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Impact of Mammography Screening Interval on Breast Cancer Diagnosis by Menopausal Status and BMI

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BACKGROUND: Controversy remains regarding the frequency of screening mammography. Women with different risks for developing breast cancer because of body mass index (BMI) may benefit from tailored recommendations.

OBJECTIVE: To determine the impact of mammography screening interval for women who are normal weight (BMI < 25), overweight (BMI 25–29.9), or obese (BMI ≥ 30), stratified by menopausal status.

DESIGN: Two cohorts selected from the Breast Cancer Surveillance Consortium. Patient and mammography data were linked to pathology databases and tumor registries.

PARTICIPANTS: The cohort included 4,432 women aged 40–74 with breast cancer; the false-positive analysis included a cohort of 553,343 women aged 40–74 without breast cancer.

MAIN MEASURES: Stage, tumor size and lymph node status by BMI and screening interval (biennial vs. annual). Cumulative probability of false-positive recall or biopsy by BMI and screening interval. Analyses were stratified by menopausal status.

KEY RESULTS: Premenopausal obese women undergoing biennial screening had a non-significantly increased odds of a tumor size > 20 mm relative to annual screeners (odds ratio [OR]=2.07; 95 % confidence interval [CI] 0.997 to 4.30). Across all BMI categories from normal to obese, postmenopausal women with breast cancer did not present with higher stage, larger tumor size or node positive tumors if they received biennial rather than annual screening. False-positive recall and biopsy recommendations were more common among annually screened women.

CONCLUSION: The only negative outcome identified for biennial vs. annual screening was a larger tumor size (> 20 mm) among obese premenopausal women. Since annual mammography does not improve stage at diagnosis compared to biennial screening and false-positive recall/biopsy rates are higher with annual screening, women and their primary care providers should weigh the harms and benefits when deciding on annual versus biennial screening.

KEY WORDS: mammography; BMI; menopausal status.
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INTRODUCTION

Randomized clinical trials confirmed that mammography screening reduces breast cancer mortality.[1,2] The majority of trials evaluated biennial screening.[3,4] In 2009, the US Preventive Services Task Force recommended biennial screening mammography for women between ages 50 and 74.[5] However, the American Cancer Society and other organizations continue to recommend annual screening.[6,7] Negative impacts of screening include additional testing, biopsies, and anxiety associated with false-positive findings,[1,8] which are more likely with annual screening.[9]

Women with excess weight present with larger, node positive and higher stage tumors.[10–17] The etiology of adverse prognostic breast cancer characteristics among individuals with excess weight is likely multi-factorial, and includes mechanisms altering tumor growth,[18–20] as well as non-biologic mechanisms such as lower rates of screening.[21–23] Additionally, the impact of excess weight on breast cancer risk varies by menopausal status. Obese premenopausal women may have a lower risk of developing breast cancer,[24] while obese postmenopausal women have a higher risk.[13]

Potential harms associated with screening may also be more frequent among women with excess weight, given that there is a higher rate of recall and biopsy with increasing adiposity.[10,25] Women with excess weight and large breasts often require an overlapping imaging technique to cover the entire breast, which can result in additional radiation.[26]

Given the rise in obesity incidence, tailored mammography screening recommendations based on body mass index (BMI) could potentially identify breast cancers at the same stage, while minimizing false-positive recall and biopsy. The screening interval that maximizes benefit and minimizes harm for overweight or obese women is currently unclear. Our objective was to determine if adverse breast cancer characteristics were more likely with biennial compared to annual mammography screening intervals across BMI categories stratified by menopausal status. We also evaluated the cumulative false-positive recall and biopsy recommendation rates after 10 years of screening for women by BMI categories and screening interval.

