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Breast cancer risk characteristics of women undergoing whole breast ultrasound screening versus mammography alone

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Abstract

Background: There are no consensus guidelines for supplemental breast cancer screening with whole breast ultrasound. However, criteria for women at high risk of mammography screening failures – interval invasive cancer or advanced cancer – have been identified. We evaluated mammography screening failure risk among women undergoing supplemental ultrasound screening in clinical practice compared to women undergoing mammography alone.

Methods: We identified 38,166 screening ultrasounds and 825,360 screening mammograms without supplemental screening during 2014–2020 within three Breast Cancer Surveillance Consortium (BCSC) registries. Risk of interval invasive cancer and advanced cancer were determined using BCSC prediction models. High interval invasive breast cancer risk was defined as heterogeneously dense breasts and BCSC 5-year breast cancer risk ≥2.5%, or extremely dense breasts and BCSC 5-year breast cancer risk ≥1.67%. Intermediate/high advanced cancer risk was defined as BCSC 6-year advanced breast cancer risk ≥0.38%.

Results: 95.3% of 38,166 ultrasounds were among women with heterogeneously or extremely dense breasts, compared to 41.8% of 825,360 screening mammograms without supplemental screening ($P<0.0001$). Among women with dense breasts, high interval invasive breast cancer risk was prevalent in 23.7% of screening ultrasounds, compared to 18.5% of screening mammograms without supplemental imaging (adjusted OR=1.35; 95%CI:1.30–1.39); intermediate/high advanced cancer risk was prevalent in 32.0% of screening ultrasounds versus 30.5% of screening mammograms without supplemental screening (adjusted OR=0.91; 95%CI:0.89–0.94).

Conclusions: Ultrasound screening was highly targeted to women with dense breasts but only a modest proportion were at high mammography screening failure risk. A clinically significant proportion of women undergoing mammography screening alone were at high mammography screening failure risk.

PRECIS

Whole breast ultrasound screening is highly targeted to women with dense breasts but only a modest proportion are at high risk of interval or advanced breast cancer. Consideration of other breast cancer risk factors beyond breast density could facilitate identification of women at high risk of mammography screening failures who may be appropriate for supplemental ultrasound screening.

Keywords

breast cancer; screening; ultrasound; mammography; risk factors; Breast Cancer Surveillance Consortium

INTRODUCTION

A number of studies have reported increased utilization of supplemental ultrasound screening following the implementation of U.S. state laws mandating breast density notification to women undergoing screening mammography.[1–5] A proposed amendment to the U.S. Mammography Quality Standards Act to require density notification nationally has further increased attention to limitations of mammography in women with dense breasts (heterogeneously dense or extremely dense) and the potential role for supplemental screening to increase early detection of breast cancer.[6, 7] However, there remain no consensus guidelines in the U.S. regarding which women undergoing screening mammography should receive supplemental ultrasound screening,[8–10] and uncertainty persists among women, primary care providers, and radiologists.[8, 11–16]

Supplemental ultrasound screening has the potential to detect cancers missed by mammography, though this gain is accompanied by potential harms including recall for additional imaging and benign breast biopsy among women who do not have breast cancer (false-positives).[8] The balance of benefits and harms may potentially be improved by targeting ultrasound screening to women at high risk of mammography screening failure, defined as a symptomatic interval invasive cancer or an advanced breast cancer diagnosis after mammography screening.[17, 18] In addition to breast density, other breast cancer risk factors (e.g., family history of breast cancer, prior benign breast disease diagnosis, and obesity) have been shown to be associated with likelihood of a mammography screening failure.[19] In the current clinical setting of variable referrals for ultrasound screening it is unclear how closely utilization of ultrasound screening is associated with a woman's risk of mammography screening failures.

We sought to evaluate the breast cancer risk characteristics of women undergoing ultrasound screening in a large sample of breast imaging facilities within three regional registries of the Breast Cancer Surveillance Consortium (BCSC). We contrasted the exam-level risk characteristics of women undergoing ultrasound screening to those of women undergoing mammography screening alone (no supplemental screening with ultrasound or MRI) at the same facilities, and characterized risks of interval invasive cancer and advanced cancer. The results inform understanding of ultrasound screening practice patterns in the U.S. and provide evidence regarding the extent to which ultrasound screening is utilized by women at high risk of mammography screening failures.

METHODS

Study Setting and Design

We analyzed observational clinical data from the Metro Chicago Breast Cancer Registry (2014–2018), San Francisco Mammography Registry (2014–2020), and Vermont

Breast Cancer Surveillance System (2014–2020), within the BCSC (https://www.bcsc-research.org/).[20] These three registries were chosen because they include a number of facilities performing screening ultrasound, whereas screening ultrasound remains rare within other BCSC registries. Each registry prospectively collected clinical breast imaging data from participating facilities within its catchment area. The registries and a central Statistical Coordinating Center (SCC) received Institutional Review Board approval to enroll participants, link data, and perform analyses. All procedures were Health Insurance Portability and Accountability Act compliant, and registries and the SCC received a Federal Certificate of Confidentiality and other protections for the identities of women, physicians, and facilities.

