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Breast biopsy patterns and findings among older women undergoing screening mammography: the role of age and comorbidity

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Abstract

Introduction: Limited evidence exists on the impact of age and comorbidity on biopsy rates and findings among older women.

Materials and Methods: We used data from 170,657 women ages 66–94 enrolled in the United States Breast Cancer Surveillance Consortium (BCSC). We estimated one-year rates of biopsy by type (any, fine-needle aspiration (FNA), core or surgical) and yield of the most invasive biopsy finding (benign, ductal carcinoma in situ (DCIS) and invasive breast cancer) by age and comorbidity. Statistical significance was assessed using Wald statistics comparing coefficients estimated from logistic regression models adjusted for age, comorbidity, BCSC registry, and interaction between age and comorbidity.

Results: Of 524,860 screening mammograms, 9830 biopsies were performed following 7930 exams (1.5%) within one year, specifically 5589 core biopsies (1.1%), 3422 (0.7%) surgical biopsies and 819 FNAs (0.2%). Biopsy rates per 1000 screens decreased with age (66–74:15.7, 95%CI:14.8–16.8), 75–84:14.5(13.5–15.6), 85–94:13.2(11.3,15.4), $p_{\text{trend}} < 0.001$) and increased with Charlson Comorbidity Score (CCS=0:14.4 (13.5–15.3), CCS=1:16.6 (15.2–18.1), CCS>=2:19.0 (16.9–21.5), $p_{\text{trend}} < 0.001$). Biopsy rates increased with CCS at ages 66–74 and 75–84 but not 85–94. Core and surgical biopsy rates increased with CCS at ages 66–74 only. For each biopsy type, the yield of invasive breast cancer increased with age irrespective of comorbidity.

Discussion: Women aged 66–84 with significant comorbidity in a breast cancer screening population had higher breast biopsy rates and similar rates of invasive breast cancer diagnosis than their counterparts with lower comorbidity. A considerable proportion of these diagnoses may represent overdiagnoses, given the high competing risk of death from non-breast-cancer causes among older women.

Keywords

Biopsy; breast cancer; overtreatment; overdiagnosis

Introduction

In the US, 18% of breast cancer cases are diagnosed among women age 75 and older.[1] Although many clinical guidelines and recommendations such as those from the United States (US) Preventive Services Task Force do not recommend for or against screening among women ages 75 and older due to insufficient evidence, 52% of these women continue to undergo screening.[2, 3] Yet, the likely benefit from screening mammography in this older population is highly variable due to the heterogeneity in health status and life expectancy.[4, 5]

Women with an abnormal screening mammogram may be recommended for tissue sampling with fine needle aspiration (FNA), core-needle biopsy, or surgical excision.[6, 7] Compared to surgical biopsy, core needle biopsy procedures are less invasive and associated with fewer complications while equally diagnostically effective.[8] Core biopsy uses a hollow core needle to remove breast tissue, while surgical biopsy involves surgical incision under general or local anesthesia, and has higher complication rates (1.5% for core vs 2–10% for surgical). [9] However, the choice of biopsy type depends on multiple factors including the location and size of the lesion, the woman's clinical characteristics including age and comorbidity burden, and provider and workforce factors.[10] [9]

Limited population-based evidence exists on how breast biopsy patterns and pathologic findings vary by age and comorbidity. In a population based study, Friese *et al.* used data from the Surveillance, Epidemiology and End Results (SEER) program to assess patterns in use of needle versus surgical biopsy among women with breast cancer and downstream consequences including surgical procedures.[6] Nelson *et al.* examined rates of biopsy recommendation following a screening mammogram among women aged 70–79 versus 80–89 but did not examine how comorbidity may impact biopsy rates.[11]

The present study leverages the Medicare-linked Breast Cancer Surveillance Consortium (BCSC) data to assess how biopsy rates and severity of biopsy findings vary with age and comorbidity burden among older women ages 66 to 94. We hypothesized that biopsy rates and severity of findings increase with age and comorbidity burden (overall and within age groups). Results of this study will help to characterize breast cancer screening practice—and potential benefits versus harms—among older women for whom screening guidelines remain unclear.

Methods

Inclusion/Exclusion Criteria

The sample included women ages 66–94 without a history of breast cancer who underwent screening mammography in 1999–2010 at a mammography registry participating in the Medicare-linked BCSC database: Carolina Mammography Registry, New Hampshire

Mammography Network, San Francisco Mammography Registry, and Vermont Breast Cancer Surveillance System. We also included Medicare-comparable claims data for women in the Kaiser Permanente Washington Registry. Screening mammograms included mammograms indicated as screening by a radiologist among women with no breast imaging in the prior 9 months.[12] Mammograms in women with a history of breast cancer or mastectomy were excluded. Claims data from Kaiser Permanente Washington and Medicare claims data from the other four registries were linked to patient, mammography, biopsy, pathology, and cancer data. Because the comorbidity measure is computed from claims data during the year before the screening mammogram, and Medicare eligibility begins at age 65, we included women who were at least 66 years old at screening. For BCSC-Medicare linked data we restricted the sample to women with continuous enrollment in fee-for-service Medicare (parts A and B) and no enrollment in a Medicare Advantage plan for 12 months before the screening mammogram to allow a full year of claims to define comorbidity. [13, 14] All eligible screening mammograms with 1 year of follow-up to ascertain biopsies were included in the analysis.

BCSC registries collect information on demographics, risk factors, clinical history, pathology, and mammography indication and results. [15] Breast cancer diagnoses and tumor characteristics are obtained by linking BCSC data to pathology services and regional SEER programs or state tumor registries. Data are pooled at a central Statistical Coordinating Center (SCC). Each registry and the SCC received institutional review board approval for active or passive consenting processes or a waiver of consent to enroll participants, link data, and perform analyses. All procedures are Health Insurance Portability and Accountability Act compliant, and all registries and the SCC received a Federal Certificate of Confidentiality and other protections for the identities of women, physicians, and facilities.

