lobular carcinoma in situ (19). Detailed breast pathologic findings at prior breast biopsy are difficult to collect by self-report; thus, we used what each woman could report: either "none (no prior biopsy)" or "prior benign biopsy, unknown diagnosis."

We considered a mammogram to be a woman's baseline (first) mammogram if no prior examinations were cited in the current mammography report and no prior screening mammography reports were available in our system (PenRad Mammography module [commercially available], version 6; PenRad Technologies, Buffalo, Minn). Like investigators in previously published studies, we categorized mammographic intervals on the basis of the date of the prior screening mammogram as annual (9–18 months), biennial (19–30 months), or longer than biennial (>30 months) (20,21). Breast density was derived from each woman's prior mammography report and was categorized by using a scale on which a level of A indicated almost entirely fat; a level of B, scattered fibroglandular density; a level of C, heterogeneously dense; and a level of D, extremely dense. Breast density would not be available for risk calculation before a baseline mammogram. Therefore, for baseline studies, we considered this variable unknown. In addition, if the prior mammography report did not contain information on breast density (a rare circumstance)

Table 1: Distribution of Risk Factors Recorded for Screening Mammograms by Age

Risk Factor	Women 40–44 Years of Age (n = 9405)		Women 45–49 Years of Age (n = 11 134)		Women 50–74 Years of Age (n = 50 609)	
	No Cancer (n = 9385)	Cancer (n = 20)	No Cancer (n = 11 098)	Cancer (n = 36)	No Cancer (n = 50 332)	Cancer (n = 277)
Race/ethnicity						
White, not Hispanic	9212 (98.2)	19 (95.0)	10 667 (96.0)	36 (100.0)	48 801 (97.0)	269 (97.1)
Black, not Hispanic	40 (0.4)	0	131 (1.2)	0	491 (1.0)	2 (0.7)
Asian, not Hispanic	45 (0.5)	1 (5.0)	110 (1.0)	0	461 (0.9)	2 (0.7)
Hispanic	1 (0.0)	0	1 (0.0)	0	2 (0.0)	0
Native American/Other	21 (0.2)	0	35 (0.3)	0	101 (0.2)	1 (0.4)
Unknown	66 (0.7)	0	154 (1.4)	0	476 (0.9)	3 (1.1)
No. of first-degree relatives with breast cancer						
0	8114 (86.5)	14 (70.0)	9287 (83.7)	26 (72.2)	40 928 (81.3)	205 (74.0)
≥1	1271 (13.5)	6 (30.0)	1811 (16.3)	10 (27.8)	9404 (18.7)	72 (26.0)
BI-RADS breast density at prior mammogram						
A: Almost entirely fat	267 (2.8)	0	494 (4.5)	0	5862 (11.6)	26 (9.4)
B: Scattered fibroglandular	2142 (22.8)	4 (20.0)	3461 (31.2)	6 (16.7)	25 705 (51.1)	143 (51.6)
C: Heterogeneously dense	3702 (39.4)	7 (35.0)	5644 (50.9)	22 (61.1)	15 975 (31.7)	94 (33.9)
D: Extremely dense	728 (7.8)	2 (10.0)	969 (8.7)	5 (13.9)	1895 (3.8)	3 (1.1)
Baseline examination	2544 (27.1)	7 (35.0)	527 (4.8)	3 (8.3)	882 (1.8)	11 (4.0)
Left blank/missing	2 (0.0)	0	3 (0.0)	0	13 (0.0)	0
No. of prior breast biopsies						
None	9042 (96.3)	20 (100.0)	10 529 (94.9)	31 (86.1)	47 321 (94.0)	257 (92.8)
≥1	343 (3.7)	0	569 (5.1)	5 (13.9)	3011 (6.0)	20 (7.2)

Note.—Data are numbers of women, with percentages in parentheses. BI-RADS = Breast Imaging Reporting and Data System.

(Table 1), we also performed risk assessment using "unknown" for the breast density variable.