METHODS

Study Setting and Data Sources

Data were derived from seven national breast imaging registries in the Breast Cancer Surveillance Consortium (BCSC) (http://breastscreening.cancer.gov).[27] Registries collected patient characteristics and clinical information from community radiology facilities. Radiologists' assessments and recommendations were based on the American College of Radiology's Breast Imaging Reporting and Data System (BI-RADS®).[28] Breast cancer diagnoses and tumor characteristics were obtained by linking BCSC data to regional Surveillance, Epidemiology, and End Results (SEER) programs or state tumor registries, and to pathology databases for five of the seven registries. Details of cancer linkage, which is at least 94.3 % complete, is described in a prior publication.[29] Data were pooled at a central Statistical Coordinating Center. Registries and the Coordinating Center received Institutional Review Board approval for active or passive consenting processes or a waiver of consent to enroll participants, link data, and perform analysis. All procedures were Health Insurance Portability and Accountability Act compliant, and registries and the Coordinating Center received a Federal Certificate of Confidentiality and other protections for the identities of women, physicians, and facilities.

Participants in the Breast Cancer Cohort and False Positive Cohort

For the cohort of women with breast cancer, analyses were restricted to cancers diagnosed within a specified follow-up period after each woman's most recent screening mammogram prior to diagnosis (the index mammogram): within 1 year for annual intervals and within 2 years for biennial intervals. To allow adequate follow-up for breast cancer, we included only index mammograms that occurred at least 1 year before the end of complete cancer data collection for annual intervals and at least 2 years for biennial intervals, as previously described elsewhere.[30] Figure 1 outlines the study design and illustrates the two ways a longer screening interval leads to a more advanced cancer diagnosis: (1) advanced disease detected at screening due to longer time for tumor growth since the previous screen, and (2) advanced disease detected clinically due to the longer interval in which cancers can become symptomatic or palpable.

Mammograms were excluded for women self-reporting a history of breast cancer and those with a history of breast cancer noted in the central database. Women reporting hormone therapy use (HT) were excluded, because the impact of obesity on breast cancer risk has been shown to vary with HT use,[21] and HT use significantly declined within the years included in the analysis.[31]

Analyses of cumulative risk of false-positive test results included a cohort of women age 40–74 years receiving screening mammography from 1994 to 2008 without a diagnosis of breast cancer. We censored follow-up for women at the time of a cancer diagnosis and excluded the prior screening mammogram if it occurred within 12 months of diagnosis. We also censored women if self-reported time since last examination differed from that in the database by more than 6 months.

Measures and Definitions

Demographic and risk factor information were obtained using a questionnaire (http://breastscreening.cancer.gov) completed at each screening. Women were considered postmenopausal if they reported that their periods had stopped naturally or that their ovaries had been surgically removed. Women who had undergone a hysterectomy were considered postmenopausal if they were older than 55 and premenopausal if they were age 55 or younger. BMI (kg/m^2) was calculated using self-reported height and weight. We used three standard BMI categories based on National Heart Blood and Lung Institute definitions: normal (18.5–24.9), overweight (25.0–29.9), obese class I/II/III (≥ 30.0).[32]

Mammography examinations were considered screening based on the indication reported by the radiology facility. To avoid misclassifying diagnostic mammograms as screening, we excluded mammograms that were unilateral or were preceded by a breast-imaging examination within the prior 9 months.

For each mammogram, the screening interval was defined by time since the most recent mammogram. Screening intervals were categorized as: 9 to 18 months for annual and >18 to 30 months for biennial intervals. Breast cancers were classified according to the American Joint Committee on Cancer staging system, 6th edition.[33] We defined large tumors as > 20 mm and advanced stage disease as stages IIB, III, or IV.