Study Population

This study included screening ultrasound and screening mammography examinations performed at 32 breast imaging facilities with at least 10 screening ultrasounds during the study period, 2014–2020 (40 facilities at the three participating BCSC registries had no screening ultrasounds or fewer than 10 screening ultrasounds and were not included). Exams among adult women age ≥18 years with no personal history of breast cancer were eligible for inclusion. Eligible screening ultrasound examinations were included regardless of mammography utilization before or after the ultrasound exam. As a comparison group, screening mammograms performed in women with no evidence of supplemental screening (ultrasound or MRI) within the next 12 months were identified from the same facilities and years.

Data Collection

Participating breast imaging facilities provided type of breast imaging modality (digital mammography, tomosynthesis, ultrasound, MRI), examination indication (screening vs. diagnostic), and mammographic breast density data to BCSC registries using standard nomenclature from the Breast Imaging Reporting and Data System (BI-RADS).[21] Breast density was recorded by radiologists during clinical interpretation of mammography using four categories: almost entirely fatty, scattered fibroglandular densities, heterogeneously dense, or extremely dense.[21] For screening ultrasounds, breast density was taken from the closest mammogram within 18 months (if available; otherwise breast density was defined as missing). Demographic, risk factor, and health history information was self-reported by women at the time of breast imaging or extracted from electronic medical records. Prior benign breast biopsy results were abstracted from clinical pathology reports. For the purposes of determining personal history of breast cancer (an exclusion criteria), we used clinical records and breast cancer diagnosis data ascertained by BCSC registries' linkage of women's breast imaging records to pathology databases; regional Surveillance, Epidemiology, and End Results programs; and state tumor registries, as previously described.[20]

Key Measures and Definitions

Women's characteristics were defined at each breast imaging examination. Women with heterogeneously or extremely dense breasts on mammography were considered to have dense breasts, consistent with conventional clinical and regulatory definitions.[22, 23] We

grouped prior benign diagnoses based on risk of developing subsequent breast cancer using published taxonomy[24–27] (lobular carcinoma in situ [LCIS] > atypical hyperplasia > proliferative without atypia > non-proliferative) or as unknown if a woman reported a prior biopsy with no available BCSC pathology result. First-degree family history of breast cancer included any breast cancer diagnosis in a mother, sister, or daughter. Body mass index (BMI) was categorized based on height and weight. Postmenopausal women were those with both ovaries removed, whose periods had stopped naturally, age 60 or older, current users of postmenopausal hormone therapy, or last menstrual period was over a year ago. Premenopausal women reported a period within the last 180 days or birth control hormone use. If menopausal status data was missing, women were assumed to be post-menopausal if age 52 years or older and pre-menopausal otherwise.

Risk for invasive breast cancer and interval invasive breast cancer were determined using the BCSC 5-year risk model version 2.0, which is applicable to women ages 35–74 with no prior history of DCIS or invasive breast cancer.[27] Five-year invasive breast cancer risk is based on age, race and ethnicity, first degree family history of breast cancer, prior history of benign breast disease, and breast density.[27] Using previously developed definitions,[17] we classified women as having high interval invasive breast cancer risk after mammography if they had heterogeneously dense breasts and BCSC 5-year invasive breast cancer risk ≥2.5% or extremely dense breasts and BCSC 5-year invasive breast cancer risk ≥1.67%. Women in these groups have interval invasive cancer rates exceeding 1 per 1000 exams after mammography screening.[17]

We estimated advanced breast cancer risk (defined as prognostic pathologic stage II or higher)[28] using the BCSC 6-year advanced breast cancer risk model (https://tools.bcsc-scc.org/AdvBC6yearRisk/#/), which is applicable to women aged 40–74 with no prior history of LCIS, DCIS, or invasive breast cancer.[29] The model is based on age, race and ethnicity, menopausal status, BMI, first-degree family history of breast cancer, prior history of benign breast disease, breast density, and mammography screening interval.[29] For all women, we estimated advanced cancer risk under an annual mammography screening regimen in the absence of supplemental screening. We classified women's advanced cancer risk according to previously defined thresholds for low/average (<0.38%) and intermediate/high advanced cancer risk (≥0.38%).[29]

Statistical Analyses

Screening breast imaging examinations were the unit of analysis. We described exam-level demographics and breast cancer risk characteristics of women undergoing ultrasound screening examinations and compared them to those of women undergoing screening mammography alone. We tested the association of demographic and risk characteristics with receipt of screening ultrasound using logistic regression adjusted for BCSC registry and estimated by generalized estimating equations with a working independence correlation structure to account for clustering of multiple exams per woman. Secondary analyses were restricted to exams among women with dense breasts. All analyses were conducted using SAS version 9.4 (SAS Institute, Cary, NC).

RESULTS

The study included 38,166 ultrasound screening exams among 29,112 women and 825,360 mammography screening exams among 377,140 women, yielding a ratio of one ultrasound screening exam for every 22 mammography alone screening episodes. Most ultrasound screening exams (75%) were the woman's first ultrasound screen and 63% of screening ultrasounds occurred within 9 months following a mammogram. Two percent of ultrasound screens occurred among women who had a prior MRI screening exam recorded in the BCSC database, compared to 0.4% among the mammography alone group. Approximately 69% of ultrasound screening exams occurred among women aged 40–59 years and 25.7% were among women who identified as Asian, Black, or Hispanic (Table 1). 95.3% of ultrasound screening exams were among women with dense breasts, while 21.7% occurred among women with a first-degree family history of breast cancer, 24.3% had a prior benign breast disease diagnosis, and 43.7% were among women who were overweight or obese. There were statistically significant differences in the distribution of demographic and risk characteristics between ultrasound screening exams and mammography screening alone exams (Table 1; $p<0.0001$). In comparison to mammography, ultrasound screening exams were much more likely to occur in women who were younger than age 50 years, premenopausal, had dense breasts, and normal body mass index. Small differences were observed in race/ethnicity, family history of breast cancer, and personal history of benign breast disease.