Study Population
We included prospectively interpreted consecutive screening mammograms as recorded in PenRad that were acquired in average-risk women 40–49 years old at our academic medical center from January 1, 2006, to December 31, 2013. The appropriate population for risk-based screening is women at an average rather than high risk for breast cancer. In fact, high-risk women may be screened by using protocols that include supplemental modalities like MRI. Therefore, we excluded mammograms in high-risk women (ie, those with a personal history of breast cancer [n = 5652] or a known high-risk genetic mutation like *BRCA* [n = 174]). We also excluded screening mammograms in women who had undergone mammography within the previous 9 months to avoid misclassifying a diagnostic examination as a screening examination (20), and we excluded mammograms that resulted in a diagnosis of non-breast cancers metastatic to the breast (n = 6) (Fig 1).

First, we constructed an age-based (≥45 years) screening scenario similar to the ACS guidelines (4) by removing all women younger than 45 years of age. Second, we constructed a risk-based screening strategy by designating the Surveillance, Epidemiology, and End Results, or SEER, average race-specific risk of invasive breast cancer plus ductal carcinoma in situ (DCIS)

for a 50-year-old woman as a threshold for screening eligibility. For example, the average SEER 5-year risk for white women is 1.23% (16) for invasive breast cancer and 0.35% for DCIS; therefore, the threshold for risk-based screening was the sum of these two risks: 1.58%.

Outcomes
We took a population perspective, viewing outcomes from the vantage point of the screening program as a whole. Breast cancer characteristics (invasive cancer vs DCIS, estrogen and progesterone receptor status, nodal status, and grade) were obtained by matching data with our Comprehensive Cancer Center cancer registry, which draws from the local health system and checks this population against the Wisconsin statewide cancer registry (22). If the registry recorded a diagnosis of invasive breast cancer or DCIS within 12 months after a mammogram, the mammogram, if positive, was a true-positive result or, if negative, was a false-negative result. False-positive results included a false-positive screening mammogram (a recommendation for additional testing) or a benign biopsy result and no registry match within 12 months.

Our primary outcome variables were numbers of cancers detected at mammography, false-positive mammograms, and benign biopsy results. The secondary outcome was the proportion of DCIS diagnosed at screening. Although we did not do statistical comparisons to our screening practice starting at age 40
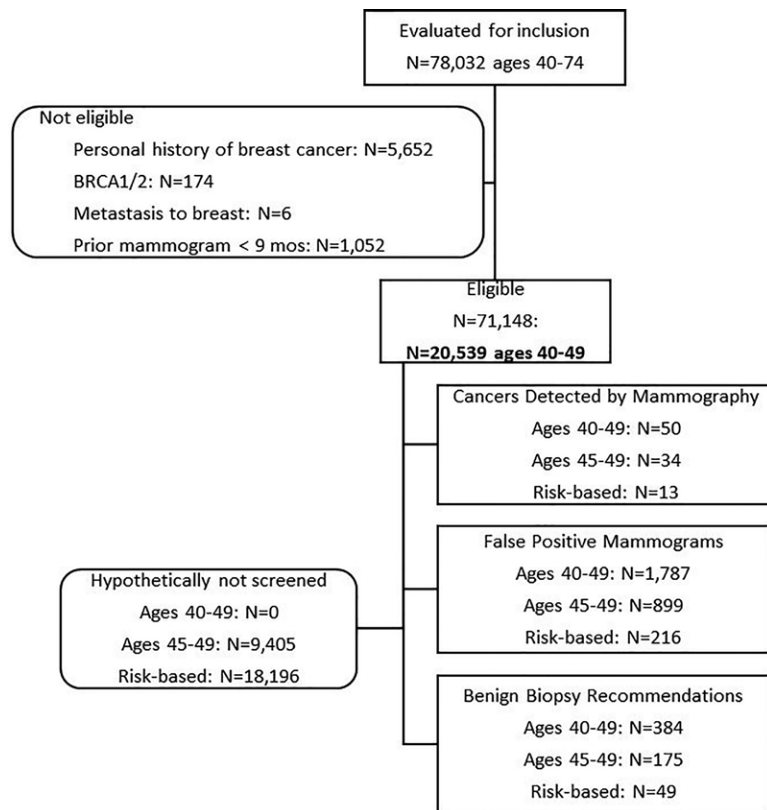
Figure 1: Flow diagram enumerates the mammograms included in this study.

