

Utilization of breast cancer screening with magnetic resonance imaging in community practice

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BACKGROUND: Breast cancer screening with magnetic resonance imaging (MRI) may be a useful adjunct to screening mammography in high-risk women, but MRI uptake may be increasing rapidly among low- and average-risk women for whom benefits are unestablished. Comparatively little is known about use of screening MRI in community practice.

OBJECTIVE: To assess relative utilization of MRI among women who do and do not meet professional society guidelines for supplemental screening, and describe utilization according to breast cancer risk indications.

DESIGN: Prospective cohort study conducted between 2007 and 2014.

PARTICIPANTS: In five regional imaging registries participating in the Breast Cancer Surveillance Consortium (BCSC), 348,955 women received a screening mammogram, of whom 1499 underwent screening MRI.

MAIN MEASURES: Lifetime breast cancer risk (< 20% or ≥ 20%) estimated by family history of two or more first-degree relatives, and Gail model risk estimates. Breast Imaging Reporting and Data System breast density and benign breast diseases also were assessed. Relative risks (RR) for undergoing screening MRI were estimated using Poisson regression.

KEY RESULTS: Among women with < 20% lifetime risk, which does not meet professional guidelines for supplementary MRI screening, and no first-degree breast cancer family history, screening MRI utilization was elevated among those with extremely dense breasts [RR 2.2; 95% confidence interval (CI) 1.7–2.8] relative to those with scattered fibroglandular densities and among women with atypia (RR 7.4; 95% CI 3.9–14.3.) or lobular carcinoma in situ (RR 33.1; 95% CI 18.0–60.9) relative to women

with non-proliferative disease. Approximately 82.9% (95% CI 80.8%–84.7%) of screening MRIs occurred among women who did not meet professional guidelines and 35.5% (95% CI 33.1–37.9%) among women considered at low-to-average breast cancer risk.

CONCLUSION: Utilization of screening MRI in community settings is not consistent with current professional guidelines and the goal of delivery of high-value care.

KEY WORDS: breast neoplasms; magnetic resonance imaging; guideline adherence; early detection of cancer; risk factors.

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INTRODUCTION

Magnetic resonance imaging (MRI) has become much more widely utilized for breast cancer screening^{1, 2} since guidelines for MRI use in high-risk women were first issued in 2007. MRI is currently recommended for breast cancer screening among women with 20% or greater lifetime breast cancer risk by the American Cancer Society, the American College of Radiology, and the Society of Breast Imaging.³ The American College of Physicians advises against MRI screening for average-risk women.⁴ While much of the data regarding potential harms and benefits of screening MRI are derived from studies in high-risk populations,^{5–9} evidence is accumulating that screening MRI is diffusing to average-risk women,^{1, 2} for whom the benefit/harm ratio is unknown, and possibly lower.

Among women with a high breast cancer risk, annual screening with MRI in conjunction with mammography has led to increased cancer detection rates compared with mammography alone.^{5–9} In high-risk women, cancers detected by MRI are more likely to be earlier stage and node negative than

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those detected by mammography.^{5, 10} However, providers do not always recognize when women meet criteria for high breast cancer risk and should be referred for related services.¹¹ Although benefits of MRI screening of high-risk women are often accompanied by higher false-positive rates than mammography screening^{5, 7, 12} and direct evidence of decreased mortality with MRI use is lacking, low rates of supplemental MRI screening of women with 20% or greater lifetime risk could be considered a missed opportunity to utilize a technology that demonstrates promise for early detection.

Despite lack of data regarding benefit, results of several studies suggest that MRI screening is diffusing to lower risk women not covered by professional society recommendations.^{1, 2} Among women with less than 20% lifetime risk, performance of screening breast MRI, including cancer detection rates, false-positive rates, and recalls for biopsy and other diagnostic tests, has not been determined. In decision analytic models, screening MRI is not cost-effective unless utilized in extremely high-risk populations.^{13, 14} In the absence of data on the balance of benefits and harms, MRI screening among women with less than 20% lifetime risk might be considered unwarranted use of the technology. Relatively little is known about MRI utilization patterns in community practice.

Professional guidelines for screening MRI recommend that lifetime risk be determined by prediction models that use family history or high-risk mutation status as primary risk determinants. In models of lifetime risk based on family history, such as the Claus model, the International Breast Cancer Intervention Model, or the Breast and Ovarian Analysis of Disease Incidence and Carrier Estimation Algorithm,^{15–17} generally, a woman with two first-degree relatives with breast cancer has at least 20% lifetime risk and meets the threshold for annual MRI screening.