In analyses restricted to exams among women with dense breasts, there were 35,616 ultrasound screening exams and 342,343 mammography alone screening episodes, corresponding to a ratio of 1:10 (Table 2). In this subset of exams, ultrasound screening was more likely to occur in White women, and slightly more likely to occur among women who were younger than 50 years, premenopausal, had extremely dense breasts, a family history of breast cancer, and a history of benign breast disease. The distribution of body mass index was very similar across groups.

Among screening ultrasound exams in women ages 35–74, 27.2% occurred in women with intermediate BCSC 5-year invasive breast cancer risk (1.67–2.49%) and 18.1% occurred among women with high or very high BCSC 5-year invasive breast cancer risk (≥2.50%) (Figure 1A). In the comparator group of mammography alone exams, 19.6% occurred in women with intermediate BCSC 5-year invasive breast cancer risk and 9.5% occurred among women with high or very high BCSC 5-year invasive breast cancer risk. In analyses restricted to exams among women aged 35–74 years with dense breasts, 46.4% of screening ultrasound exams occurred in women with intermediate or higher BCSC 5-year invasive breast cancer risk, whereas 40.7% of mammography alone screening exams occurred in women with intermediate or higher BCSC 5-year invasive breast cancer risk (Figure 1B).

The joint distribution of breast density and BCSC 5-year invasive breast cancer risk across screening ultrasound and mammography screening examinations is shown in Figure 2. A total of 22.6% of screening ultrasounds were performed in women at high risk of interval invasive cancer after mammography due to having either heterogeneously dense breasts and BCSC 5-year invasive breast cancer risk of ≥2.5%, or extremely dense breasts and BCSC

5-year invasive risk ≥1.67%. Among the mammography alone comparator group, 8.0% of exams were in women at high interval invasive cancer risk (adjusted odds ratio [aOR]=3.28; 95%CI:3.17–3.39 for high interval invasive cancer risk, ultrasound vs. mammography). Among women with dense breasts, 23.7% of screening ultrasounds were performed in women at high risk of interval invasive cancer, whereas 18.5% of mammography alone exams were in women at high risk of interval invasive cancer (aOR=1.35; 95%CI:1.30–1.39).

Figure 3A illustrates that 30.7% of ultrasound screens among women ages 40–74 years occurred in women with intermediate or high BCSC 6-year advanced breast cancer risk (≥0.38%). Among the mammography alone comparator group, 18.6% of exams occurred in women with intermediate or higher advanced breast cancer risk (aOR=1.60; 95%CI:1.55–1.64 for intermediate or higher advanced cancer risk, ultrasound vs. mammography). In analyses restricted to exams among women aged 40–74 years with dense breasts, 32.0% of screening ultrasound exams occurred in women with intermediate or high BCSC 6-year advanced breast cancer risk, whereas 30.5% of mammography screening alone exams occurred in women with intermediate or high BCSC 6-year advanced breast cancer risk (aOR=0.91; 95%CI:0.89–0.94; Figure 3B).

DISCUSSION

Our results from a geographically diverse sample of breast imaging facilities in the United States demonstrate that ultrasound screening was predominantly utilized by women with dense breasts. Other breast cancer risk factors were also more common, and risk of mammography failures – interval invasive breast cancer and advanced cancer – was higher among ultrasound screening exams compared to mammography screening alone. Analyses restricted to exams among women with dense breasts indicated only modest differences in risk of interval or advanced cancer between the ultrasound and mammography alone groups. Overall, our findings indicate strong selection of women for ultrasound screening based on breast density alone and moderate selection based on other breast cancer risk factors, corresponding to a wide distribution in risk of mammography screening failure among women undergoing breast ultrasound screening.

The moderate differences in the risk distributions for invasive breast cancer, interval cancer, and advanced breast cancer observed in the full study population between ultrasound screening exams versus mammography alone exams narrowed substantially when restricted to exams among women with dense breasts. Most notably, the prevalence of intermediate or high 6-year advanced breast cancer risk among women with dense breasts was higher among mammography alone screening exams compared to supplemental ultrasound screening exams after adjusting for BCSC registry. This reinforces our conclusion that, aside from breast density, other factors associated with mammography failure risk such as obesity[29] are not commonly used to select women for supplemental ultrasound screening.

Our results also demonstrate that a clinically significant proportion of women at high risk of advanced cancer underwent mammography screening alone with no supplemental screening.

These findings suggest a potential role for risk assessment at the time of mammography screening or during primary care visits when screening strategies are discussed.