Exposures and Outcomes

The primary exposures of interest were age and comorbidity score at the screening mammogram. Comorbidity was measured using the 2000 Klabunde Comorbidity Index, a variation of the Charlson Comorbidity Index/Score (CCS).[16] The CCS is a weighted index that predicts one-year risk of death using Medicare procedure and diagnostic claims data, derived from the sum of weighted disease conditions (n=16) and classified as 0, 1, 2 or 3.[16–18] CCS scores were computed based on claims during the year before the screening mammogram.[19] We categorized CCS scores into 0, 1 or 2 (i.e. CCS0, CCS1, and CCS2+, respectively).[20]

Demographic and clinical information including age, race/ethnicity, education level, family history of breast cancer, body mass index, and breast biopsy/aspiration history were obtained from self-report at mammogram or from electronic medical records. Breast density was recorded by radiologists using the Breast Imaging Reporting and Data System (BI-RADS) scale as almost entirely fatty, scattered fibroglandular densities, heterogeneously dense, or extremely dense.[21] Time since prior mammogram was determined from the BCSC database and self-report. Women's home addresses at each exam were geocoded using

census block group for median household income (based on 2010 US Census data) and zip code for rurality.[22]

Biopsy types examined included fine needle aspiration (FNA), core biopsy, and surgical biopsy performed within one year after the screening mammogram and prior to the following screen (if any). Multiple biopsy types could be linked to a screen. The most invasive biopsy finding within each biopsy type was categorized as (from most to least severe): invasive breast cancer, DCIS, and benign findings (high-risk and other benign findings, such as non-proliferative, calcifications, fibroadenoma, cystosarcoma phyllodes, lobular carcinoma in situ, and proliferative with or without atypia).

Statistical Analysis

Frequency distributions of demographic and clinical characteristics at the time of each screening mammogram were examined by comorbidity score and biopsy type. Unadjusted rates of each biopsy type (per 1000 screening mammograms) were computed using the total number of screening mammograms followed by a specific biopsy type divided by the total number of screening mammograms. To obtain adjusted rates, logistic regression models were fit including age group, comorbidity group, BCSC registry, and the interaction between age and comorbidity groups. The outcome for each model was the presence of a specific biopsy type within one year after the screening mammogram. Predicted probabilities were computed for each combination of age group, comorbidity group and registry. To obtain adjusted probabilities for each age (or comorbidity) group, the predicted probabilities were weighted by comorbidity (or age) group and mammography registry distributions and then summed across those categories. To obtain adjusted probabilities for each age by comorbidity group, the predicted probabilities were weighted by the frequency distribution of mammography registries then summed across mammography registry categories.

Biopsy yield was defined as the percent of a specific type of biopsy with a specific finding (benign, DCIS, or invasive breast cancer). For example, the invasive breast cancer yield for core biopsies was computed as total number of core biopsies with at least one finding of invasive breast cancer divided by total number of core biopsies (multiplied by 100). Only one of each biopsy type was included per screen, and biopsy yield was computed using the most invasive biopsy finding following that biopsy type. For example, if a screen was followed by two core biopsies then we used the most invasive result; the core biopsy was counted once, and the most invasive outcome was counted once. The primary difference between models for biopsy rates and those for biopsy yield was that the latter were fit on the subset of screens that were followed by a specific biopsy type. Separate models were fit for each combination of biopsy type (any biopsy, FNA, core biopsy, surgical biopsy) and biopsy result (invasive breast cancer, DCIS, benign), adjusted for age, comorbidity score, and BCSC registry. Due to small numbers we combined DCIS with invasive results for FNAs found within one year after a screening mammogram. Trends across comorbidity level within age groups were evaluated using a two-sided p-value based on the Wald Chi-square statistic obtained by testing for a linear trend across comorbidity score parameter estimates. To look at trends within age or comorbidity group we used similar trend tests based on

models without an interaction between age and comorbidity. SAS 9.4 was used for statistical analysis (SAS Institute Inc., Cary, NC).

Results

Participant Characteristics

We identified 170,657 women ages 66–94 who underwent 524,860 screening mammograms that were eligible for analysis. A woman could have multiple screens in the analysis (median=2, IQR=1–4). The median age was 73 years (IQR: 69–78 years) (Table 1). Overall, the women were mostly white (86%), had some college education or more (51%), reported no first-degree family history of breast cancer (81%) and had scattered fibroglandular or almost entirely fatty breast density (64%). The distribution of comorbidity levels (CCS0, CCS1 and CCS2) was 72%, 20%, and 7%, respectively. Compared to women with CCS0, women with CCS 2 were more likely to be older, black, not have a high school diploma, live in a lower income area, and have higher BMI.

Biopsy Rates by Age and Comorbidity Burden

During the follow up period, 7930 (1.5%) screening exams were followed by at least one biopsy and 1805 (0.3%) had at least two biopsy types (Table 2). The prevalence of any biopsy by comorbidity score was: CCS0: 1.4%, CCS1: 1.6%, and CCS2: 1.8%. The prevalence of any biopsy by age was 66–74: 1.6%, 75–84: 1.5%, and 85–94: 1.4%. The percentage of screening mammograms followed by any biopsy was higher among women with no prior mammogram (3.8%) or a mammogram at least three years ago (2.5%), with prior biopsy or aspiration (2.1%), and who were obese (BMI 30 to <35: 2.1%, BMI ≥35: 2.3%). The percentage of screening mammograms followed by any biopsy was lower among Black women (1.2%), women without a high school degree (1.3%), and women with lower breast density (almost entirely fat: 1.0%, scattered fibroglandular densities: 1.3%). The percentage of FNA, core and surgical biopsies following a screening mammogram was 0.2%, 1.1% and 0.7%, respectively, and 0.3% of screens were followed by at least two biopsy types.

Adjusted rates of any biopsy per 1000 screening mammograms decreased with age (66–74: 15.7 (95% CI=14.8–16.8), 75–84: 14.5 (95% CI=13.5–15.6), 85–94: 13.2 (95% CI=11.3–15.4), $p_{\text{trend}} < 0.001$) and increased with comorbidity (CC0: 14.4 (95% CI=13.5–15.3), CC1: 16.6 (95% CI=15.2–18.1), CC2: 19.0 (95% CI=16.9–21.5), $p_{\text{trend}} < 0.001$) (Table 3). We found increasing rates of any biopsy with increasing comorbidity score at ages 66–74 (CCS0: 14.9 (95% CI=14.1–15.7), CCS1: 17.0 (95% CI=15.7–18.3), CCS 2: 21.1 (95% CI 19.0–23.5), $p_{\text{trend}} < 0.001$) and 75–84 (CCS0: 13.8 (95% CI=13.0–14.7), CCS1: 16.4 (95% CI=15.0–17.8), CCS≥2: 16.7 (95% CI=14.7–18.9), $p_{\text{trend}} = 0.003$) but not 85–94 (CCS0: 12.9 (95% CI=11.3–14.6), CCS1: 14.2 (95% CI=11.6–17.4), CCS≥2: 13.4 (95% CI=10.0–17.9), $p_{\text{trend}} = 0.79$). We did not observe trends in FNA rates across age or comorbidity groups overall. However, adjusted FNA rates per 1000 screens increased with comorbidity score at ages 75–84 ($p_{\text{trend}} = 0.02$). In contrast, core biopsy rates decreased with age and increased with comorbidity score overall. However, core biopsy rates increased with comorbidity score only at ages 66–74 ($p_{\text{trend}} < 0.001$). Rates of surgical biopsy overall increased with

comorbidity score but not age. Within age groups, the increase in surgical biopsy rates with comorbidity score was seen only at ages 66–74 ($p_{\text{trend}} < 0.001$). Figure 1 illustrates biopsy rates by age, CCS, and biopsy type.