years, for each hypothetical screening scenario, we calculated the following: mammograms not obtained, mammographically detectable cancers not diagnosed, false-positive mammograms avoided, and benign biopsy results avoided. We also calculated the time from the actual screening detection to the time that the woman became eligible for the given hypothetical screening scenario (age based or risk based) to determine the potential time lapse for screening detection associated with each strategy.

The cancer detection rate and the recall rate were calculated on the basis of the Breast Imaging Reporting and Data System, or BI-RADS, 5th Edition (23). All physicians interpreting mammograms in the context of routine clinical care (*n* = 19, including E.S.B.) were certified under the Mammography Quality Standards Act and had 5–15 years of experience; four were breast imaging fellowship trained.

Statistical Analysis
We limited our analysis to predefined primary and secondary outcome variables for the two hypothetical screening strategies using the χ^2 statistical test, defining a *P* value of less than .05 as indicating a statistically significant difference. We also estimated 95% confidence intervals (CIs) using generalized estimating equations, with an independence correlation structure to account for correlation among examinations for the same woman (24). We did not adjust for multiplicity of inferences in the study. We calculated the accuracy of the BCSC model in terms of discrimination and calibration to predict invasive cancer for comparison with prior literature (12,19). We calculated the

discrimination by using areas under the receiver operating characteristic curve (AUCs) and 95% CIs, using logistic regression for the BCSC 5-year breast cancer risk estimate. We determined the calibration of the BCSC risk prediction model by calculating the ratio of the expected breast cancers to the observed breast cancers in the subset of mammograms obtained from 2006 to 2009, because 5-year outcomes were available in this group. Statistical computations were performed by using SAS, version 9.4 (SAS Institute, Cary, NC). To account for dependencies between women who had more than one mammogram, we performed a similar analysis with one randomly selected mammogram per individual woman. We included all baseline mammograms, which are associated with higher rates of false-positive results than subsequent mammograms (for which comparison to prior mammograms is available [25]) in a secondary analysis (Appendix E1 [online]).

Results
The mean age at screening mammography for our screening population, which included 71 148 screening mammograms in 24 928 women, was 55.5 years ± 8.9 (age range, 40–74 years) (Fig 1). The younger age group (40–49 years) was comparable to the overall screening population in terms of race and ethnicity and demonstrated the following expected differences: higher breast density, less family history of breast cancer, and fewer breast biopsies (Table 1). The 56 women aged 40–49 years given a diagnosis of breast cancer showed a higher proportion of known risk factors than did women without breast cancer in each age group. Fifty of the 56 cancers were screening detected—there were 33 invasive cancers (24 local, seven regional, and two unclassified) and 17 instances of DCIS.

Age-based versus Risk-based Screening Outcomes
In women 40–49 years old, age-based (≥45 years) screening (Table 2) detected more cancers than did risk-based screening (34 of 50; 68%; 95% CI: 55.1%, 80.9% vs 13 of 50; 26%; 95% CI: 13.8%, 38.2%) (*P* < .001), while prompting more false-positive mammograms (899 of 1787; 50.3%; 95% CI: 48.0%, 52.7% vs 216 of 1787; 12.1%; 95% CI: 10.6%, 13.6%) (*P* < .001) and benign biopsy results (175 of 384; 45.6%; 95% CI: 40.6%, 50.6% vs 49 of 384; 12.8%; 95% CI: 9.4%, 16.1%) (*P* < .001). The proportion of breast cancers diagnosed as DCIS at mammography in the risk-based strategy was greater than that in the age-based strategy (five of 13; 38.5%; 95% CI: 12.0%, 64.9% vs 10 of 34; 29.4%; 95% CI: 14.1%, 44.7%) (*P* = .05). We demonstrated similar results when we included only one randomly selected record per woman within the 40–49-year age range and all baseline mammograms were included in the hypothetical scenarios (Appendix E1 [online]).