A screening examination was considered positive for recall if the BI-RADS assessment was: 0 (needs additional

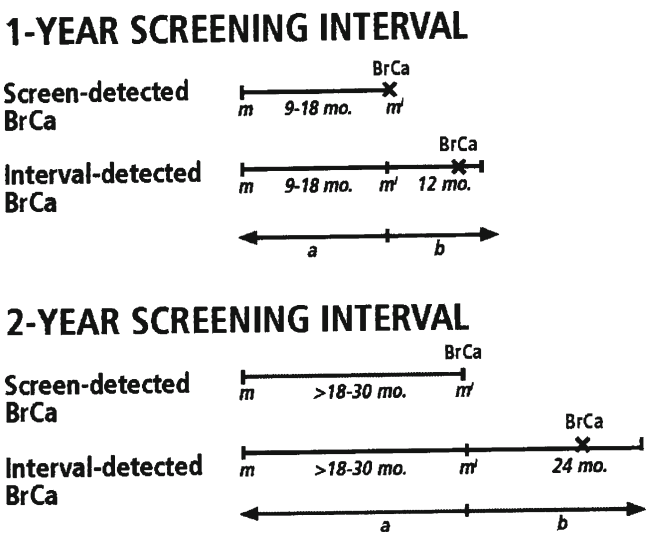

Figure 1. Overview of study design. ***m*** **= screening mammogram;** ***ml*****= index mammogram;** ***BrCa*** **= breast cancer;** ***a*** **= screening interval;** ***b*** **= follow-up period for cancer ascertainment.**

imaging); 4 (suspicious abnormality); 5 (highly suggestive of malignancy); or 3 (probably benign) with a recommendation for immediate follow-up. A screening mammogram was considered positive for biopsy if the BI-RADS assessment after all imaging and within 90 days after the screening exam was 4 or 5, or was 0 or 3 with a recommendation for biopsy, fine needle aspiration, or surgical consult. Exams were excluded if the final assessment, 90 days after the screening mammogram, was BI-RADS 0 with a recommendation for additional imaging, a non-specified workup, or missing a recommendation.

Statistical Analysis

We described the population characteristics in each of the two study cohorts. Among the breast cancer cohort, we estimated the proportion with invasive cancer versus ductal carcinoma in situ (DCIS) by screening interval, BMI, and menopausal status. For women with invasive cancer, we estimated distributions of tumor characteristics (stage, tumor size, and lymph node status) at diagnosis by interval, BMI, and menopausal status. We fit separate logistic regression models for each tumor characteristic to estimate odds ratios and 95 % confidence intervals (CI) associated with biennial versus annual screening by BMI and menopausal status. Models were adjusted for BCSC registry, race/ethnicity, age at index mammogram, and family history of breast cancer. We did not adjust for multiple comparisons. Our outcomes are highly correlated making, any standard adjustment overly conservative. Importantly, adjustment for multiple comparisons reduces type I errors, but increases type II errors.[34] The least desirable error for these analyses would be to miss differences when they do exist (type II error), as this would result in suggesting that screening less often is acceptable.

We estimated the probability of a false-positive (FP) first mammogram using logistic regression including breast density and screening interval in the model, and adjusted for BCSC registry. Probability estimates were standardized to the BCSC registry distribution using indirect (marginal) standardization. Using previously developed methods for screening tests, we modeled the cumulative probability of FP results (recall and biopsy recommendation) after 10 years of subsequent screening.[35] Briefly, we fit logistic regression models for FP results at each subsequent screening round conditional on screening round number, total number of screenings before censoring, screening interval, BMI, and BCSC registry. Estimates were stratified by age (40–49 vs. 50–74). We combined estimates of the FP risk at each subsequent screening round to obtain cumulative FP probabilities after 10 years of repeat screening. We report fitted values from this model by BMI, screening interval, and age. We report separate p values for the association between BMI and odds of a FP result from our models for first mammograms and subsequent mammograms.

Analyses were performed in SAS® software, Version 9.2 (SAS Institute, Cary, NC). FP risk analyses were performed using R 2.10.1 (R Foundation for Statistical Computing, Vienna, Austria).

Role of the Funding Source

The study was funded by a Grand Opportunity grant from the National Cancer Institute (NCI). Data collection was supported by the NCI-funded BCSC cooperative agreements. The FP recall/ biopsy analysis was also supported by

an NCI grant. The funding agency had no role in the design, conduct, interpretation or writing of the study.