Biopsy Yield by Age and Comorbidity Burden

We found no significant trends in biopsy yield for benign, DCIS, or invasive findings by comorbidity score, overall or within age groups (Table 4). The adjusted biopsy yield for benign findings decreased with age (66–74: 58.8 (95% CI=56.0–61.5), 75–84: 51.3 (95% CI: 48.1–54.6), 85–94: 43.8 (37.1–50.7), $p_{\text{trend}} < 0.001$), whereas the biopsy yield for invasive findings increased with age (66–74: 31.3 (95% CI=28.8–34.0), 75–84: 38.6 (95% CI:35.4–41.8), 85–94: 45.9 (39.2–52.8), $p_{\text{trend}} < 0.001$) (Supplemental Figure 1a–1c). Similar trends were observed when stratified by biopsy type.

Discussion

Given the complex interplay of age, comorbidity and competing risk of death due to the comorbidity burden that impacts life expectancy among older women, it is imperative to identify benefits versus harms associated with procedures and treatments following screening mammography among women aged 75 and older for whom guidelines remain unclear. [23, 24] We found that overall biopsy rates within one year following screening mammography decreased with age group among women ages 66–94 and increased with comorbidity burden at ages 66–74 and 75–84. Further, biopsy yield for invasive cancer increased with age while yield for benign findings decreased with age, with no differences in yield observed by comorbidity score. This pattern was similar across biopsy types. Our results suggest that the risk of downstream procedures following mammography screening in older women, including biopsy, is higher among women with more versus fewer comorbidities.[25, 26] For example, an 80 year-old woman with a CCS score of 1 or 2 has the same risk of biopsy as a 70 year-old woman with a CCS score of 0. Further, women diagnosed with breast cancer may receive treatment such as surgery, radiation, or chemotherapy, with associated complications, possibly representing overtreatment without significant survival benefit in women with limited life-expectancy due to comorbidities.

The association of comorbidity score with biopsy rates has not been previously evaluated for women of any age. When looking by age, we found overall biopsy rates increased with CCS among women ages 66–74 and 75–85 but not 85–94. The threshold to recommend biopsy is based on the BI-RADS assessment from mammography. A BI-RADS 4 assessment represents >2% risk of invasive breast cancer, with biopsy recommendation as standard, whereas a BI-RADS 3 assessment represents <2% risk, with a recommendation for short term follow up at six months as standard.[27] However, simulation modeling has identified that while the 2% threshold for recommending biopsy fits well for women ages 42–75, the threshold increases with age as older women are less likely to benefit from biopsy.[27] Burnside et al. emphasized the need to consider age and comorbidity when determining risk thresholds for biopsy, given the harms versus benefits of biopsy including complications.[10, 28] Hence a decision to undergo biopsy in older women should consider factors including

the risk threshold, balance of benefits versus harms and the nature and aggressiveness of breast cancer, which change with age.

Women with higher comorbidity burden may be more likely to experience health problems or visit their physicians, which may lead to greater likelihood of biopsy. Though overall biopsy rates after screening mammography decreased with age in our study, we found that older women continued to undergo biopsy procedures despite high comorbidity burden, which suggests that older women—especially those with multiple chronic conditions—may undergo unnecessary surgical procedures that offer limited benefits. Further, current literature shows that 55–85% of breast biopsies have benign findings, resulting in overtreatment and unnecessary anxiety and cost. [10] We found that biopsy yield of benign findings decreased with age, suggesting that healthcare providers may take age, risk threshold, and comorbidity status into consideration when recommending biopsy. Still, benign biopsies may represent unnecessary procedures, especially among women with multiple comorbidities who may be at increased risk of discomfort, infection and other complications coupled with fear and anxiety associated with benign findings. [26, 29] Hence it is crucial to incorporate age, risk threshold, and comorbidity into shared decision-making about breast cancer screening.

We evaluated rates of different types of biopsy by age and comorbidity among older women. FNA rates did not differ by age and comorbidity overall, but we observed increased FNA rates with higher comorbidity among women ages 75–84. Rates of core and surgical biopsy increased with comorbidity burden at ages 65–74. Our results are in line with findings of Friese et al. that core-needle biopsy was the initial procedure for 24.3% of women identified with stage I-II breast cancer.[6] They found no difference in use of core versus surgical biopsy by comorbidity. However, their analysis compared comorbidity scores between women who underwent core versus surgical biopsy (versus separate analyses by biopsy type), did not report patterns by age and comorbidity, and was limited to patients with cancer (versus a screening cohort). [6]

The decision to undergo screening mammography and subsequent downstream procedures should be part of patient-clinician shared decision-making to tailor screening to risk and preferences.[28] Shared decision-making is important to informing women of the benefits and harms of screening, including downstream procedures. This process should be guided by key shared decision-making elements: introducing choice, describing options, and helping patients explore preferences and make decisions. [30]

Limitations of our study include lack of access to data on post-biopsy outcomes including complications, which limits our understanding of benefits versus harms of downstream procedures after screening mammography. Due to the relatively low comorbidity burden in this screening population, our biopsy estimates may differ from other populations of older women. We used data through 2010, which may not reflect more recent breast imaging trends including increased use of digital breast tomosynthesis. Further, our study is US-based and may not be generalizable to women in other countries. However, it is notable that the reduction in FNA and increase in core biopsy we observe has also been observed in other countries.[31] Finally, our sample size does not support further subgroup analysis

to explore patterns by age and comorbidity in greater detail. Our study also has major strengths. The BCSC is the largest longitudinal population-based cohort study of women undergoing screening mammography in the U.S. The BCSC registries follow women after mammography to ascertain follow-up procedures, including biopsy, and outcomes. BCSC linkage to Medicare data allowed us to ascertain comorbidity in older women. Thus, we were able to assess patterns by age, comorbidity, biopsy type, and biopsy finding.

In conclusion, our study found that biopsy rates increased with comorbidity burden among women aged 66–74 and 75–84. Although biopsy rates declined with age, older women with higher comorbidity burden undergo biopsy procedures at a greater rate than older women with lower comorbidity, which may result in unnecessary procedures with little or no benefit. Future studies should evaluate factors beyond age and comorbidity, such as life expectancy and risk thresholds using breast density and other breast cancer risk factors.[32] This work coupled with work from other investigators can help refine screening mammography guidelines among older women.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Availability of data and materials:

Information about the data used in this study is available from the Breast Cancer Surveillance Consortium; restrictions apply to data availability (<https://www.bsc-research.org/>).