We sought to determine the utilization of supplemental screening with breast MRI among 348,955 women receiving mammography screening in the Breast Cancer Surveillance Consortium (BCSC). We examined MRI screening according to established breast cancer risk factors, using two or more first-degree relatives with breast cancer as an indicator of 20% or greater lifetime breast cancer risk.

METHODS

Study Setting and Data Sources

The study was conducted in five regional registries of the BCSC, a breast imaging network that collects risk factor, imaging, and pathology information as well as cancer diagnoses and vital statistics data for women undergoing breast cancer screening. Cancer diagnosis information is obtained from linkage to state tumor registries or to National Cancer Institute (NCI)-funded Surveillance, Epidemiology, and End Results (SEER) registries. Women who received mammograms during 2007–2014 at imaging facilities participating in the BCSC were eligible for this study. Data for this analysis

were collected from registries in California (San Francisco Mammography Registry, SFMR), Vermont (Vermont Breast Cancer Surveillance System, VBCSS), Washington State (Group Health Breast Cancer Surveillance Registry, GH), North Carolina (Carolina Mammography Registry, CMR), and New Hampshire (New Hampshire Mammography Network, NHMN).¹⁸ Each registry obtained Institutional Review Board approval for either active or passive consent processes or a waiver of consent to enroll participants, link data, and perform analysis. All procedures were Health Insurance Portability and Accountability Act (HIPAA) compliant. All registries and the Statistical Coordinating Center obtained a Federal Certificate of Confidentiality and other protections for the identities of women, physicians, and facilities who are subjects of this research.

Measures, Definitions, and Outcomes

All women aged 35–69 years without a personal history of ductal carcinoma in situ, invasive breast cancer, or breast augmentation who received a screening mammogram at a BCSC facility between 2007 and 15 months prior to the end of follow-up (NHMN December 2011; GH September 2013; SFMR and CMR December 2013; VBCSS September 2014) were eligible. A screening mammogram was defined as a bilateral mammogram with indication of “screening” recorded by the radiologist or technologist, which was not preceded by a mammography examination within the previous 9 months. A minimum of 15 months of follow-up was required to allow capture of receipt of screening MRI, our primary outcome. We restricted analyses to women screened at facilities that reported at least five MRI examinations during the study period to insure that MRI was available to attendees.

Demographic and risk factor information was collected using self-administered forms at the time of mammography. Women reported age, race/ethnicity, highest level of educational attainment, and first-degree family history of breast cancer. Prior biopsy results obtained from pathology reports were categorized as: non-proliferative disease, which included unknown; proliferative disease without atypia, atypical hyperplasia, and lobular carcinoma in situ (LCIS).¹⁹ Breast mammographic density obtained from radiologist assessment of mammograms was classified according to American College of Radiology Breast Imaging-Reporting and Data System (BI-RADS) criteria as almost entirely fat, scattered fibroglandular tissue, heterogeneously dense, and extremely dense.²⁰

The primary exposure of interest was 20% or greater lifetime breast cancer risk as defined by family history of two or more first-degree relatives with breast cancer, which usually exceeds the 20% threshold.^{15–17} We also calculated lifetime risk according to the NCI Breast Cancer Risk Assessment Tool, also known as the Gail model.²¹ Standard breast cancer risk factors included in the Gail model are current age, age at menarche and first live birth, number of first-degree relatives

with breast cancer, number of breast biopsies, and history of breast atypia.

Women were considered to have received supplemental screening MRI if an MRI with clinical indication “screening (asymptomatic)” was performed within 15 months before or 15 months following the screening mammogram.

Statistical Analysis

We compared the probability of being screened with MRI by patient characteristics, estimating adjusted relative risks (RR) of receiving a screening MRI and 95% confidence limits using modified Poisson regression estimated via generalized estimating equations. We used robust standard errors to account for violation of the Poisson mean-variance relationship.²² To allow for the additional opportunity to obtain a screening MRI among women who received more than one mammogram during the study period, the total number of mammography examinations observed for each woman was included as an offset in the Poisson model. All RR estimates were adjusted for age at first examination during the study period and for BCSC registry. Analyses were stratified by high risk ($\geq 20\%$ lifetime risk) vs. average/low-risk ($< 20\%$ lifetime risk) and age at screening examination (< 50 years, ≥ 50 years). As the BCSC is an open cohort, women receiving mammograms at a BCSC facility may have received screening MRI at a facility outside BCSC catchment. Thus, we report RRs for patient characteristics associated with MRI use, which are unbiased under imperfect outcome ascertainment.²³ All analyses were performed using SAS software v9.4 (Cary, NC).