While consensus guidelines for supplemental ultrasound screening do not exist in the U.S., the American College of Radiology's Expert Panel on Breast Imaging recently concluded that ultrasound screening may be appropriate for high-risk women with non-dense breasts (almost entirely fatty and scattered fibroglandular densities) and intermediate or high-risk women with dense breasts, whereas supplemental ultrasound screening is usually not appropriate for average or intermediate risk women with non-dense breasts.[10] The panel disagreed as to whether ultrasound screening may be appropriate for average-risk women with dense breasts. In our study, mammography failure risk varied widely among women undergoing breast ultrasound screening. Approximately half of ultrasound screening exams occurred among women with dense breasts and low or average breast cancer risk who are not at high risk of screening failures. One-fifth of women undergoing ultrasound screening in our study were classified as having high interval invasive breast cancer risk with mammography based on their breast density and BCSC 5-year risk.[17] Approximately 1 in 3 women undergoing ultrasound screening had intermediate or higher advanced cancer risk. These observations underscore the need for additional research to determine in what population ultrasound screening reduces the risk of screening failures.

Ultrasound screening was relatively rare at the participating breast imaging facilities (1 per 22 mammography alone screening episodes, and 1 per 10 mammography alone exams among women with dense breasts). Almost 20% of mammography alone screening exams (corresponding to over 126,000 screening episodes) occurred among women with intermediate or high advanced cancer risk, exceeding by far the total number of ultrasound screening episodes (38,166) and demonstrating that a large group of women at high advanced cancer risk did not undergo supplemental ultrasound or MRI screening. Efforts to increase supplemental ultrasound or MRI screening utilization among women at high risk of mammography failure may improve breast cancer screening outcomes.[17, 18, 29] Numerous studies have demonstrated that the addition of supplemental ultrasound to mammography increases cancer detection rates,[8, 30] and evidence is also emerging that supplemental ultrasound screening is associated with reduced interval cancer rates compared to mammography alone.[31, 32]

While breast density notification laws have focused attention on the limitations of mammography for women with dense breasts, a growing literature has highlighted the importance of additional risk factors in contributing to risk of mammography screening failures.[17, 18, 29] Laws and policies that mandate breast density notification without consideration of other risk factors may be inadequate to direct supplemental screening efforts to women at risk of mammography failures. Tools for estimating breast cancer risk and risk of mammography screening failure are available, though consensus on which measures are most appropriate has not been established and further research on implementation strategies in clinical practice will be needed. The BCSC 5-year breast cancer risk model v2.0 calculator is freely available online,[33] and can be combined with breast density to identify women at elevated risk of mammography interval invasive breast cancer as done in this study.[17] The BCSC 6-year advanced cancer risk model was developed

to directly estimate advanced cancer risk as a function of age, race/ethnicity, menopausal status, screening interval, BMI, first degree family history of breast cancer, prior history of benign breast disease, and breast density.[29] To facilitate use, the risk model publication[29] includes look-up tables showing advanced cancer risk for combinations of risk factors and is available as an online calculator.

Our results are consistent with prior work showing that ultrasound screening utilization is associated with age, breast density, and family history of breast cancer.[4] In the prior BCSC analysis of ultrasound screening in the BCSC during 2006–2013, 74% of ultrasound screening exams occurred among women with dense breasts; 46% occurred among women with intermediate or higher BCSC 5-year invasive cancer risk.[34] While BI-RADS guidelines for breast density assessment changed in 2013,[21, 35] our prior work indicates that density assessment in clinical practice remained consistent within the BCSC[36] and thus is unlikely to explain the change in breast density prevalence between the prior BCSC ultrasound study and the current study. While our current study indicates that ultrasound screening during 2014–2020 was more narrowly targeted to women with dense breasts, the distribution of breast cancer risk among women undergoing ultrasound remained similar between the two studies. Our analyses provide new evidence regarding the distribution of mammography failure risk among women undergoing ultrasound screening.

Interpretation of our results must be tempered by the limited data on ultrasound screening performance according to risk characteristics and uncertainty about the appropriateness of ultrasound screening in population subgroups.[10] While prior work has characterized women at high risk of mammography screening failures,[17, 18, 29] evidence on the impact of supplemental ultrasound screening on breast cancer outcomes among women at high mammography screening failure risk is not yet available. Ultrasound screening is not without potential harms in the form of false-positives. A prior BCSC study estimated that supplemental ultrasound screening was associated with an approximate doubling of the false-positive biopsy recommendation rate compared to mammography alone.[34] Further study is needed to characterize ultrasound screening performance and long-term outcomes according to risk of mammography screening failure. In the current absence of consensus recommendations, the decision to undergo supplemental ultrasound screening should involve a consideration of both potential benefits and harms, personal preferences, and values.[11]

Strengths of our study include a geographically and racially diverse sample of breast imaging facilities from U.S. community practice, prospectively collected breast imaging and risk factor data via three BCSC registries, and the use of established BCSC risk prediction models. Notably, the three registries were selected because they included a number of breast imaging facilities offering screening ultrasound; thus, the rate of ultrasound screening is higher than would be observed across all BCSC registries. We did not examine the impact of density notification laws in this study, which were enacted in 2013, 2017, and 2019 for California, Vermont, and Illinois, respectively (Illinois mandated insurance coverage of supplemental screening for women with dense breasts beginning in 2009). However, our study characterizes utilization of screening ultrasound during a contemporary era of increased breast density awareness following national patient advocacy efforts,[37–40] which undoubtedly contributed to the observed enrichment of ultrasound screening exams among

women with dense breasts. The BCSC risk models have moderate discrimination, they do not consider potentially useful predictors such as family history of breast cancer in second-degree relatives, genetic polymorphisms, or quantitative image-based mammographic features, and it is unclear how commonly they are used in clinical practice. However, the BCSC invasive breast cancer risk model is well calibrated in comparison to other models and externally validated in three cohorts.[41–43] To our knowledge, the BCSC advanced cancer risk model is the only available risk model for advanced breast cancer. Our study does not directly address the degree to which ultrasound screening may be targeted based on other breast cancer risk models commonly used in clinical practice. Finally, we were unable to examine the frequency of high penetrance genetic mutations (e.g., *BRCA1/2*). However, the modest frequency of first-degree family history among women undergoing ultrasound screening suggests that these were unlikely to be common, and supplemental MRI screening is recommended for *BRCA* mutation carriers.[44] Further study is needed of sociodemographic predictors of ultrasound screening, barriers to ultrasound screening access, and implementation strategies for delivery of information on risk of breast cancer and mammography failures.