List of abbreviations:

BCSC	Breast Cancer Surveillance Consortium
CCS	Charlson Comorbidity Score
CI	Confidence Interval
DCIS	Ductal Carcinoma in Situ
FNA	Fine Needle Aspiration

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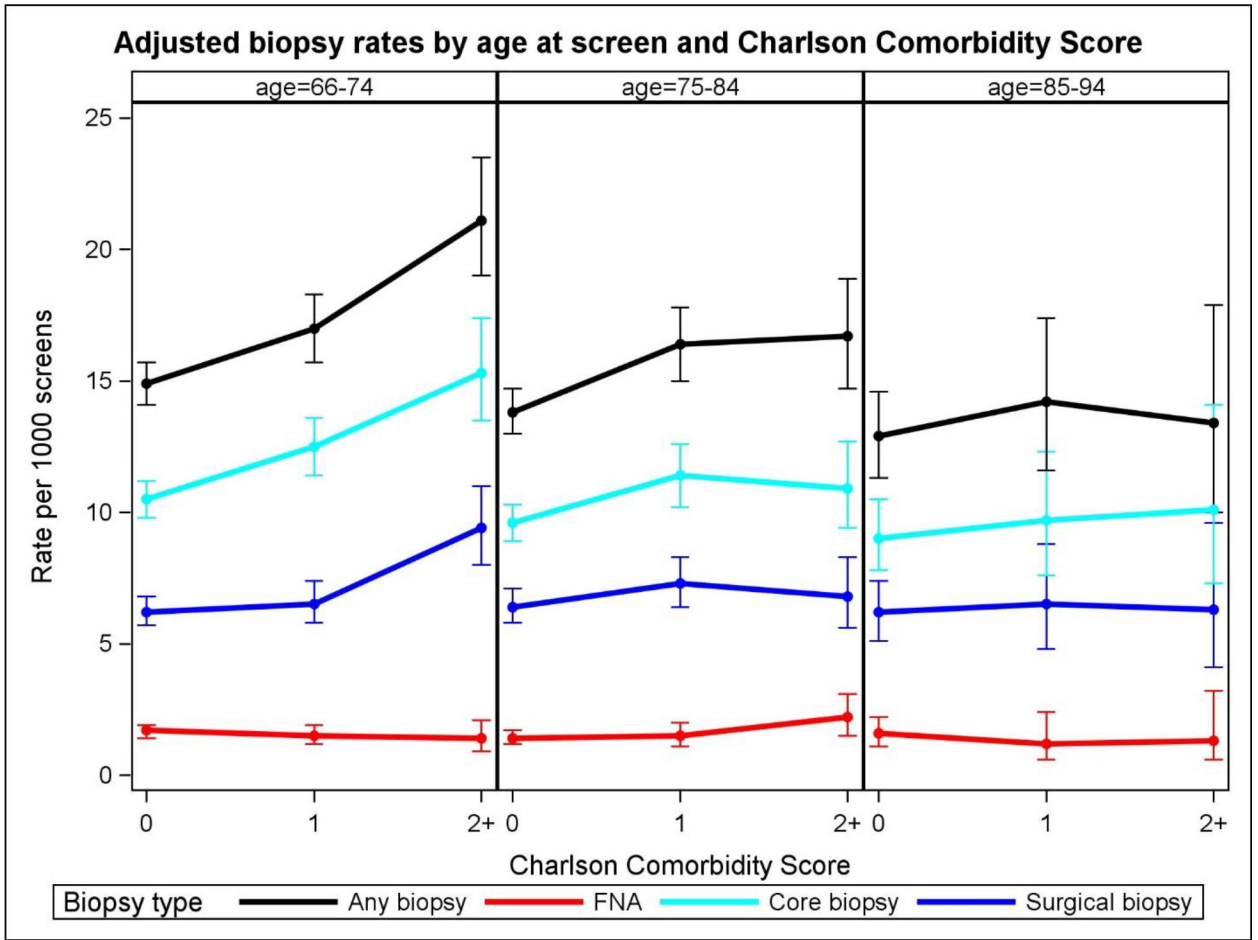


Figure 1: Adjusted rates (95% CI) of biopsy after screening mammography (overall and by biopsy type) by age and comorbidity score. Data from the Breast Cancer Surveillance Consortium, 1999–2010. Adjusted biopsy rates were calculated using logistic regression models that included age group, comorbidity group, BCSC registry, and the interaction between age and comorbidity groups. BCSC: Breast Cancer Surveillance Consortium, CI: Confidence Interval, FNA: Fine Needle Aspiration.

Table 1.

Characteristics of 524,860 screening mammograms by comorbidity score in the Breast Cancer Surveillance Consortium, 1999–2010

	Charlson Comorbidity Score[17]			
	Overall	0	1	2+
Characteristics at screen	N (column %)*	N (column %)*	N (column %)*	N (column %)*
Total N	524860	379958	105889	39013
Age in years (median, interquartile range)	73 (69, 78)	73 (69, 78)	74 (70, 78)	75 (70, 80)
Age group, years, N (%)				
66–74	304334 (58.0)	227031 (59.8)	58292 (55.1)	19011 (48.7)
75–84	190180 (36.2)	132603 (34.9)	40916 (38.6)	16661 (42.7)
85–94	30346 (5.8)	20324 (5.3)	6681 (6.3)	3341 (8.6)
Race/ethnicity, N (%)				
White	421162 (86.0)	313459 (88.2)	79580 (81.0)	28123 (78.5)
Black	41000 (8.4)	22950 (6.5)	12528 (12.8)	5522 (15.4)
Hispanic	6539 (1.3)	4590 (1.3)	1360 (1.4)	589 (1.6)
Asian/Pacific Islander	15043 (3.1)	10588 (3.0)	3361 (3.4)	1094 (3.1)
Other	5735 (1.2)	3853 (1.1)	1363 (1.4)	519 (1.4)
<i>Missing</i>	<i>35381 (6.7)</i>	<i>24518 (6.5)</i>	<i>7697 (7.3)</i>	<i>3166 (8.1)</i>
Education, N (%)				
<High School Graduate	63112 (14.4)	38672 (12.2)	17137 (19.5)	7303 (22.8)
High School Graduate or GED	150575 (34.4)	106433 (33.5)	32420 (36.9)	11722 (36.6)
Some College or Technical School	111872 (25.5)	83405 (26.2)	21126 (24.0)	7341 (22.9)
College Graduate	112320 (25.7)	89470 (28.1)	17228 (19.6)	5622 (17.6)
<i>Missing</i>	<i>86981 (16.6)</i>	<i>61978 (16.3)</i>	<i>17978 (17.0)</i>	<i>7025 (18.0)</i>
Median income, N (%)				
\$36,000	46834 (13.4)	30874 (12.1)	11640 (16.7)	4320 (17.2)
\$36,001–\$47,500	74861 (21.3)	52562 (20.5)	16254 (23.3)	6045 (24.1)
\$47,501–\$64,600	106064 (30.2)	77925 (30.5)	21116 (30.3)	7023 (28.0)
\$64,601	122883 (35.0)	94435 (36.9)	20717 (29.7)	7731 (30.8)
<i>Missing</i>	<i>174218 (33.2)</i>	<i>124162 (32.7)</i>	<i>36162 (34.2)</i>	<i>13894 (35.6)</i>
Rurality, N (%)				
Urban focused	288631 (56.3)	211534 (57.0)	55397 (53.4)	21700 (56.9)
Large rural	108877 (21.2)	77265 (20.8)	23542 (22.7)	8070 (21.2)
Small rural	62912 (12.3)	44709 (12.1)	13670 (13.2)	4533 (11.9)
Isolated rural	52222 (10.2)	37382 (10.1)	11036 (10.6)	3804 (10.0)
<i>Missing</i>	<i>12218 (2.3)</i>	<i>9068 (2.4)</i>	<i>2244 (2.1)</i>	<i>906 (2.3)</i>
Body mass index, kg/m², N (%)				
<25	94358 (43.5)	75180 (46.7)	14536 (35.8)	4642 (30.6)