RESULTS

Women screened with mammography included in the analysis ($n = 348,955$) underwent 1499 screening MRIs and were predominantly non-Hispanic white (69.9%) and college educated (53.3%) (Table 1). More than 43,000 of these women (12.5%) reported a first-degree family history of breast cancer. Approximately 1.4% of included women had a lifetime breast cancer risk of 20% or more according to the Gail risk model.

Women who reported either no or one first-degree relative with breast cancer, and who were therefore not eligible for screening MRI according to published guidelines, were 98.8% of included women ($n = 344,858$; 95% CI 98.8–98.9%) (Table 2). Among these women, those with established breast cancer risk factors were much more likely to undergo screening MRI. Women with one first-degree relative with breast cancer had a greater than eight-fold increased risk of undergoing a screening MRI compared with women with no affected first-degree relatives; an estimated 47.4% (710/1499; 95% CI 44.8–49.9%) of all screening MRIs was received by these women.

Among women who did not have a first-degree family history, we investigated other risk factors that might have prompted MRI screening. Women who reported a prior biopsy were 4.0 times more likely to undergo supplemental MRI than

Table 1 Characteristics of Women Who Received Breast Cancer Screening in the Breast Cancer Surveillance Consortium ($n = 348,955$)

Characteristic	N	%
Age at first examination (years)		
35–39	16,141	4.6
40–49	129,122	37.0
50–59	123,249	35.3
60–69	80,443	23.1
Race/ethnicity		
Non-Hispanic White	222,951	69.9
Non-Hispanic Black	23,155	7.3
Hispanic	20,453	6.4
Other	52,368	16.4
Missing	30,028	
Highest level of education		
HS grad/GED or less	62,092	21.2
Some college/technical	74,868	25.5
College grad or higher	156,586	53.3
Missing	55,409	
First-degree family history of breast cancer		
No	305,503	87.6
Yes	43,452	12.4
Had prior biopsy	16,737	5.2
Highest severity of prior biopsy		
Non-proliferative disease	11,157	66.7
Proliferative disease without atypia	4684	28.0
Proliferative disease with atypia	728	4.4
Lobular carcinoma in situ	168	1.0
BI-RADS density		
Almost entirely fat	32,166	10.3
Scattered fibroglandular tissue	121,751	39.1
Heterogeneously dense	124,730	40.0
Extremely dense	32,909	10.6
Missing	37,399	
Gail lifetime risk		
High $\geq 20\%$	4705	1.4
Average ($< 20\%$)	343,951	98.6
Missing	299	

BI-RADS: American College of Radiology Breast Imaging Reporting and Data System

women without a prior biopsy. Among biopsied women, the likelihood of MRI increased substantially with increasing degree of high-risk benign lesions. Compared to women whose biopsies had non-proliferative disease, risk of MRI receipt was over seven-fold higher among those with atypia and 33-fold higher among those with LCIS (p -trend < 0.001). Use of screening MRI also increased with BI-RADs breast density category. Women classified as having heterogeneously dense tissue were 1.5-fold more likely and those with extremely dense tissue were 2.2-fold more likely to be screened with MRI (p -trend < 0.001) than women with scattered fibroglandular tissue. Screening MRI utilization did not differ by age, except that women with a family history were more likely to obtain an MRI if age < 50 years (RR 11.2) vs. older (RR 6.6) (p -value heterogeneity < 0.0001). Women without a first-degree family history, who have low-to-average risk by family history-based guidelines, received 35.5% (532/1499; 95% CI 33.1–37.9%) of all MRIs.

The collective influence of breast cancer risk factors on use of supplemental MRI among women without a family history was reflected in the relationship between MRI use and Gail risk score (Table 2). Women with a Gail risk score of 15–19% lifetime breast cancer risk underwent MRI almost three times more often than women with less than 15% lifetime risk.

Table 2 Utilization of Breast Screening Magnetic Resonance Imaging (MRI) Among Women Undergoing Mammography with Less Than 20% Lifetime Risk of Breast Cancer, as Defined by Family History (Fewer Than Two Affected First-Degree Relatives) (n = 344,858).