In summary, we found that ultrasound screening in this geographically-diverse multi-site study was strongly targeted to women with dense breasts. The distributions of breast cancer risk, interval invasive breast cancer risk, and advanced cancer risk varied widely among women undergoing ultrasound screening. Many women at high risk of screening mammography failure did not undergo supplemental screening following mammography. Consideration and further public awareness of other breast cancer risk factors beyond breast density could facilitate identification of women at high risk of mammography screening failures who may be appropriate for supplemental ultrasound screening.

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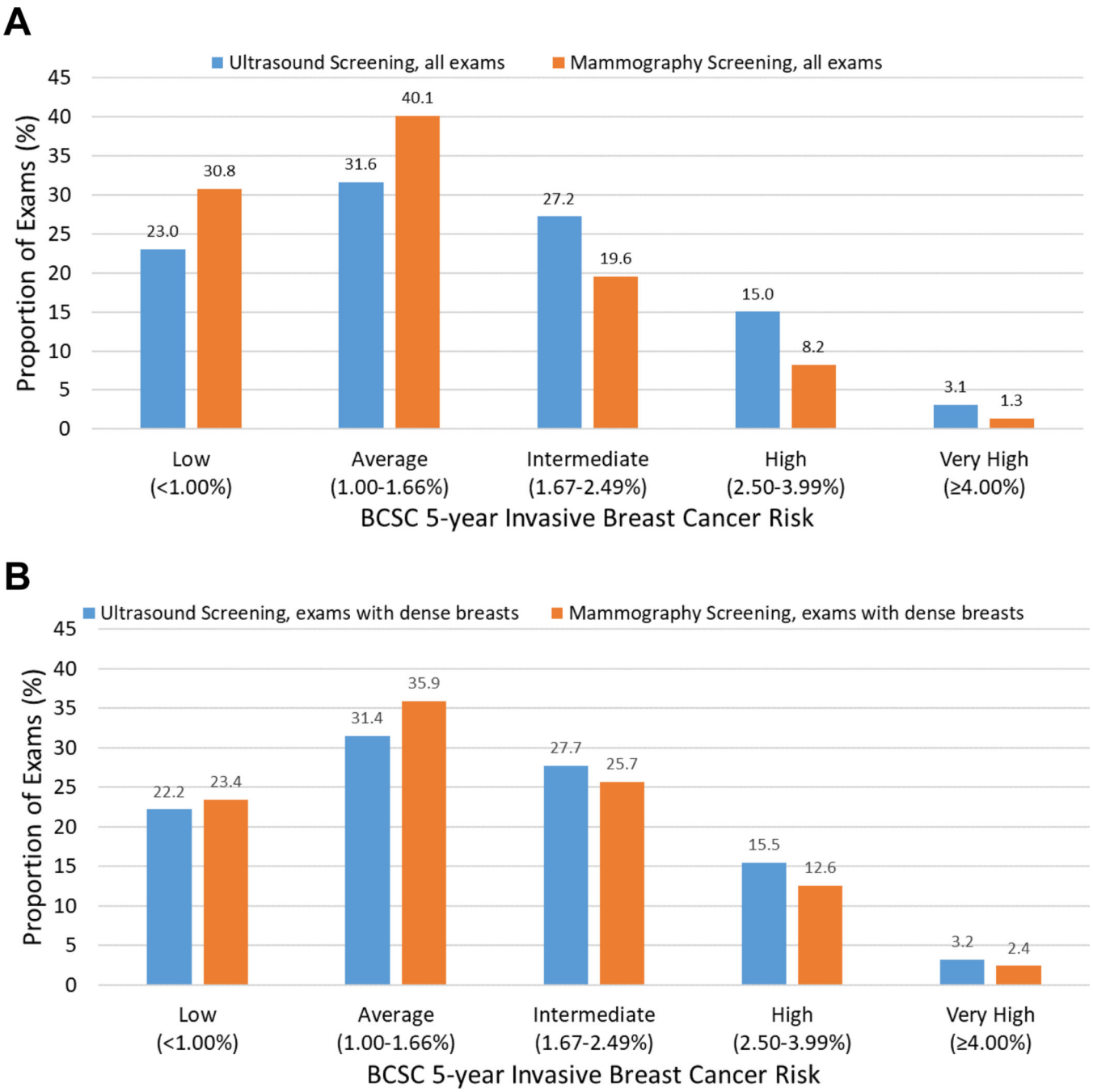

Figure 1. Distribution of BCSC 5-year invasive breast cancer risk.