	Overall	Charlson Comorbidity Score[17]		
		0	1	2+
Characteristics at screen	N (column %) *	N (column %) *	N (column %) *	N (column %) *
25 to <30	72722 (33.6)	54621 (33.9)	13400 (33.0)	4701 (31.0)
30 to <35	33537 (15.5)	22219 (13.8)	7888 (19.5)	3430 (22.6)
35	16125 (7.4)	8986 (5.6)	4723 (11.6)	2416 (15.9)
<i>Missing</i>	<i>308118 (58.7)</i>	<i>218952 (57.6)</i>	<i>65342 (61.7)</i>	<i>23824 (61.1)</i>
Breast density, N (%)				
Almost entirely fat	50895 (11.0)	34707 (10.4)	11627 (12.3)	4561 (13.0)
Scattered fibroglandular densities	246465 (53.1)	175343 (52.4)	51939 (54.9)	19183 (54.8)
Heterogeneously dense	151412 (32.6)	112683 (33.7)	28350 (30.0)	10379 (29.7)
Extremely dense	15283 (3.3)	11765 (3.5)	2639 (2.8)	879 (2.5)
<i>Missing</i>	<i>60805 (11.6)</i>	<i>45460 (12.0)</i>	<i>11334 (10.7)</i>	<i>4011 (10.3)</i>
First-degree family history of breast cancer, N (%)				
No	382400 (81.2)	275717 (81.2)	77840 (81.7)	28843 (80.8)
Yes	88283 (18.8)	63979 (18.8)	17463 (18.3)	6841 (19.2)
<i>Missing</i>	<i>54177 (10.3)</i>	<i>40262 (10.6)</i>	<i>10586 (10.0)</i>	<i>3329 (8.5)</i>
Time since prior mammogram, N (%)				
No prior	4756 (0.9)	3189 (0.9)	1057 (1.0)	510 (1.3)
<1 year	5203 (1.0)	3727 (1.0)	1037 (1.0)	439 (1.2)
1–2 years	469791 (91.8)	342514 (92.3)	93897 (91.0)	33380 (88.3)
3 years	32166 (6.3)	21500 (5.8)	7179 (7.0)	3487 (9.2)
<i>Missing</i>	<i>12944 (2.5)</i>	<i>9028 (2.4)</i>	<i>2719 (2.6)</i>	<i>1197 (3.1)</i>
History of breast biopsy or aspiration, N (%)				
No	383250 (74.1)	276785 (73.9)	77922 (74.7)	28543 (74.6)
Yes	134000 (25.9)	97916 (26.1)	26378 (25.3)	9706 (25.4)
<i>Missing</i>	<i>7610 (1.4)</i>	<i>5257 (1.4)</i>	<i>1589 (1.5)</i>	<i>764 (2.0)</i>

* Column percentages based on non-missing values (except percentages shown for missing data)

Table 2.

Breast biopsy patterns* after 524,860 screening mammograms in the Breast Cancer Surveillance Consortium, 1999–2010

	No biopsy	At least 1 biopsy	Fine needle aspiration	Core biopsy	Surgical biops	At least 2 types of biopsies
Characteristics at screen	N (row %)	N (row %)	N (row %)	N (row %)	N (row %)	N (row %)
Total N (%)	516930 (98.5)	7930 (1.5)	819 (0.2)	5589 (1.1)	3422 (0.7)	1805 (0.3)
Days to first biopsy or FNA (median, interquartile range)		29 (18, 55)	37 (18, 144)	27 (16, 45)	49 (31, 86)	
Charlson Comorbidity Score, N (%)						
0	374461 (98.6)	5497 (1.4)	603 (0.2)	3865 (1.0)	2405 (0.6)	1302 (0.3)
1	104170 (98.4)	1719 (1.6)	151 (0.1)	1222 (1.2)	710 (0.7)	350 (0.3)
2	38299 (98.2)	714 (1.8)	65 (0.2)	502 (1.3)	307 (0.8)	153 (0.4)
Age group, years, N (%)						
66–74	299614 (98.4)	4720 (1.6)	479 (0.2)	3365 (1.1)	1959 (0.6)	1021 (0.3)
75–84	187390 (98.5)	2790 (1.5)	291 (0.2)	1926 (1.0)	1268 (0.7)	668 (0.4)
85–94	29926 (98.6)	420 (1.4)	49 (0.2)	298 (1.0)	195 (0.6)	116 (0.4)
Race/ethnicity, N (%)						
White	414722 (98.5)	6440 (1.5)	675 (0.2)	4572 (1.1)	2810 (0.7)	1534 (0.4)
Black	40511 (98.8)	489 (1.2)	40 (0.1)	306 (0.7)	210 (0.5)	65 (0.2)
Hispanic	6426 (98.3)	113 (1.7)	18 (0.3)	80 (1.2)	45 (0.7)	27 (0.4)
Asian/Pacific Islander	14833 (98.6)	210 (1.4)	32 (0.2)	148 (1.0)	96 (0.6)	63 (0.4)
Other	5645 (98.4)	90 (1.6)	6 (0.1)	65 (1.1)	47 (0.8)	25 (0.4)
<i>Missing</i>	<i>34793 (98.3)</i>	<i>588 (1.7)</i>	<i>48 (0.1)</i>	<i>418 (1.2)</i>	<i>214 (0.6)</i>	<i>91 (0.3)</i>
Education, N (%)						
<High School Graduate	62273 (98.7)	839 (1.3)	74 (0.1)	503 (0.8)	444 (0.7)	170 (0.3)
High School Graduate or GED	148232 (98.4)	2343 (1.6)	242 (0.2)	1625 (1.1)	1066 (0.7)	557 (0.4)
Some College or Technical School	110077 (98.4)	1795 (1.6)	200 (0.2)	1290 (1.2)	777 (0.7)	449 (0.4)
College Graduate	110405 (98.3)	1915 (1.7)	232 (0.2)	1376 (1.2)	840 (0.7)	510 (0.5)
<i>Missing</i>	<i>85943 (98.8)</i>	<i>1038 (1.2)</i>	<i>71 (0.1)</i>	<i>795 (0.9)</i>	<i>295 (0.3)</i>	<i>119 (0.1)</i>
Median income, N (%)						
\$36,000	46114 (98.5)	720 (1.5)	63 (0.1)	478 (1.0)	316 (0.7)	127 (0.3)
\$36001–\$47500	73759 (98.5)	1102 (1.5)	86 (0.1)	713 (1.0)	521 (0.7)	211 (0.3)
\$47501–\$64600	104368 (98.4)	1696 (1.6)	183 (0.2)	1210 (1.1)	759 (0.7)	429 (0.4)
\$64601	120603 (98.1)	2280 (1.9)	263 (0.2)	1770 (1.4)	855 (0.7)	586 (0.5)
<i>Missing</i>	<i>172086 (98.8)</i>	<i>2132 (1.2)</i>	<i>224 (0.1)</i>	<i>1418 (0.8)</i>	<i>971 (0.6)</i>	<i>452 (0.3)</i>
Rurality, N (%)						
Urban focused	284394 (98.5)	4237 (1.5)	441 (0.2)	3132 (1.1)	1677 (0.6)	965 (0.3)