Characteristic	Mammograms	MRIs	Relative risk		95% Confidence interval
Total	344,858	1242			
All ages: number of first-degree relatives with breast cancer					
None	305,503	532	1.0		
One	39,355	710	8.1	7.2	9.1
Among women with no family history of breast cancer	305,503	532			
Prior biopsy					
No	255,893	338	1.0		
Yes	13,683	91	4.0	3.1	5.1
Prior biopsy result					
Non-proliferative disease	9130	35	1.0		
Proliferative disease without atypia	3867	29	2.0	1.2	3.3
Proliferative disease with atypia	559	14	7.4	3.9	14.2
Lobular carcinoma in situ	127	13	33.1	18.0	60.9
Breast density (BI-RADS)					
Almost entirely fat	28,119	15	0.4	0.2	0.6
Scattered fibroglandular tissue	106,690	143	1.0		
Heterogeneously dense	108,594	227	1.5	1.2	1.9
Extremely dense	28,506	93	2.2	1.7	2.8
Missing	33,324	54			
Gail lifetime risk among all women at < 20% familial risk					
< 15%	303,984	511	1.0		
15–19%	1040	8	2.8	1.4	5.6
> 20%	216	13	20.5	11.7	36.1
Missing	263	0			
Age < 50 years at screening	144,240	707			
Number of first-degree relatives with breast cancer					
None	129,012	276	1.0		
One	15,228	431	11.2	9.6	13.0
Among women with no family history of breast cancer	129,012	276			
Prior biopsy					
No	114,977	196	1.0		
Yes	4702	45	4.1	3.0	5.7
Prior biopsy result					
Non-proliferative disease	3130	17	1.0		
Proliferative disease without atypia	1425	15	2.0	1.0	4.2
Proliferative disease with atypia	123	7	10.2	4.2	25.0
Lobular carcinoma in situ	24	6	38.0	16.6	87.0
Breast density (BI-RADS)					
Almost entirely fat	7568	8	0.62	0.3	1.3
Scattered fibroglandular tissue	37,424	58	1.0		
Heterogeneously dense	51,876	127	1.6	1.2	2.2
Extremely dense	17,482	55	2.1	1.4	3.0
Missing	14,662	28			
Gail lifetime risk among all women at < 20% familial risk					
< 15%	128,077	263	1.0		
15–19%	766	7	3.2	1.5	6.8
> 20%	100	6	21.2	9.5	47
Missing	69	0			
Age ≥ 50 years at screening	200,618	535			
Number of first-degree relatives with breast cancer					
None	176,491	256	1.0		
One	24,127	279	6.6	5.6	7.9
Among women with no family history of breast cancer	176,491	256			

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Table 2. (continued)

Characteristic	Mammograms	MRIs	Relative risk	95% Confidence interval	
Prior biopsy					
No	140,916	142	1.0		
Yes	8981	46	3.8	2.7	5.3
Prior biopsy result					
Nonproliferative disease	6000	18	1.0		
Proliferative disease without atypia	2442	14	1.9	1.0	3.9
Proliferative disease with atypia	436	7	5.5	2.3	13.0
Lobular carcinoma in situ	103	7	26.3	11.2	62.1
Breast density (BI-RADS)					
Almost entirely fat	20,551	7	0.3	0.1	0.5
Scattered fibroglandular tissue	69,536	85	1.0		
Heterogeneously dense	56,718	100	1.4	1.1	1.9
Extremely dense	11,024	38	2.6	1.8	3.9
Missing	18,662	26			
Gail lifetime risk among all women at < 20% familial risk					
< 15%	175,907	248	1.0		
15–19%	274	1	N.C.		
> 20%	116	7	23.1	11.0	48.7
Missing	194	0			

BI-RADS: American College of Radiology Breast Imaging Reporting and Data System
MRI, magnetic resonance imaging. N.C. Not calculated because of small cell sizes

Women with more than 20% lifetime risk were over 20-fold more likely to receive MRI and generally had breast biopsy results such as atypia. Thus, the Gail model, when applied among women who did not have a first-degree family history, may have influenced MRI use.