RESULTS

Characteristics of Women in the Two Study Cohorts

Figure 2 identifies the women included in the two study cohorts. All women ages 40 to 74 in the BCSC registries between 1994 and 2008 were eligible. Initial decision for inclusion into the two cohorts is based on a diagnosis of breast cancer.

Population characteristics of the two cohorts (women with and without breast cancer) are presented in Table 1. Over 50 % of women had a BMI within the overweight or obese range. Women with a breast cancer diagnosis appeared to be older and postmenopausal and more likely to have a family history of breast cancer. Because of the large numbers of women without breast cancer, all comparisons between the two cohorts are significantly different ($p<0.0001$).

Screening Interval and Tumor Characteristics

Most women diagnosed with breast cancer had invasive, node negative and stage I breast cancer across all BMI categories (Table 2). The data were similar for premenopausal and postmenopausal women.

Odds of Biennial Versus. Annual Screening by Tumor Characteristics

Adjusted odds ratios for presenting with adverse tumor characteristics by BMI category and screening interval stratified by menopausal status are shown in Table 3. Premenopausal obese women had double the odds of being diagnosed with a tumor > 20 mm if they received biennial screening rather than annual (OR=2.07; 95 % CI 0.997 to 4.304, $p=0.051$). Across all BMI categories, premenopausal women with breast cancer did not present with higher stage or node positive tumors if they received biennial rather than annual screening.

Biennial screening interval increased the odds of normal weight postmenopausal women presenting with invasive cancer rather than DCIS (OR=1.43; 95 % CI 1.02 to 2.02, $p=0.04$). Across all BMI categories, postmenopausal women with breast cancer did not present with higher stage, larger tumor size or node positive tumors if they received biennial rather than annual screening.

Cumulative Probability of False-Positive Mammography and Biopsy

Irrespective of age or BMI, individuals screened yearly, had a higher 10-year cumulative risk of a FP screening mammogram and biopsy recommendation than those screened biennially (Table 4). Women age 40–49 had more FP recalls and biopsy recommendations than women 50 or older. Compared to normal weight women, overweight and obese women were more likely to have a FP recall at their first exam; however, overweight women 40–49 and obese women 40–49 and 50–74 were less likely to have FP recalls over 10 years of subsequent exams (Table 4). Obese women 40–49 had a higher risk of a FP biopsy recommendation at the first exam compared to normal weight women ($p<0.001$), but risk was similar after 10 years of subsequent screening. In contrast, obese women 50–74 had similar FP