Table 2: Short-term Outcomes of Mammography in Women 40–49 Years of Age

Parameter	Usual Care in Women 40–49 Years of Age (n = 20 539)*	Age-based (≥45 Years) Screening (n = 11 134)†	Risk-based Screening in Women 40–49 Years of Age (n = 2343)†
Baseline mammography	2073 (10.1)	331 (3.0)	41 (1.7)
Primary outcome			
Cancers detected at mammography	50 (0.24)	34 (0.31)	13 (0.55)
False-positive mammograms	1787 (8.70)	899 (8.07)	216 (9.22)
Benign biopsy results	384 (1.87)	175 (1.57)	49 (2.09)
Secondary outcome: percentage DCIS‡	17/50 (34)	10/34 (29)	5/13 (39)
Comparison to age-based screening at ≥ 40 years			
Cancers not detected	…	16	37
Mammograms not performed	…	9405	18 196
False-positive mammograms avoided	…	888	1571
Benign biopsy results avoided	…	209	335

Note.—Unless otherwise specified, data are numbers of women, with percentages in parentheses. DCIS = ductal carcinoma in situ.

* Observed usual-care screening outcomes.

† Hypothetical screening strategies in women 40–49 years of age.

‡ No. of instances of DCIS detected/total no. of cancers detected at mammography.

Age-based (≥45 years) screening included 6390 (62.2%; 95% CI: 61.2%, 63.1%) of the 10 280 women aged 40–49 years and 11 134 (54.2%; 95% CI: 53.5%, 54.9%) of the 20 539 mammograms, while risk-based screening included 1339 (13.0%; 95% CI: 12.4%, 13.7%) of the 10 280 women aged 40–49 years and 2343 (11.4%; 95% CI: 11.0%, 11.8%) of the 20 539 mammograms (Fig 2). The differences between hypothetical age-based (≥45 years) and risk-based screening included 21 of 50 detectable cancers (42.0%; 95% CI: 28.3%, 55.7%), 683 of 1787 false-positive mammograms (38.2%; 95% CI: 36.0%, 40.5%), and 126 of 384 benign biopsy results (32.8%; 95% CI: 28.1%, 37.5%). Of the 50 screening-detected cancers diagnosed in the 40–49-year age group, 13 (26.0%; 95% CI: 13.8%, 38.2%) were detected in women who had no risk factors.

In women 40–44 years old, 16 cancers (nine invasive, seven DCIS) were detected on 9405 mammograms in our screening practice starting at age 40 years. In the 40–44-year age group, by definition, age-based (≥45 years) screening included no mammograms, no recalls, no biopsies, and no cancers detected. Risk-based screening included 480 mammograms, 46 recalls, 12 biopsies, and a single cancer detected (a case of DCIS).

The majority of cancers in our study were estrogen receptor positive and lymph node negative, with cancer characteristics for each hypothetical screening scenario listed in Table 3. The difference in time-to-detection that would have occurred between cancer detection in our screening practice starting at age 40 years and aged-based program eligibility varied from 1 year to 5 years. This same difference for the risk-based program varied between 1 year to 10 years. The average hypothetical delay for risk-based screening (3.9 years) was longer than that for age-based (≥45 years) screening (2.4 years). The time difference between actual detection and eligibility for a given hypothetical scenario did not appear to differ according to tumor subtype (invasive vs DCIS), hormone receptor status, or nodal status (Table 3).

### Risk Model Discrimination and Calibration

In screening mammograms in women aged 40–74 years, the BCSC model produced an AUC of 0.61 (95% CI: 0.58, 0.65) and a calibration expected/observed ratio of 1.06. In women aged 40–49 years, the BCSC model demonstrated an AUC of 0.678 (95% CI: 0.595, 0.761) and a calibration expected/observed ratio of 0.91.