In contrast, women with two or more first-degree relatives with breast cancer ($n = 4097$; 1.2% of all women; 95% CI 1.1–1.2%) constituted a high-risk group who met the criteria for MRI (20% or greater lifetime risk) established by professional guidelines (Table 3). In this group, women with additional established breast cancer risk factors were also more likely to undergo screening MRI. Women with a history of breast biopsy were more than two-fold more likely than women without a prior biopsy to be screened (Table 3). The small number of women with high-risk lesions (e.g., LCIS) screened with MRI precluded analysis of trend. Women with heterogeneously dense or extremely dense tissue also were 1.6–1.9 times more likely to undergo supplemental MRI than those with scattered fibroglandular densities. MRI screening was not more common among women with Gail model scores indicating 30% or greater lifetime risk than women with 20% or greater lifetime risk. Age at screening did not modify MRI utilization.

Overall, 82.9% (1242/1499) of all screening MRI examinations were obtained by women for whom MRI was not recommended by professional guidelines because of minimal familial risk (95% CI 80.8–84.7%). Thus, only 17.1% of MRI imaging examinations (95% CI 15.3–19.1%) would be considered guideline-appropriate. Women with no family history and 15% or lower lifetime risk as calculated by the Gail model received more than one of three (34.0%; 511/1499; 95% CI 31.7–36.5%) screening MRIs.

DISCUSSION

Our data suggest use of screening MRI is not in concordance with professional society recommendations. We found that at least 6.3% (257/4097; 95% CI 5.6–7.1%) of women at high-risk for breast cancer, defined as two or more first-degree relatives with breast cancer, underwent screening MRI. In contrast, screening MRI was received by at least 0.36% (1242/344858; 95% CI 0.34–0.38%) of women who had fewer than two first-degree relatives with breast cancer. While the latter finding might seem of limited consequence, the continued growth of MRI use in a low-risk population poses issues for effective resource utilization; in the context of 39.3 million mammograms annually in the United States,²⁴ 0.36% implies more than 140,000 MRI screening examinations yearly in low- to average-risk women.

Screening guidelines from professional organizations recommend MRI use only among women deemed at elevated breast cancer risk: high-risk genetic mutation carriers, recipients of chest irradiation prior to age 30, and women at increased risk as calculated by models that largely depend on family history. Such recommendations are based on the limited evidence available from observational studies, in which women with a high genetic breast cancer risk who received MRI screening had an increased cancer detection rate,^{5–9} and identified cancers were often earlier stage than those detected through screening mammography.^{5, 10} However, the absence of data on mortality, the most clinically relevant outcome, together with higher false-positive rates for MRI than mammography, prompted restriction of MRI screening recommendations to women in whom the higher cancer detection rates might

Table 3 Utilization of Breast Screening Magnetic Resonance Imaging (MRI) Among Women Undergoing Mammography with 20% or more Lifetime Risk of Breast Cancer, as Defined by Family History (2 or more Affected First-Degree Relatives) (n = 4097)

Risk factor group	Mammography	MRI	Relative risk	95% Confidence interval	
Total	4097	257			
All ages					
Prior biopsy					
No	2898	152	1.0		
Yes	370	54	2.2	1.6	2.9
Prior biopsy result					
Non-proliferative disease	248	35	1.0		
Proliferative disease	95	12	1.0	0.5	1.8
Without atypia proliferative disease	22	4		N.C.	
With atypia lobular carcinoma in situ	5	3		N.C.	
BI-RADS density					
Almost entirely fat	451	12	0.5	0.3	0.9
Scattered fibroglandular tissue	1461	71	1.0		
Heterogeneously dense	1433	115	1.6	1.2	2.2
Extremely dense	383	45	1.9	1.3	2.7
Missing	369	14			
Gail model lifetime risk					
20–29%	2193	139	1.0		
30%+	952	93	1.1	0.8	1.4
Missing	952	25			
Age < 50 years at screening	891	107			
Screening prior biopsy					
No	792	86	1.0		
Yes	99	21	1.6	1.0	2.3
Prior biopsy result					
Non-proliferative disease	66	13	1.0		
Proliferative disease	28	5	1.0	0.4	2.3
Without atypia proliferative disease	4	2		N.C.	
With atypia lobular carcinoma in situ	1	1		N.C.	
BI-RADS density					
Almost entirely fat	70	6	0.8	0.4	1.7
Scattered fibroglandular tissue	293	29	1.0		
Heterogeneously dense	392	58	1.6	1.1	2.4
Extremely dense	171	21	1.4	0.8	2.2
Missing	97	6			
Gail model lifetime risk					
20–29%	401	55	1.0		
30%+	411	56	1.1	0.8	1.5
Missing	211	9			
Age ≥ 50 years at screening	2377	99			
Prior biopsy					
No	2106	66	1.0		
Yes	271	33	2.9	1.9	4.5
Prior biopsy result					
Non-proliferative disease	182	22	1.0		
Proliferative disease	67	7	1.0	0.4	2.2
Without atypia proliferative disease	18	2		N.C.	
With atypia lobular carcinoma in situ	4	2		N.C.	
BI-RADS density					
Almost entirely fat	381	6	0.4	0.2	0.9
Scattered fibroglandular tissue	1168	42	1.0		
Heterogeneously dense	1041	57	1.7	1.2	2.5