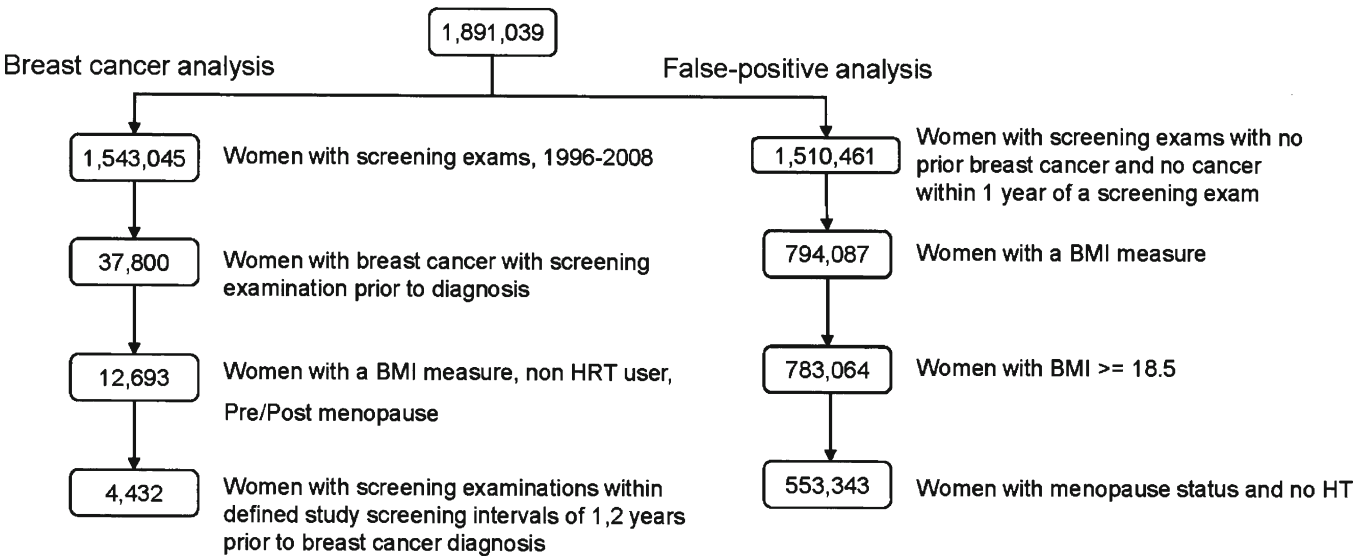

Figure 2. Characteristics of women in the two study cohorts.

Table 1. Population Characteristics by Screening Interval for Women in the Two Study Cohorts

	Breast cancer cohort		Cohort without breast cancer for false-positive analysis
	1-year screen * (%)	2-year screen† (%)	
Total number of women	2,766	1,666	553,343
Menopausal status			
Pre-menopausal	675 (24.4)	516 (31.0)	257,681 (46.6)‡
Post-menopausal	2,091 (75.6)	1,150 (69.0)	295,662 (53.4)‡
Age (years)			
40–49	502 (18.2)	406 (24.4)	219,470 (39.7)‡
50–74	2,264 (81.8)	1,260 (75.6)	333,873 (60.3)‡
BMI			
18.5–25	1,189 (43.6)	668 (40.8)	257,198 (46.5)‡
25–30	907 (33.3)	514 (31.4)	164,074 (29.7)‡
≥ 30	630 (23.1)	457 (27.8)	132,071 (23.9)‡
Race/ethnicity			
White, Non-Hispanic	2,213 (80)	1,287 (77.3)	399,865 (72.3)‡
Black, Non-Hispanic	45 (1.6)	37 (2.2)	13,074 (2.4)‡
Hispanic	241 (8.7)	151 (9.1)	63,522 (11.5)‡
Asian/Pacific Islander	132 (4.8)	119 (7.1)	41,242 (7.5)‡
American Indian /Alaska Native	18 (0.6)	17 (1.0)	8,990 (1.6)‡
Other (includes mixed)	52 (1.9)	27 (1.6)	8,702 (1.6)‡
Unknown	65 (2.4)	38 (1.7)	17,948 (3.2)‡
Family history			
Yes	634 (22.9)	318 (19.1)	71,747 (13.0)‡
No	1,792 (64.8)	1,171 (70.3)	461,957 (83.5)‡
Unknown	340 (12.3)	177 (10.6)	19,639 (3.5)‡
	Mean (SD)	Mean (SD)	
Screening interval	13.7 (1.7) mos	24.1 (3.0) mos	

**Cancers diagnosed within 12 months of screening examination*
†Cancers diagnosed within 24 months of screening examination
‡$p < 0.0001$ between the cohort without breast cancer and breast cancer cohort (1-year screen and 2-year screen combined) for all comparisons

biopsy rates at their first exam compared to normal weight women, but higher rates after 10 years of screening (9.2 % annually, 5.4 % biennially, vs. 7.9 % annually, 4.6 % biennially $p<0.001$).

DISCUSSION

A goal of mammography screening is to balance a reduction in breast cancer morbidity and mortality with adverse events related to screening. Women with excess weight are more likely to present with unfavorable tumor characteristics.[10–13,21] Therefore, it is important to understand whether a longer screening interval would cause harms due to delayed diagnosis. This observational study examined whether biennial screening mammography led to a breast cancer diagnosis with larger size tumors or higher stage for overweight and obese women relative to annual screening.