Among (A) all women ages 35–74 and (B) women ages 35–74 with dense breasts undergoing ultrasound screening exams or mammography screening alone at 32 breast imaging facilities participating in the Vermont, San Francisco and Chicago Breast Cancer Surveillance Consortium registries, 2014–2020. The BCSC 5-year invasive breast cancer risk model is not applicable for women under age 35 or over age 74 years. Among women aged 35–74 years, invasive breast cancer risk could not be calculated due to missing breast

density for 1.8% of eligible ultrasound screening exams and 0.7% of eligible mammography screening exams.

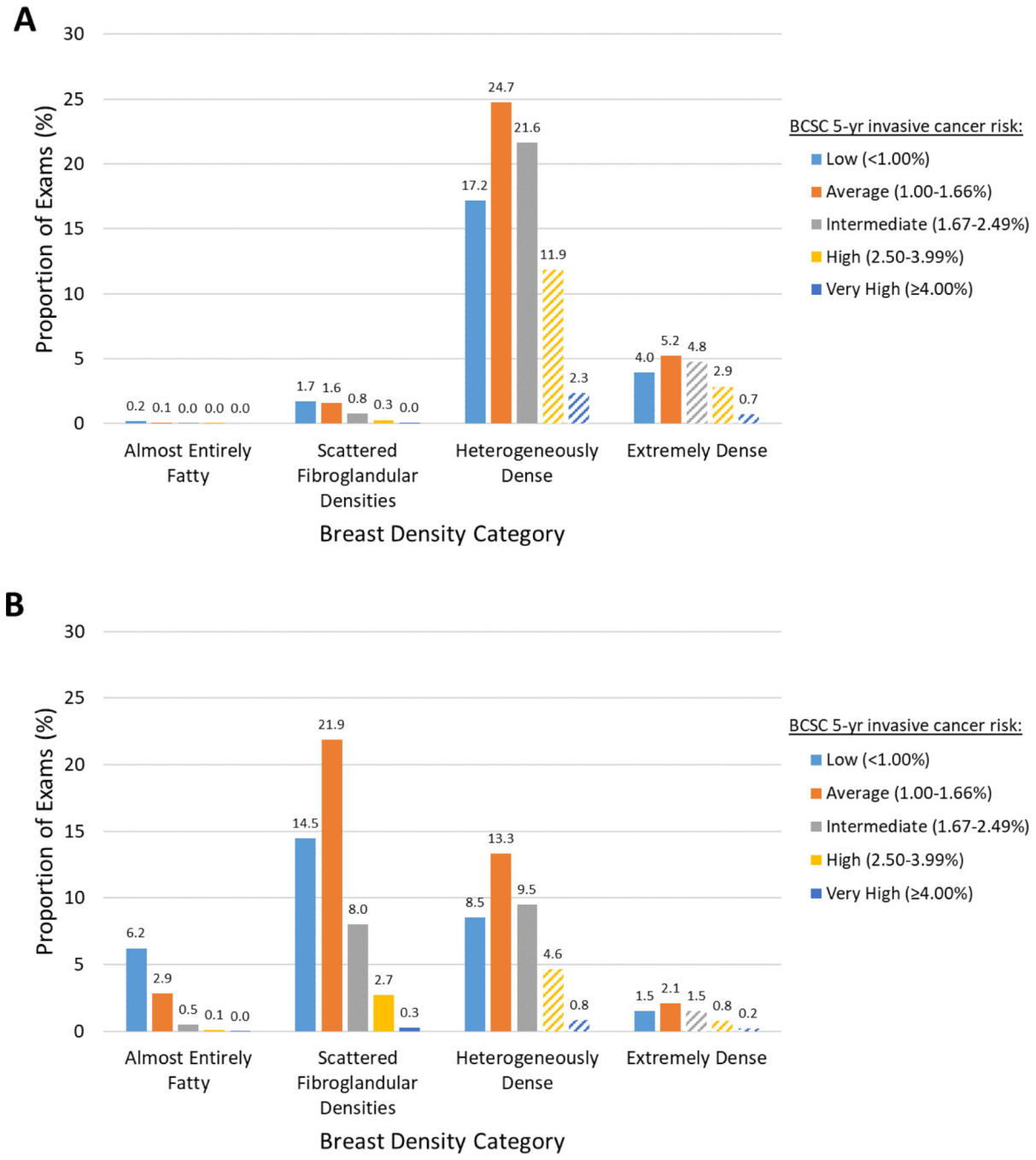

Figure 2. Joint distribution of breast density and BCSC 5-year invasive breast cancer risk.

Among women ages 35–74 undergoing (A) ultrasound screening or (B) mammography screening alone at 32 breast imaging facilities participating in the Vermont, San Francisco and Chicago Breast Cancer Surveillance Consortium registries, 2014–2020. Diagonally striped bars represent groups with high interval invasive cancer risk based on breast density and estimated BCSC 5-year invasive breast cancer risk [17]. The BCSC 5-year invasive breast cancer risk model is not applicable for women under age 35 or over age 74 years. Among women aged 35–74 years, breast density and invasive breast cancer risk were missing for

1.8% of eligible ultrasound screening exams and 0.7% of eligible mammography screening exams.