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Table 3. (continued)

Risk factor group	Mammography	MRI	Relative risk	95% Confidence interval	
Extremely dense	212	24	3.1	1.9	5.1
Missing	272	8			
Gail model lifetime risk					
20–29%	1792	84	1.0		
30%+	541	37	1.3	0.9	2.0
Missing	741	16			

BI-RADS: American College of Radiology Breast Imaging Reporting and Data System. N.C. not calculated because of small cell sizes

offset possible harms, such as the cascade of additional imaging and diagnostic procedures that can accompany a suspicious finding.²⁵ Increased cancer detection rates in high-risk populations without definitive proof of survival benefit also suggests possible harm from overdiagnosis. However, for high-risk women, the balance of benefits and harms has been judged to favor annual screening by MRI as one component of a comprehensive cancer surveillance plan.^{3, 26}

The supplemental MRI screening of women with low-to-average risk suggests that women and/or their physicians²⁷ use MRI for reasons not identified by our study. Concerns about mammography effectiveness or breast density notification laws may lead women at lower risk to seek advanced imaging, while physicians may be influenced by women's expectations, reimbursement mechanisms, risk aversion in a litigious legal climate, and confidence in the clinical effectiveness of MRI.^{27, 28} Our data suggest that women with atypia, LCIS, or extremely dense breast tissue in particular appear to receive MRI screening more frequently than women without those characteristics. Limited evidence is available regarding the benefits and harms of MRI among intermediate-risk women (above average risk and < 20% lifetime risk).^{5, 29–32} For women at intermediate risk, cancer detection rates by MRI appear similar⁵ or higher^{29–32} than by screening mammography, and recall rates are generally greater. However, even if sensitivity and specificity were equal among intermediate- and high-risk women, the lower cancer incidence in the intermediate-risk population (and thus lower positive predictive value) might preclude routine MRI use. Results of several analyses suggest that MRI screening is currently cost-effective, using standard criteria, only among women with high lifetime breast cancer risk.^{13, 14, 33, 34} Cancer yield and survival benefit with MRI may have to be high to support annual MRI screening of intermediate risk women.

As the complex balance of potential harms and benefits for screening MRI has been determined to result in a net benefit to women at familial high breast cancer risk,^{3, 26} MRI receipt by only a fraction of high-risk women presents an opportunity to improve identification of these women and offer MRI screening. Our data suggest that, after high familial risk was taken into account, other established risk factors for breast cancer played only a modest role in shaping MRI screening decisions.

For instance, women with over 30% lifetime risk according to the Gail score were no more likely to undergo MRI than women with 20–29% lifetime risk. Barriers to screening MRI receipt include access, out-of-pocket costs, and ability to tolerate the procedure; these may affect up to 40% of high-risk women.³⁵ These factors, coupled with a lack of recognition of high-risk women who might benefit from additional services,¹¹ suggest that if mortality benefits are clearly established, optimizing MRI screening benefits for high-risk women may require reduction of multiple barriers.

Limitations of our study include lack of data on high-risk mutation status, although this should correlate closely with breast cancer family history. We also lack pedigree information on ovarian cancer and on breast and ovarian cancer history in second-degree relatives. As a result, a small proportion of women may have been misclassified as low or average risk. Our analysis is limited to examinations performed in facilities that participate in the BCSC. Some women who received a screening mammogram at a BCSC facility may have received a screening MRI at a non-participating facility. By limiting the analysis to facilities that performed both mammography and MRI, we minimized potential under-ascertainment of MRI use. We are not able to estimate the actual prevalence of MRI use. However, the relative risk of undergoing MRI, comparing risk groups, is unbiased even with incomplete capture of MRIs.²³ Our study strengths include the availability of screening information from breast imaging facilities in five geographic regions, allowing inferences beyond the specifics of a single practice.