	No biopsy	At least 1 biopsy	Fine needle aspiration	Core biopsy	Surgical biops	At least 2 types of biopsies
Characteristics at screen	N (row %)	N (row %)	N (row %)	N (row %)	N (row %)	N (row %)
Large rural	107159 (98.4)	1718 (1.6)	181 (0.2)	1152 (1.1)	796 (0.7)	392 (0.4)
Small rural	61966 (98.5)	946 (1.5)	81 (0.1)	617 (1.0)	435 (0.7)	181 (0.3)
Isolated rural	51457 (98.5)	765 (1.5)	87 (0.2)	476 (0.9)	408 (0.8)	190 (0.4)
<i>Missing</i>	<i>11954 (97.8)</i>	<i>264 (2.2)</i>	<i>29 (0.2)</i>	<i>212 (1.7)</i>	<i>106 (0.9)</i>	<i>77 (0.6)</i>
Body mass index, N (%), kg/m²						
<25	92796 (98.3)	1562 (1.7)	203 (0.2)	1122 (1.2)	671 (0.7)	411 (0.4)
25 to <30	71445 (98.2)	1277 (1.8)	164 (0.2)	941 (1.3)	537 (0.7)	346 (0.5)
30 to <35	32834 (97.9)	703 (2.1)	66 (0.2)	550 (1.6)	294 (0.9)	198 (0.6)
35	15748 (97.7)	377 (2.3)	47 (0.3)	274 (1.7)	182 (1.1)	116 (0.7)
<i>Missing</i>	<i>304107 (98.7)</i>	<i>4011 (1.3)</i>	<i>339 (0.1)</i>	<i>2702 (0.9)</i>	<i>1738 (0.6)</i>	<i>734 (0.2)</i>
Breast density, N (%)						
Almost entirely fat	50370 (99.0)	525 (1.0)	45 (0.1)	390 (0.8)	230 (0.5)	135 (0.3)
Scattered fibroglandular densities	243242 (98.7)	3223 (1.3)	283 (0.1)	2313 (0.9)	1317 (0.5)	662 (0.3)
Heterogenously dense	148802 (98.3)	2610 (1.7)	273 (0.2)	1818 (1.2)	1151 (0.8)	592 (0.4)
Extremely dense	15022 (98.3)	261 (1.7)	34 (0.2)	162 (1.1)	125 (0.8)	58 (0.4)
<i>Missing</i>	<i>59494 (97.8)</i>	<i>1311 (2.2)</i>	<i>184 (0.3)</i>	<i>906 (1.5)</i>	<i>599 (1.0)</i>	<i>358 (0.6)</i>
Family history of breast cancer, N (%)						
No	376568 (98.5)	5832 (1.5)	620 (0.2)	4160 (1.1)	2458 (0.6)	1336 (0.3)
Yes	86648 (98.1)	1635 (1.9)	158 (0.2)	1189 (1.3)	745 (0.8)	434 (0.5)
<i>Missing</i>	<i>53714 (99.1)</i>	<i>463 (0.9)</i>	<i>41 (0.1)</i>	<i>240 (0.4)</i>	<i>219 (0.4)</i>	<i>35 (0.1)</i>
Time since prior mammogram, N (%)						
No prior	4577 (96.2)	179 (3.8)	17 (0.4)	102 (2.1)	85 (1.8)	24 (0.5)
1 year	5083 (97.7)	120 (2.3)	22 (0.4)	68 (1.3)	61 (1.2)	30 (0.6)
1–2 years	463251 (98.6)	6540 (1.4)	688 (0.1)	4628 (1.0)	2833 (0.6)	1525 (0.3)
3 years	31346 (97.5)	820 (2.5)	66 (0.2)	599 (1.9)	351 (1.1)	189 (0.6)
<i>Missing</i>	<i>12673 (97.9)</i>	<i>271 (2.1)</i>	<i>26 (0.2)</i>	<i>192 (1.5)</i>	<i>92 (0.7)</i>	<i>37 (0.3)</i>
History of breast biopsy or aspiration, N (%)						
No	378199 (98.7)	5051 (1.3)	503 (0.1)	3629 (0.9)	2144 (0.6)	1161 (0.3)
Yes	131226 (97.9)	2774 (2.1)	302 (0.2)	1893 (1.4)	1229 (0.9)	620 (0.5)
<i>Missing</i>	<i>7505 (98.6)</i>	<i>105 (1.4)</i>	<i>14 (0.2)</i>	<i>67 (0.9)</i>	<i>49 (0.6)</i>	<i>24 (0.3)</i>

* Biopsy patterns are based on biopsies found within 12 months after screening exam and prior to next screen. If multiple biopsy types are found after a single screen the screen would appear in multiple columns.

FNA: Fine Needle Aspiration.