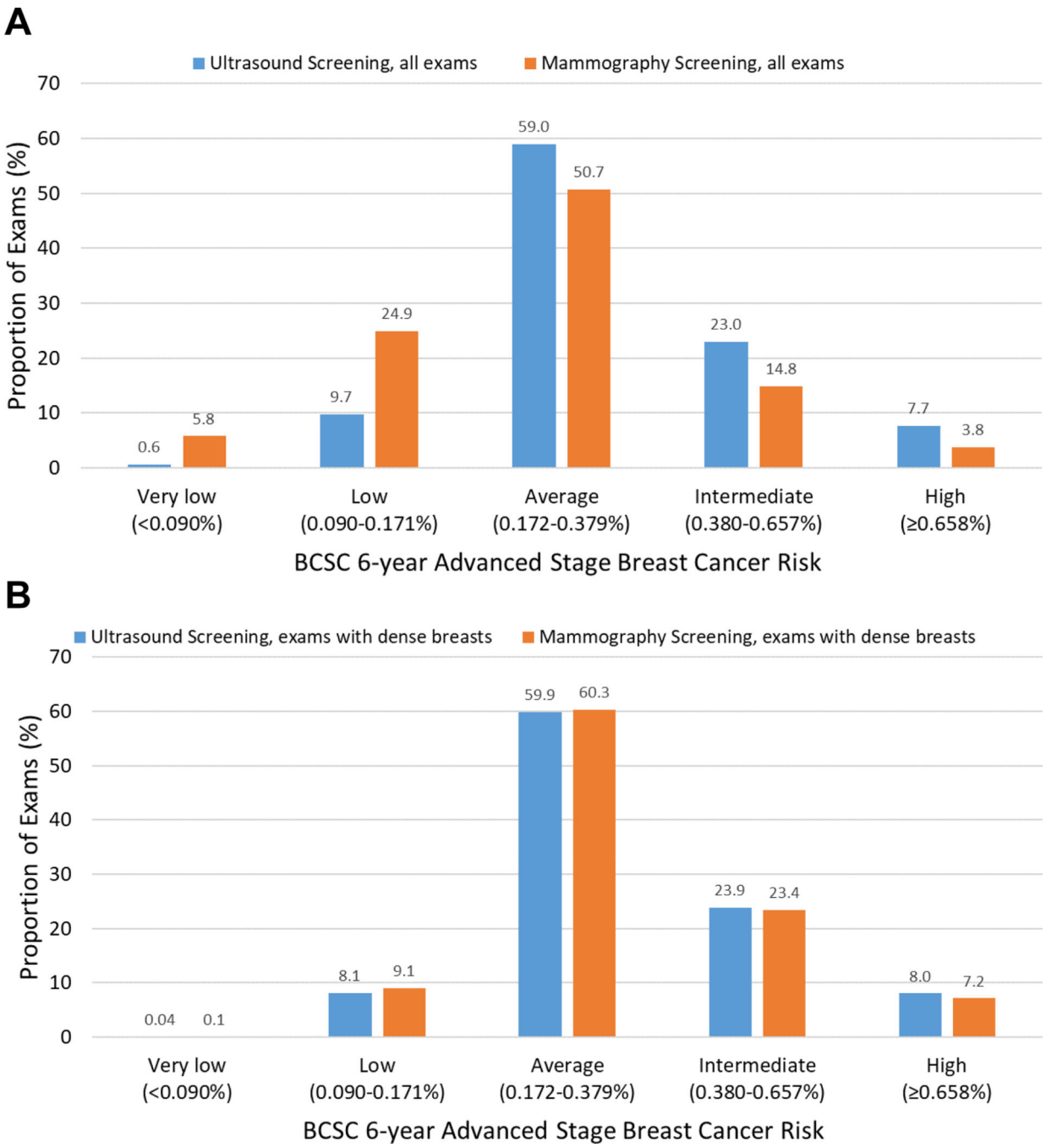

Figure 3. Distribution of BCSC 6-year advanced stage breast cancer risk.

Among (A) all women ages 40–74 and (B) women ages 40–74 with dense breasts undergoing ultrasound screening exams and mammography screening exams at 32 breast imaging facilities participating in the Vermont, San Francisco and Chicago Breast Cancer Surveillance Consortium registries, 2014–2020. The BCSC advanced cancer risk model is not applicable for women under age 40 or over age 74 years. Among women aged 40–74 years, advanced cancer risk could not be calculated due to missing body mass index or breast density or prior LCIS for 6.2% of ultrasound screening exams (4.6% for women with

dense breasts and 9.4% of mammography screening exams (10.3% for women with dense breasts).

Table 1.

Exam-level demographic and risk characteristics for women undergoing ultrasound screening exams or mammography screening alone at 32 breast imaging facilities participating in the Vermont, San Francisco and Chicago Breast Cancer Surveillance Consortium registries, 2014–2020.