Breast MRI use that is not concordant with guidelines, as documented in this study, poses distinct challenges to effective resource allocation in breast cancer screening. Our data suggest that women with less than 20% lifetime risk based on family history, but who have high breast density, breast atypia, or LCIS, undergo MRI at many times the rate of other women, although the harms and benefits in this population are uncertain and the cost-benefit ratio may exceed established benchmarks.^{13, 14, 33, 34} Such women may not be at substantially increased risk of cancers missed by mammography (interval cancers) and thus not in need of screening MRI, in part because interval cancer rates are high among women at higher overall breast cancer risk.³⁶ In contrast, among women who meet professional guidelines for screening MRI, only a fraction received this service; thus, potential benefits may be missed.

Our data illustrate the substantial gap between current practice and supplemental MRI breast cancer screening that is both consistent with professional guidelines and the goal of delivery of high-value care.^{4,37} MRI performance measures should be evaluated in non-mutation carriers using validated risk models and consideration of survival benefit to guide MRI utilization.

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Compliance with ethical standards:

Conflict of interest: None of the authors have identified a conflict of interest in relation to this manuscript.

REFERENCES

1. Stout NK, Nekhlyudov L, Li L, et al. Rapid increase in breast magnetic resonance imaging use: trends from 2000 to 2011. *JAMA internal medicine*. 2014;174: 114-121.
2. Wernli KJ, DeMartini WB, Ichikawa L, et al. Patterns of breast magnetic resonance imaging use in community practice. *JAMA Intern Med*. 2014;174: 125-132.
3. Lee CH, Dershaw DD, Kopans D, et al. Breast cancer screening with imaging: recommendations from the Society of Breast Imaging and the ACR on the use of mammography, breast MRI, breast ultrasound, and other technologies for the detection of clinically occult breast cancer. *J Am Coll Radiol*. 2010;7: 18-27.
4. Wilt TJ, Harris RP, Qaseem A. High Value Care Task Force of the American College of P. Screening for cancer: advice for high-value care from the American college of physicians. *Ann Intern Med*. 2015;162: 718-725.
5. Kriege M, Brekelmans CT, Boetes C, et al. Efficacy of MRI and mammography for breast-cancer screening in women with a familial or genetic predisposition. *N Engl J Med*. 2004;351: 427-437.
6. Kuhl CK, Schrading S, Leutner CC, et al. Mammography, breast ultrasound, and magnetic resonance imaging for surveillance of women at high familial risk for breast cancer. *J Clin Oncol*. 2005;23: 8469-8476.
7. Leach MO, Boggis CR, Dixon AK, et al. Screening with magnetic resonance imaging and mammography of a UK population at high familial risk of breast cancer: a prospective multicentre cohort study (MARIBS). *Lancet*. 2005;365: 1769-1778.
8. Warner E, Plewes DB, Hill KA, et al. Surveillance of BRCA1 and BRCA2 mutation carriers with magnetic resonance imaging, ultrasound, mammography, and clinical breast examination. *JAMA*. 2004;292: 1317-1325.
9. Sardaneli F, Podo F, D'Agnolo G, et al. Multicenter comparative multimodality surveillance of women at genetic-familial high risk for breast cancer (HIBCRT study): interim results. *Radiology*. 2007;242: 698-715.
10. Warner E, Hill K, Causer P, et al. Prospective study of breast cancer incidence in women with a BRCA1 or BRCA2 mutation under surveillance with and without magnetic resonance imaging. *J Clin Oncol*. 2011;29: 1664-1669.
11. Bellcross CA, Leadbetter S, Alford SH, Peipins LA. Prevalence and healthcare actions of women in a large health system with a family history meeting the 2005 USPSTF recommendation for BRCA genetic counseling referral. *Cancer Epidemiol Biomarkers Prev*. 2013;22: 728-735.
12. Berg WA, Zhang Z, Lehrer D, et al. Detection of breast cancer with addition of annual screening ultrasound or a single screening MRI to mammography in women with elevated breast cancer risk. *JAMA*. 2012;307: 1394-1404.