Comparison with Other Studies

It is biologically plausible that tumors identified with biennial screening intervals could be larger and more likely node positive than tumors detected among annual screeners. In our analysis, obese premenopausal women screened biennially compared to annually were more likely to present with tumors > 20 mm, a difference that approached significance. However, biennial screeners were not more likely to be node positive or late stage. Among obese postmenopausal women, the ORs for late-stage disease, large tumor size, and node positivity for biennial vs. annual screening were higher than the same ORs for normal weight women, in the range of 1.3–1.4; however, none were significantly different. This could be due to lack of statistical power in this smaller group of obese women. Only postmenopausal normal weight women were more likely to present with invasive tumors compared to DCIS when screened biennially rather than annually. A longer screening interval did not result in a significant increase in frequency of invasive carcinomas among women with excess weight, though the odds ratios were similar. DCIS is considered to be a precursor to invasive breast cancer, and a longer screening interval may provide time for invasion to develop.[36] However, most cases of DCIS do not progress to invasive disease.[37–39]

As expected, FP mammograms and biopsy recommendations are more frequent with annual screening intervals.[9] It is not surprising that women 40–49 years old have higher 10-year cumulative rates of FP mammograms than older women. Women aged 40–49 and 50–74 who were obese experienced fewer FP recalls but similar or higher biopsy recommendations than normal weight women over 10 years

Table 2. Distribution of Tumor Characteristics by Screening Interval, BMI Category, and Menopausal Status

	Normal weight		Overweight		Obese	
	1 year	2 years	1 year	2 years	1 year	2 years
Premenopausal						
N=1,175	391	263	169	137	109	106
DCIS (%)	24.8	30.8	21.9	25.5	20.2	24.5
Invasive (%)	75.2	69.2	78.1	74.5	79.8	75.5
Stage, invasive only	289	176	126	98	85	87
Stage I (%)	54.3	55.1	49.2	53.1	50.6	41.6
Stage IIA (%)	25.6	25.0	24.6	20.4	18.8	31.2
Stage IIB (%)	9.0	6.8	10.3	9.2	12.9	7.8
Stage III/IV (%)	11.1	13.1	15.9	17.3	17.6	19.5
Stage, invasive only	291	177	128	99	85	77
Early (%)	80.1	80.2	74.2	73.7	69.4	72.7
Late (%)	19.9	19.8	25.8	26.3	30.6	27.3
Tumor size (mm), invasive only	283	178	128	97	85	77
<10 (%)	22.6	21.3	20.3	19.6	18.8	22.7
10–<15 (%)	26.9	23.6	23.4	18.6	22.4	18.7
15–20 (%)	23.7	29.2	25.0	24.7	28.3	12.0
>20 (%)	26.9	25.8	31.3	37.1	30.6	46.7
Lymph node, invasive only	292	177	128	99	85	77
Positive (%)	30.5	31.6	33.6	30.3	40.0	35.1
Negative (%)	69.5	68.4	66.4	69.7	60.0	64.9
Post-menopausal						
N=3,190	798	405	738	377	521	351
DCIS (%)	25.8	17.5	20.1	16.2	20.7	18.2
Invasive (%)	74.2	82.5	79.9	83.8	79.3	81.8
Stage, invasive only	572	324	564	307	387	278
Stage I (%)	59.8	63.6	65.4	63.2	65.1	64.0
Stage IIA (%)	22.4	20.4	20.6	21.5	17.6	18.3
Stage IIB (%)	5.9	5.9	5.3	4.9	5.7	6.8
Stage III/IV (%)	11.9	10.2	8.7	10.4	11.6	10.8
Stage, invasive only	582	329	575	314	396	281
Early (%)	82.5	84.2	86.1	85.0	82.8	82.6
Late (%)	17.5	15.8	13.9	15.0	17.2	17.4
Tumor size (mm), invasive only	568	320	561	299	402	278
<10 (%)	28.2	29.7	31.9	27.1	31.1	24.1
10–<15 cm (%)	26.4	23.4	26.9	25.1	24.9	27.7
15–20 (%)	24.0	26.8	20.7	22.8	23.4	25.1
> 20 (%)	21.5	20.0	20.5	25.1	20.6	23.0
Lymph node, invasive only	584	329	579	314	396	282
Positive (%)	25.0	25.5	22.1	21.0	23.5	26.2
Negative (%)	75.0	74.5	77.9	79.0	76.5	73.8