Screening Practice and Performance

In women aged 40–74 years, 42 332 (59.5%; 95% CI: 59.1%, 59.9%) of 71 148 mammograms were annual, 16 729 (23.5%; 95% CI: 23.2%, 23.8%) were biennial, and 8113 (11.4%; 95% CI: 11.2%, 11.6%) were greater than biennial. In women aged 40–49 years, 9218 (44.9%; 95% CI: 44.2%, 45.6%) of 20 539 mammograms were annual, 5324 (25.9%; 95% CI: 25.3%, 26.5%) were biennial, and 2916 (14.2%; 95% CI: 13.7%, 14.7%) were greater than biennial. The majority of baseline mammograms were obtained in the 40–49-year age group (n = 3081) as compared with those in the 50–74 age group (n = 893). Performance metrics for all 71 148 mammograms showed a cancer detection rate of 4.19 per 1000 women and a recall rate of 8.19%.

Discussion

From a population perspective, our study showed that age-based (≥45 years) screening detected more cancers with more false-positive mammograms and benign biopsy results compared with a risk-based strategy. Because almost all women younger than 45 years old have a breast cancer risk lower than that of an average 50-year-old according to the Breast Cancer Surveillance Consortium (BCSC) model, risk-based screening in the 40–44-year age group generated fewer mammograms and detected only one out of 16 screening-detectable cancers, making the age-based (≥45 years) and the risk-based scenarios similar in this younger age range. Our study illustrates the short-term implications of changing practice from screening
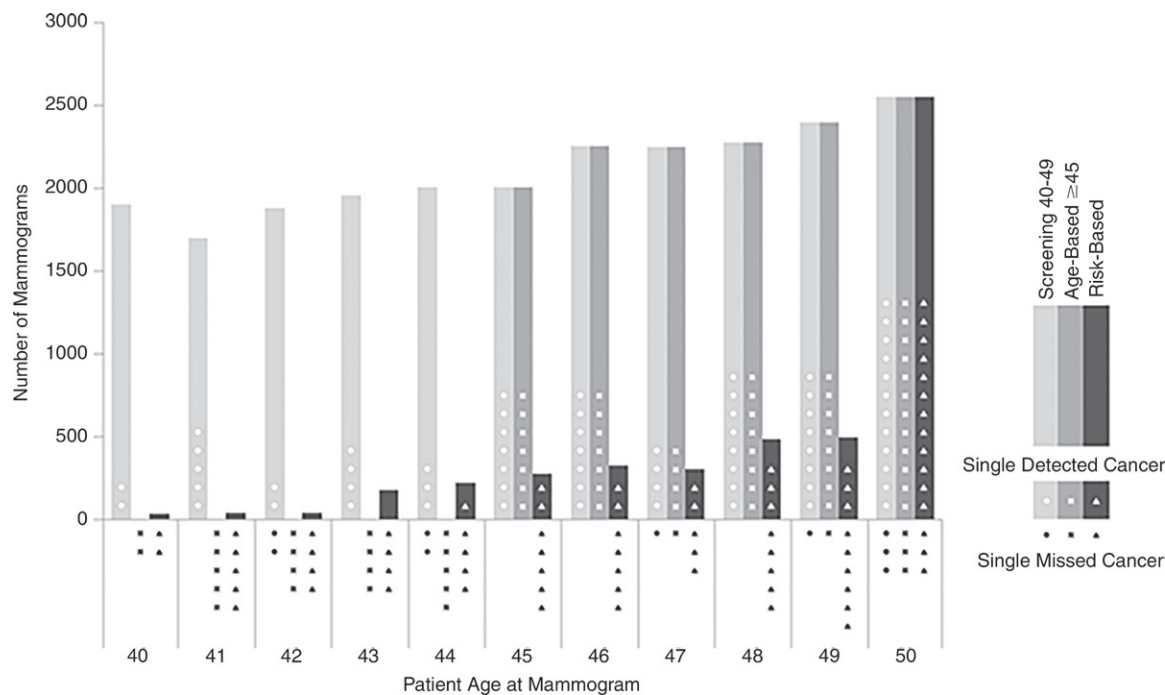
Figure 2: Bar graph shows the numbers of mammograms in usual care (screening at ages 40–49 years) (light gray bar) and for the hypothetical screening strategies of age-based (≥45 years) screening (medium gray bar) and risk-based screening (dark gray bar). The shapes within or below the respective bars represent screening-detectable breast cancers either detected at mammography (white shapes) or not detected at mammography (black shapes) according to screening strategy.