13. Saadatmand S, Tilanus-Linthorst MM, Rutgers EJ, et al. Cost-effectiveness of screening women with familial risk for breast cancer with magnetic resonance imaging. *J Natl Cancer Inst*. 2013;105: 1314-1321.
14. Plevritis SK, Kurian AW, Sigal BM, et al. Cost-effectiveness of screening BRCA1/2 mutation carriers with breast magnetic resonance imaging. *JAMA*. 2006;295: 2374-2384.
15. Tyrer J, Duffy SW, Cuzick J. A breast cancer prediction model incorporating familial and personal risk factors. *Stat Med*. 2004;23: 1111-1130.
16. Claus EB, Risch N, Thompson WD. Autosomal dominant inheritance of early-onset breast cancer. Implications for risk prediction. *Cancer*. 1994;73: 643-651.
17. Antoniou AC, Cunningham AP, Peto J, et al. The BOADICEA model of genetic susceptibility to breast and ovarian cancers: updates and extensions. *Br J Cancer*. 2008;98: 1457-1466.
18. Ballard-Barbash R, Taplin SH, Yankaskas BC, et al. Breast Cancer Surveillance Consortium: a national mammography screening and outcomes database. *AJR Am J Roentgenol*. 1997;169: 1001-1008.
19. Santen RJ MR. Benign Breast Disorders. *N Engl J Med*. 2005;353: 275-285.
20. American College of Radiology. The American College of Radiology Breast Imaging Reporting and Data System (BI-RADS). 4th ed. Reston, VA. 2003.
21. Gail MH, Brinton LA, Byar DP, et al. Projecting individualized probabilities of developing breast cancer for white females who are being examined annually. *J Natl Cancer Inst*. 1989;81: 1879-1886.
22. Zou G. A modified poisson regression approach to prospective studies with binary data. *Am J Epidemiol*. 2004;159: 702-706.
23. Chubak J, Pocobelli G, Weiss NS. Tradeoffs between accuracy measures for electronic health care data algorithms. *J Clin Epidemiol*. 2012;65: 343-349 e342.
24. Mammography Quality Standards Act Statistics <http://www.fda.gov/radiation-emittingproducts/mammographyqualitystandardsactandprogram/ucm113858.htm>. Accessed November 21, 2016.
25. Hubbard RA, Kerlikowske K, Flowers CI, Yankaskas BC, Zhu W, Miglioretti DL. Cumulative probability of false-positive recall or biopsy recommendation after 10 years of screening mammography: a cohort study. *Ann Intern Med*. 2011;155: 481-492.
26. Saslow D, Boetes C, Burke W, et al. American Cancer Society guidelines for breast screening with MRI as an adjunct to mammography. *CA: a cancer journal for clinicians*. 2007;57: 75-89.
27. Kadivar H, Goff BA, Phillips WR, Andrilla CH, Berg AO, Baldwin LM. Guideline-inconsistent breast cancer screening for women over 50: a vignette-based survey. *J Gen Intern Med*. 2014;29: 82-89.
28. Hendee WR, Becker GJ, Borgstede JP, et al. Addressing overutilization in medical imaging. *Radiology*. 2010;257: 240-245.
29. Schwartz T, Cyr A, Margenthaler J. Screening breast magnetic resonance imaging in women with atypia or lobular carcinoma in situ. *J Surg Res*. 2015;193: 519-522.
30. Port ER, Park A, Borgen PI, Morris E, Montgomery LL. Results of MRI screening for breast cancer in high-risk patients with LCIS and atypical hyperplasia. *Ann Surg Oncol*. 2007;14: 1051-1057.
31. Friedlander LC, Roth SO, Gavenonis SC. Results of MR imaging screening for breast cancer in high-risk patients with lobular carcinoma in situ. *Radiology*. 2011;261: 421-427.
32. Sung JS, Malak SF, Bajaj P, Alis R, Dershaw DD, Morris EA. Screening breast MR imaging in women with a history of lobular carcinoma in situ. *Radiology*. 2011;261: 414-420.

33. **Moore SG, Shenoy PJ, Fanucchi L, Tumeh JW, Flowers CR.** Cost-effectiveness of MRI compared to mammography for breast cancer screening in a high risk population. *BMC Health Serv Res.* 2009;9: 9.
34. **Taneja C, Edelsberg J, Weycker D, Guo A, Oster G, Weinreb J.** Cost effectiveness of breast cancer screening with contrast-enhanced MRI in high-risk women. *J Am Coll Radiol.* 2009;6: 171-179.
35. **Berg WA, Blume JD, Adams AM, et al.** Reasons women at elevated risk of breast cancer refuse breast MR imaging screening: ACRIN 6666. *Radiology.* 2010;254: 79-87.
36. **Kerlikowske K, Zhu W, Tosteson AN, et al.** Identifying women with dense breasts at high risk for interval cancer: a cohort study. *Ann Intern Med.* 2015;162: 673-681.