Table 3:

Rate (95% CI) of screening mammograms followed by biopsy (per 1000 screens) adjusted for age, comorbidity score and Breast Cancer Surveillance Consortium registry

Age at screen, years	Overall N (denominator)	Any biopsy	p-trend*	Fine needle aspiration	p-trend*	Core biopsy	p-trend*	Surgical biopsy	p-trend*
66–74	304334	15.7 (14.8, 16.8)	<0.001	1.6 (1.3, 2.0)	0.50	11.2 (10.4, 12.1)	<0.001	6.5 (5.9, 7.2)	0.52
75–84	190180	14.5 (13.5, 15.6)		1.5 (1.2, 1.9)		10.0 (9.2, 10.9)		6.6 (5.9, 7.4)	
85–94	30346	13.2 (11.3, 15.4)		1.5 (1.0, 2.3)		9.2 (7.7, 11.1)		6.2 (5.0, 7.9)	
Charlson Comorbidity Score (CCS)									
0	379958	14.4 (13.5, 15.3)	<0.001	1.6 (1.3, 1.9)	0.41	10.1 (9.4, 10.8)	<0.001	6.3 (5.7, 6.9)	<0.001
1	105889	16.6 (15.2, 18.1)		1.5 (1.1, 2.0)		11.9 (10.7, 13.2)		6.8 (6.0, 7.8)	
2+	39013	19.0 (16.9, 21.5)		1.7 (1.1, 2.5)		13.4 (11.6, 15.5)		8.3 (6.9, 9.9)	
Age at screen=66–74 years									
CCS=0	227031	14.9 (14.1, 15.7)	<0.001	1.7 (1.4, 1.9)	0.40	10.5 (9.8, 11.2)	<0.001	6.2 (5.7, 6.8)	<0.001
CCS=1	58292	17.0 (15.7, 18.3)		1.5 (1.2, 1.9)		12.5 (11.4, 13.6)		6.5 (5.8, 7.4)	
CCS=2+	19011	21.1 (19.0, 23.5)		1.4 (0.9, 2.1)		15.3 (13.5, 17.4)		9.4 (8.0, 11.0)	
Age at screen=75–84 years									
CCS=0	132603	13.8 (13.0, 14.7)	0.003	1.4 (1.2, 1.7)	0.02	9.6 (8.9, 10.3)	0.09	6.4 (5.8, 7.1)	0.55
CCS=1	40916	16.4 (15.0, 17.8)		1.5 (1.1, 2.0)		11.4 (10.2, 12.6)		7.3 (6.4, 8.3)	
CCS=2+	16661	16.7 (14.7, 18.9)		2.2 (1.5, 3.1)		10.9 (9.4, 12.7)		6.8 (5.6, 8.3)	
Age at screen=85–94 years									
CCS=0	20324	12.9 (11.3, 14.6)	0.79	1.6 (1.1, 2.2)	0.74	9.0 (7.8, 10.5)	0.51	6.2 (5.1, 7.4)	0.95

Age at screen, years	Overall N (denominator)	Any biopsy	p-trend*	Fine needle aspiration	p-trend*	Core biopsy	p-trend*	Surgical biopsy	p-trend*
CCS=1	6681	14.2 (11.6, 17.4)		1.2 (0.6, 2.4)		9.7 (7.6, 12.3)		6.5 (4.8, 8.8)	
CCS=2+	3341	13.4 (10.0, 17.9)		1.3 (0.6, 3.2)		10.1 (7.3, 14.1)		6.3 (4.1, 9.6)	

* The p-values testing for trend across age group and across comorbidity score are based on models that do not include an interaction between age and comorbidity. The p-values testing for trend across comorbidity within each age group are based on models with an interaction between age group and comorbidity group.

CCS: Charlson Comorbidity Score, CI: Confidence Interval.

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Table 4.

Biopsy yield (95% CI) of benign findings, ductal carcinoma in situ (DCIS) and invasive breast cancer per 100 biopsies following a screening mammogram, by age at screen and comorbidity (adjusted for age, comorbidity score and Breast Cancer Surveillance Consortium registry)

Age and comorbidity groups	All biopsies (N=9479)	p-trend*	Fine needle aspiration [‡] (N=659)	p-trend*	Core biopsy (N=5477)	p-trend*	Surgical biopsy (N=3343)	p-trend*
All Biopsies								
Benign [†]	55.2 (52.1, 58.4)		79.2 (67.3, 87.1)		57.9 (53.7, 62.1)		47.1 (41.8, 52.4)	
DCIS	9.9 (8.2, 12.1)		NA		9.8 (7.6, 12.7)		11.8 (8.8, 15.8)	
Invasive	34.8 (31.8, 37.9)		20.8 (12.9, 32.7)		32.2 (28.4, 36.3)		41.1 (36.0, 46.5)	
Benign[†]								
Age at screen, years								
66–74	58.8 (56.0, 61.5)	< 0.001	83.8 (73.9, 89.9)	0.01	61.3 (57.7, 64.8)	<0.001	50.0 (45.3, 54.7)	0.01
75–84	51.3 (48.1, 54.6)		73.7 (60.5, 82.9)		54.6 (50.2, 58.8)		43.4 (38.2, 48.7)	
85–94	43.8 (37.1, 50.7)		68.4 (43.4, 86.1)		44.5 (35.6, 53.7)		40.2 (29.5, 51.8)	
Charlson Comorbidity Score (CCS)								
0	54.7 (52.0, 57.4)	0.61	80.0 (70.2, 86.6)	0.83	56.8 (53.2, 60.3)	0.28	47.2 (42.7, 51.7)	0.77
1	57.0 (53.1, 60.9)		76.3 (60.5, 86.7)		61.5 (56.4, 66.4)		46.8 (40.3, 53.4)	
2+	55.5 (49.9, 61.1)		80.0 (57.0, 93.0)		59.4 (52.0, 66.4)		46.2 (37.1, 55.6)	
Age 66–74								
CCS=0	58.4 (56.0, 60.7)	0.49	84.7 (77.2, 89.7)	0.94	60.4 (57.2, 63.4)	0.67	50.0 (45.9, 54.1)	0.30
CCS=1	61.0 (57.6, 64.3)		80.4 (67.2, 88.8)		64.7 (60.4, 68.9)		51.4 (45.4, 57.3)	
CCS=2+	56.7 (51.9, 61.5)		84.1 (59.7, 95.0)		61.7 (55.4, 67.6)		45.9 (38.1, 53.9)	
Age 75–84								
CCS=0	50.6 (47.8, 53.4)	0.08	74.0 (62.3, 82.2)	0.50	53.1 (49.4, 56.8)	0.19	43.9 (39.4, 48.5)	0.51
CCS=1	52.4 (48.5, 56.3)		70.7 (53.7, 82.7)		58.5 (53.3, 63.6)		40.2 (34.1, 46.7)	
CCS=2+	55.8 (50.1, 61.4)		79.3 (60.6, 90.4)		58.3 (50.6, 65.6)		47.2 (37.8, 56.8)	
Age 85–94								
CCS=0	43.6 (38.1, 49.2)	0.81	70.3 (49.7, 84.4)	0.34	43.8 (36.4, 51.4)	0.92	39.6 (30.8, 49.1)	0.74