starting at age 40 years to either an American Cancer Society-like age-based (≥45 years) strategy or a WISDOM-like, risk-based strategy. Because we focused on short-term outcomes, we cannot know the long-term impact of undetected cancers. If a woman has a mammographically detectable cancer but is not eligible for screening, the impact of undetected cancers depends on the length of the diagnostic delay and tumor behavior, which tends to be more aggressive in younger women. A substantial delay would increase the likelihood that a cancer would be detected clinically, be larger, and be node positive.

A risk-based screening strategy depends on the accuracy of the risk model used and the threshold chosen. Performance for the BCSC model is available only for women 40–74 years of age (12,19). For women aged 40–74 years in our study, the BCSC model achieved an area under the receiver operating characteristic curve (AUC) of 0.614 for the task of discriminating whether a woman would develop breast cancer in 5 years—slightly lower than prior studies showing AUCs of 0.66 (95% CI: 0.61, 0.70) (12) and 0.664 (19). However, the AUC for our study population in the 40–49-year age group of 0.678 is comparable. For women aged 40–74 years in our study, the BCSC model calibration showed an expected/observed ratio of 1.06, similar to the ratio of 1.04 published previously (19). However, the expected/observed ratio for our study population in the 40–49-year age group of 0.91 is somewhat lower. We chose the risk of an average 50-year-old for invasive breast cancer plus ductal carcinoma in situ (DCIS) as our risk-based eligibility threshold. Although risk-based screening may provide the opportunity to align the decision to undergo mammography with women's risk

(and perhaps personal values and preferences if effective shared decision making is available), risk-based screening will be inherently more complicated to perform compared with age-based (≥45 years) screening (26–28), a topic that this study does not address. The decision to include DCIS may have resulted in the slightly higher proportion of DCIS in the risk-based scenario. When we included baseline mammograms in the hypothetical scenario results, conclusions do not change. Including baseline mammograms is clinically reasonable, reflecting a screening strategy that would enable breast density assessed on baseline mammograms (obtained in women older than 40 years, but otherwise without limitations of risk or age considerations), to influence the decision about future screening.

Our approach had some notable strengths. We showed that systematic risk factor collection in the clinic at the time of mammography is practical. Our method minimizes the problem of recall bias encountered in cross-sectional study designs. Importantly, our practice is well within performance benchmarks for screening mammography (23,29,30).

Our limitations included the lack of mortality follow-up, which precluded us from drawing conclusions on long-term outcomes. Potential biases of a retrospective, nonrandomized, observational study required us to draw conclusions with caution, although such investigations have been shown to provide accurate outcomes data (31,32). Reliance on patient self-report for previous breast biopsy information meant we could not collect detailed pathology data, which may have improved risk prediction performance; however, we demonstrated that the BCSC risk calculator performance is comparable to that in