	Ultrasound Screening (N=38,166 exams)		Mammography Screening Alone (N=825,360 exams)		
	n	%[a]	n	%[a]	P-value[b]
Age, years					<0.0001
<40	1,056	2.8%	8,083	1.0%	
40–49	13,581	35.6%	183,539	22.2%	
50–59	12,611	33.0%	259,759	31.5%	
60–69	7,631	20.0%	235,392	28.5%	
70+	3,287	8.6%	138,587	16.8%	
Race/ethnicity[c]					<0.0001
Asian	2,573	6.9%	109,367	13.7%	
Black	2,978	8.0%	86,652	10.9%	
Hispanic	3,981	10.7%	54,776	6.9%	
White	26,820	72.4%	530,805	66.5%	
Other/Multiple	685	1.8%	16,039	2.0%	
Unknown	1,129	(3.0%)	27,721	(3.4%)	
Menopausal status					<0.0001
Premenopausal	18,720	49.0%	250,456	30.3%	
Postmenopausal	19,446	51.0%	574,904	69.7%	
BI-RADS breast density					<0.0001
Almost entirely fat	119	0.3%	81,942	10.0%	
Scattered fibroglandular densities	1,647	4.4%	395,131	48.2%	
Heterogeneously dense	29,119	77.9%	294,442	35.9%	
Extremely dense	6,497	17.4%	47,901	5.8%	
Unknown	784	(2.1%)	5,944	(0.7%)	
First degree family history of breast cancer					<0.0001
No	29,785	78.3%	674,185	82.6%	
Yes	8,249	21.7%	142,338	17.4%	
Unknown	132	(0.3%)	8,837	(1.1%)	
History of benign breast disease					<0.0001
None	28,882	75.7%	654,132	79.3%	
Prior biopsy, diagnosis unknown	4,762	12.5%	98,506	11.9%	
Non-proliferative lesion	3,099	8.1%	49,613	6.0%	
Proliferative changes without atypia	1,036	2.7%	18,606	2.3%	
Proliferative changes with atypia	329	0.9%	3,853	0.5%	
Lobular carcinoma in situ	58	0.2%	650	0.1%	
Body Mass Index (kg/m^2)					<0.0001
Underweight (<18.5)	890	2.5%	10,468	1.4%	

	Ultrasound Screening (N=38,166 exams)		Mammography Screening Alone (N=825,360 exams)		
	n	%[a]	n	%[a]	P-value[b]
Normal (18.5-<25)	19,484	53.9%	273,983	36.7%	
Overweight (25-<30)	10,120	28.0%	225,676	30.2%	
Obese (30+)	5,682	15.7%	236,753	31.7%	
Missing	1,990	(5.2%)	78,480	(9.5%)	

BI-RADS, Breast Imaging Reporting and Data System.

[a]Percentages are among non-missing; percent missing is shown in parentheses.

[b]Comparing the distribution of the risk characteristic among women undergoing ultrasound screening vs. mammography screening, from a logistic regression model using generalized estimating equation with an independent correlation structure to account for multiple exams per woman.

[c]All race/ethnicity groups except Hispanic are non-Hispanic.

Table 2.

Exam-level demographic and risk characteristics for women with dense breasts undergoing ultrasound screening exams or mammography screening alone at 32 breast imaging facilities participating in the Vermont, San Francisco and Chicago Breast Cancer Surveillance Consortium registries, 2014–2020.

	Ultrasound Screening (N=35,616 exams)		Mammography Screening Alone (N=342,343 exams)		
	n	%[a]	n	%[a]	P-value[b]
Age, years					<0.0001
<40	839	2.4%	5,285	1.5%	
40–49	12,887	36.2%	110,495	32.3%	
50–59	11,696	32.8%	112,881	33.0%	
60–69	7,103	19.9%	75,861	22.2%	
70+	3,091	8.7%	37,821	11.0%	
Race/ethnicity[c]					<0.0001
Asian	2,453	7.1%	66,012	20.1%	
Black	2,843	8.2%	28,817	8.8%	
Hispanic	3,823	11.0%	22,493	6.8%	
White	24,855	71.8%	204,319	62.2%	
Other/Multiple	626	1.8%	6,810	2.1%	
Unknown	1,016	(2.9%)	13,892	(4.1%)	
Menopausal status					<0.0001
Premenopausal	17,489	49.1%	146,709	42.9%	
Postmenopausal	18,127	50.9%	195,634	57.1%	
BI-RADS breast density					<0.0001
Heterogeneously dense	29,119	81.8%	294,442	86.0%	
Extremely dense	6,497	18.2%	47,901	14.0%	
First degree family history of breast cancer					<0.0001
No	27,871	78.5%	280,834	83.2%	
Yes	7,646	21.5%	56,846	16.8%	
Unknown	99	(0.3%)	4,663	(1.4%)	
History of benign breast disease					<0.0001
None	26,866	75.4%	266,371	77.8%	
Prior biopsy, diagnosis unknown	4,513	12.7%	43,391	12.7%	
Non-proliferative lesion	2,922	8.2%	21,937	6.4%	
Proliferative changes without atypia	968	2.7%	8,494	2.5%	
Proliferative changes with atypia	296	0.8%	1,794	0.5%	
Lobular carcinoma in situ	51	0.1%	356	0.1%	
Body Mass Index (kg/m^2)					0.07
Underweight (<18.5)	854	2.5%	7,986	2.6%	
Normal (18.5-<25)	18,636	54.8%	165,914	54.0%	
Overweight (25-<30)	9,457	27.8%	85,831	28.0%	
Obese (30+)	5,076	14.9%	47,257	15.4%	

	Ultrasound Screening (N=35,616 exams)		Mammography Screening Alone (N=342,343 exams)		
	n	%[a]	n	%[a]	P-value[b]
Missing	1,593	(4.5%)	35,355	(10.3%)	

BI-RADS, Breast Imaging Reporting and Data System.

[a]Percentages are among non-missing; percent missing is shown in parentheses.

[b]Comparing the distribution of the risk characteristic among women undergoing ultrasound screening vs. mammography screening, from a logistic regression model using generalized estimating equation with an independent correlation structure to account for multiple exams per woman.

[c]All race/ethnicity groups except Hispanic are non-Hispanic.