Age and comorbidity groups	All biopsies (N=9479)	p-trend*	Fine needle aspiration [‡] (N=659)	p-trend*	Core biopsy (N=5477)	p-trend*	Surgical biopsy (N=3343)	p-trend*
CCS=1	45.1 (36.2, 54.4)		70.7 (34.8, 91.5)		47.7 (35.9, 59.7)		41.3 (27.3, 56.7)	
CCS=2+	41.8 (29.6, 55.1)		43.4 (6.6, 88.4)		42.8 (27.3, 59.8)		43.6 (23.7, 65.5)	
DCIS								
Age at screen, years								
66–74	9.9 (8.4, 11.8)	0.97	NA	NA	9.9 (7.9, 12.4)	0.79	11.7 (9.0, 15.2)	0.91
75–84	10.0 (8.3, 12.2)		NA		9.6 (7.4, 12.5)		12.0 (9.0, 16.0)	
85–94	10.0 (6.7, 14.9)		NA		10.4 (6.1, 17.6)		11.5 (6.4, 20.6)	
CCS								
0	10.2 (8.6, 12.0)	0.86	NA	NA	10.2 (8.2, 12.7)	0.41	11.9 (9.2, 15.2)	0.55
1	9.3 (7.2, 11.9)		NA		8.7 (6.3, 12.1)		11.2 (7.7, 16.3)	
2+	10.0 (7.1, 14.0)		NA		9.0 (5.7, 14.4)		12.9 (7.9, 20.7)	
Age 66–74								
CCS=0	9.9 (8.5, 11.5)	0.33	NA	NA	10.0 (8.2, 12.1)	0.81	11.7 (9.3, 14.7)	0.23
CCS=1	9.5 (7.7, 11.8)		NA		9.5 (7.2, 12.5)		10.7 (7.5, 15.0)	
CCS=2+	11.3 (8.6, 14.8)		NA		9.6 (6.4, 14.0)		14.8 (9.9, 21.5)	
Age 75–84								
CCS=0	10.6 (8.9, 12.4)	0.11	NA	NA	10.5 (8.4, 13.0)	0.36	12.0 (9.3, 15.4)	0.38
CCS=1	9.0 (7.0, 11.5)		NA		7.2 (5.0, 10.3)		12.9 (9.1, 17.9)	
CCS=2+	7.7 (5.1, 11.3)		NA		8.3 (4.9, 13.6)		9.2 (4.9, 16.6)	
Age 85–94								
CCS=0	10.4 (7.5, 14.2)	0.81	NA	NA	10.6 (6.8, 16.3)	0.71	12.3 (7.6, 19.4)	0.53
CCS=1	8.2 (4.4, 14.7)		NA		10.1 (4.8, 20.0)		6.5 (2.1, 18.4)	
CCS=2+	11.4 (5.5, 22.3)		NA		8.6 (2.8, 23.7)		17.0 (6.3, 38.0)	
Invasive								
Age at screen, years								
66–74	31.3 (28.8, 34.0)	<0.001	16.2 (10.1, 26.1)	0.01	28.8 (25.6, 32.2)	<0.001	38.4 (33.9, 43.1)	0.01
75–84	38.6 (35.4, 41.8)		26.3 (17.1, 39.5)		35.7 (31.7, 40.0)		44.5 (39.2, 49.9)	
85–94	45.9 (39.2, 52.8)		31.6 (13.9, 56.6)		44.8 (36.0, 54.0)		47.8 (36.9, 59.0)	
CCS								
0	35.1 (32.5, 37.8)	0.70	20.0 (13.4, 29.8)	0.83	33.0 (29.6, 36.5)	0.55	40.9 (36.5, 45.5)	0.92
1	33.8 (30.1, 37.6)		23.7 (13.3, 39.5)		29.8 (25.3, 34.7)		42.0 (35.6, 48.6)	
2+	34.5 (29.3, 40.0)		20.0 (7.0, 43.0)		31.7 (25.2, 38.8)		40.7 (32.0, 50.1)	
Age 66–74								

Age and comorbidity groups	All biopsies (N=9479)	p-trend*	Fine needle aspiration [‡] (N=659)	p-trend*	Core biopsy (N=5477)	p-trend*	Surgical biopsy (N=3343)	p-trend*
CCS=0	31.7 (29.6, 34.0)	0.91	15.3 (10.3, 22.8)	0.94	29.6 (26.8, 32.6)	0.78	38.4 (34.5, 42.4)	0.85
CCS=1	29.5 (26.5, 32.7)		19.6 (11.2, 32.8)		25.7 (22.1, 29.8)		38.1 (32.5, 44.0)	
CCS=2+	32.0 (27.7, 36.6)		15.9 (5.0, 40.3)		28.9 (23.5, 34.8)		39.1 (31.7, 47.1)	
Age 75–84								
CCS=0	38.8 (36.1, 41.6)	0.44	26.0 (17.8, 37.7)	0.50	36.4 (32.8, 40.1)	0.44	43.9 (39.4, 48.6)	0.94
CCS=1	38.5 (34.8, 42.4)		29.3 (17.3, 46.3)		34.3 (29.5, 39.4)		46.6 (40.2, 53.1)	
CCS=2+	36.5 (31.2, 42.2)		20.7 (9.6, 39.4)		33.4 (26.6, 41.0)		43.6 (34.3, 53.3)	
Age 85–94								
CCS=0	45.7 (40.2, 51.3)	0.93	29.7 (15.6, 50.3)	0.34	45.2 (37.8, 52.9)	0.73	47.4 (38.4, 56.6)	0.44
CCS=1	46.6 (37.7, 55.8)		29.3 (8.5, 65.2)		42.1 (30.8, 54.3)		52.5 (37.4, 67.1)	
CCS=2+	46.3 (33.8, 59.3)		56.6 (11.6, 93.4)		48.4 (32.3, 65.0)		38.5 (20.5, 60.1)	

* The p-values testing for trend across age group and across comorbidity score are based on models that do not include an interaction between age and comorbidity. The p-values testing for trend across comorbidity within each age group are based on models with an interaction between age group and comorbidity group.

[‡] Includes high-risk benign and other benign findings.

[‡] Results for DCIS and invasive breast cancer have been combined for fine needle aspiration due to small cell sizes.

CCS: Charlson Comorbidity Score, CI: Confidence Interval, DCIS: Ductal Carcinoma in Situ.