of annual or biennial screening, though the magnitude of the differences are not large. Other researchers have noted an increase in additional testing among women with excess weight.[10,25] Perhaps in this cohort, abnormalities on screening mammography among obese women were more likely referred directly for biopsy rather than short interval follow-up of the abnormality. There may also be more biopsies in obese women because of asymmetries identified on mammogram due to large size of breasts.

There is a potential harm from additional radiation associated with screening overweight and obese women at frequent intervals. Multiple overlapping images, known as mosaic imaging, may be required to assure complete coverage of large breasts by mammography,[26] and will result in multiple radiation exposures. For a cohort of 100,000 women, modeling suggests that radiation exposure from biennial standard two-view mammography provided to women age 40–74 is predicted to result in 86 induced breast cancers and 11 deaths due to radiation, but is outweighed by the benefit of overall mortality reduction from screening.[40] This harms/benefit ratio may change for obese women with large breasts, who may receive greater radiation from screening and diagnostic mammograms.

Strengths and Weaknesses

Use of BCSC data has several advantages. With over 2.5 million participants from community mammography facilities across the US since 1994, it is a nationally representative sample. The large numbers and time frame allow us to evaluate observed screening intervals in lieu of a clinical trial. However, the observational nature of the data has limitations. The screening interval definition and analysis are complicated by selection and length bias, although our study design reduces length bias by including both screen-detected and interval cancers and by having the follow-up interval correspond to the screening interval. Our study population had only 52 %

Table 3. Odds Ratios (95 % Confidence Interval [CI]) of Adverse Tumor Characteristics for Biennial Compared to Annual Screeners, by BMI and Adjusted for Registry, Race/Ethnicity, Age and Family History

	Normal weight odds ratios (95 % CI)	Overweight odds ratios (95 % CI)	Obese odds ratios (95 % CI)
Premenopausal			
Invasive vs. DCIS	0.71 (0.48, 1.06)	0.70 (0.38, 1.29)	0.61 (0.29, 1.24)
Among invasive cancers:			
Late stage	0.81 (0.47. 1.39)	1.18 (0.58, 2.37)	0.84 (0.39, 1.83)
Tumor size >20 mm	0.81 (0.49, 1.32)	1.21 (0.64, 2.27)	2.07 (0.997, 4.304)
Lymph node positive	1.02 (0.65, 1.61)	0.85 (0.44, 1.63)	0.72 (0.34, 1.50)
Postmenopausal			
Invasive vs. DCIS	1.43 (1.02, 2.02)*	1.21 (0.83, 1.76)	1.43 (0.94, 2.16)
Among invasive cancers:			
Late stage	0.95 (0.62, 1.47)	1.19 (0.75, 1.89)	1.32 (0.82, 2.10)
Tumor size >20 mm	0.93 (0.62, 1.38)	1.21 (0.82, 1.80)	1.38 (0.90, 2.13)
Lymph node positive	1.14 (0.79, 1.64)	0.92 (0.62, 1.36)	1.41 (0.93, 2.13)

**Significant result with p= 0.04*

of women in overweight or obese BMI categories compared with national studies that report 66–68 % in the 40 and older age groups.[41] As a primarily screening cohort, the BCSC may include more health conscious individuals who are more likely to have a normal weight. Additionally, there is evidence that women with excess weight obtain fewer screening mammograms,[22,23] and self-reports of weight may be biased.[42] Our population reflects the racial and ethnic diversity of women 40 and older in the US population in being primarily Caucasian.[43] We are unable to assess racial and ethnic differences on the effects of obesity on outcomes by screening interval, given the small samples sizes after stratification. We evaluated numerous comparisons: some may be significant by chance alone. Thus, it is important to consider the magnitude of differences and confidence interval widths.