Table 3: Cancer Characteristics and Time to Detection in Hypothetical Scenarios

Parameter	Total No. of Cancers	Invasive Cancers/in Situ Cancers	ER+/ER-/ER Status Unknown	PR+/PR-/PR Status Unknown	Nodal Status Negative/Positive	Cancer Grade 1/2/3/ Unknown
		Cancer Characteristics				
Cancers detected						
Screening scenario						
Usual care	50	33/17	43/2/5	36/6/8	43/7	13/20/9/8
Age based	34	24/10	28/1/5	25/1/8	29/5	10/13/7/4
Risk based	13	8/5	10/0/3	8/2/3	12/1	4/4/2/3
Cancers not detected						
Screening scenario						
Age based	16	9/7	15/1/0	11/5/0	14/2	3/7/2/4
Risk based	37	25/12	33/2/2	28/4/5	31/6	9/16/7/5
Time to detection (y)*						
Age-based screening						
1	3	0/3	3/0/0	1/2/0	3/0	1/0/2/0
2	4	4/0	4/0/0	4/0/0	2/2	0/3/0/1
3	2	0/2	2/0/0	2/0/0	2/0	1/1/0/0
4	5	5/0	4/1/0	3/2/0	5/0	1/1/0/3
5	2	0/2	2/0/0	1/1/0	2/0	0/2/0/0
Risk-based screening						
1	6	4/2	5/1/0	6/0/0	3/3	1/3/2/0
2	7	6/1	6/0/1	6/0/1	6/1	4/3/0/0
3	4	4/0	3/1/0	2/1/1	4/0	1/0/1/2
4	3	1/2	3/0/0	2/0/1	3/0	1/1/1/0
5	5	4/1	4/0/1	3/0/2	4/1	0/3/2/0
6	2	0/2	2/0/0	1/1/0	2/0	1/0/1/0
7	4	4/0	4/0/0	3/1/0	3/1	0/2/0/2
8	2	0/2	2/0/0	2/0/0	2/0	1/1/0/0
9	2	2/0	2/0/0	2/0/0	2/0	0/1/0/1
10	2	0/2	2/0/0	1/1/0	2/0	0/2/0/0

Note.—Data are numbers of cancers with a given characteristic. ER = estrogen receptor, PR = progesterone receptor.

* The time difference between actual detection in the screening program starting at age 40 years and the hypothetical scenario (age-based or risk-based) eligibility.

prior literature (12,19). In our primary analysis, hypothetical screening scenarios disproportionately excluded baseline mammograms in younger age groups, thereby potentially underestimating false-positive mammograms. However, subsequent analysis including all baseline examinations reinforced our initial results and conclusion. Our single-institution study had limited precision because of its modest sample size. Our study population had a high proportion of white women (the population of our screening mammography practice and catchment area), so results may not be generalizable to a more diverse group. We did not shed light on patient decision making or the practicality or cost of program implementation. We included only women reporting for screening rather than all women in the health system or region (ie, those that elect/do not elect to undergo screening).

In conclusion, we demonstrated that outcomes in an age-based (≥45 years) screening strategy versus a risk-based screening strategy in a high-quality screening practice differed significantly in the 45–49-year age group but not in the 40–44-year age group. The risk-based screening strategy exposed more women to delays in diagnosis prior to eligibility, and these delays were, on average, longer than those with age-based (≥45 years) screening. However, savings related to lower mammogram utilization and fewer false-positive mammograms and benign biopsy results accompany these missed detections. Understanding the projected differences in short-term outcomes between age-based and risk-based strategies—in the context of screening starting at 40 years of age—will enable researchers to predict outcomes that might occur in prospective studies. When choosing a screening strategy, physicians, patients, and policymakers will need to determine whether the trade-offs in both short-term and long-term outcomes are acceptable, while also weighing the practicality and complexity of each strategy.

Author contributions: Guarantors of integrity of entire study, E.S.B., L.G.W.; study concepts/study design or data acquisition or data analysis/interpretation, all authors; manuscript drafting or manuscript revision for important intellectual content, all authors; approval of final version of submitted manuscript, all authors; agrees to ensure any questions related to the work are appropriately resolved, all au-

thors; literature research, E.S.B., C.M.S.; clinical studies, E.S.B., S.B.S., L.G.W.; experimental studies, E.S.B., O.A., L.G.W.; statistical analysis, A.T., C.M.S., J.M.H., O.A.; and manuscript editing, all authors

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