CLINICAL IMPLICATIONS AND FUTURE RESEARCH

Results suggest that biennial screening does not increase the frequency of adverse tumor characteristics compared to annual screening among overweight or obese women, but it is associated with fewer FP recall and biopsy recommendations. Premenopausal women who are obese are more likely to present with larger tumors if they are screened biennially rather than annually. Larger tumors require a larger surgical excision and larger radiation fields. Howev-

Table 4. Percentage (95 % CI) of False-Positive First Mammograms and Percentage of Women (95 % CI) with at Least One False-Positive Recall at Subsequent Mammography After 10 Years of Mammography. All Estimates are Adjusted for Registry

	Normal weight	Overweight	Obese
False-positive recall			
Age 40–49			
First mammography (p value*)	Ref	<0.001	<0.001
Risk for first exam	16.5 (16.1, 16.9)	18.4 (17.8, 18.9)	18.3 (17.7, 18.9)
10 years of screening (p value)	Ref	0.96	<0.001
Cumulative risk for annual screening	66.5 (64.9, 68.1)	66.5 (64.9, 68.1)	60.8 (59.1, 62.5)
Cumulative risk for biennial screening	44.8 (43.8, 45.9)	44.8 (43.7, 45.9)	39.9 (38.8, 40.9)
Age 50–74			
First mammography (p value)	Ref	0.007	0.011
Risk for first exam	16.0 (15.3, 16.7)	17.5 (16.7, 18.4)	17.5 (16.6, 18.4)
10 years of screening (p value)	Ref	0.013	<0.001
Cumulative risk for annual screening	54.4 (53.4, 55.3)	53.4 (52.4, 54.3)	52.1 (51.1, 53.1)
Cumulative risk for biennial screening	34.3 (33.6, 35.1)	33.6 (32.9, 34.3)	32.6 (31.9, 33.3)
False-positive biopsy recommendation			
Age 40–49			
First mammography (p value)	Ref	0.17	<0.001
Risk for first exam	2.1 (1.9, 2.3)	2.3 (2.1, 2.5)	2.7 (2.4, 2.9)
10 years of screening (p value)	Ref	0.99	0.54
Cumulative risk for annual screening	11.2 (9.8, 12.8)	11.2 (9.8, 12.8)	11.5 (10.0, 13.1)
Cumulative risk for biennial screening	6.0 (5.4, 6.6)	6.0 (5.4, 6.6)	6.2 (5.6, 6.8)
Age 50–74			
First mammography (p value)	Ref	0.12	0.14
Risk for first exam	2.2 (2.5, 3.2)	3.2 (2.8, 3.6)	3.2 (2.8, 3.7)
10 years of screening (p value)	Ref	0.16	<0.001
Cumulative risk for annual screening	7.9 (7.3, 8.5)	8.2 (7.6, 8.8)	9.2 (8.6, 9.9)
Cumulative risk for biennial screening	4.6 (4.3, 4.9)	4.8 (4.5, 5.2)	5.4 (5.0, 5.8)

**p values are based on hypothesis tests for differences in odds of false-positive results for overweight or obese women compared to normal weight*

er, with the increasing use of gene expression assays, chemotherapy decisions are less likely to be made on tumor size.[44,45] Ideally, a randomized controlled trial of annual vs. biennial screening intervals for women with different BMI and menopausal status would elucidate appropriate screening recommendations. However, the financial burden and long duration of such a trial makes it highly unlikely. Given the disparity in breast cancer mortality between African American and white women,[46] understanding racial differences in screening intervals by BMI and menopausal status is an important area for future research.

CONCLUSIONS

Biennial versus annual screening does not appear to increase adverse breast cancer characteristics among overweight and obese women. Furthermore, biennial screening results in lower cumulative false-positive recall and biopsy recommendations for all women and therefore less radiation. Biennial screening appears to be safe for overweight and obese women; however, women with excess weight and their primary care providers should continue to weigh the potential harms and benefits of annual vs. biennial screening.

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