Detection of Ductal Carcinoma *In Situ* in Women Undergoing Screening Mammography

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Background: **With the large number of women having mammography—an estimated 28.4 million U.S. women aged 40 years and older in 1998—the percentage of cancers detected as ductal carcinoma *in situ* (DCIS), which has an uncertain prognosis, has increased. We pooled data from seven regional mammography registries to determine the percentage of mammographically detected cancers that are DCIS and the rate of DCIS per 1000 mammograms.** ***Methods:*** **We analyzed data on 653 833 mammograms from 540 738 women between 40 and 84 years of age who underwent screening mammography at facilities participating in the National Cancer Institute's Breast Cancer Surveillance Consortium (BCSC) throughout 1996 and 1997. Mammography results were linked to population-based cancer and pathology registries. We calculated the percentage of screen-detected breast cancers that were DCIS, the rate of screen-detected DCIS per 1000 mammograms by age and by previous mammography status, and the sensitivity of screening mammography. Statistical tests were two-sided.** ***Results:*** **A total of 3266 cases of breast cancer were identified, 591 DCIS and 2675 invasive breast cancer. The percentage of screen-detected breast cancers that were DCIS decreased with age (from 28.2% [95% confidence interval (CI) = 23.9% to 32.5%] for women aged 40–49 years to 16.0% [95% CI = 13.3% to 18.7%] for women aged 70–84 years). However, the rate of screen-detected DCIS cases per 1000 mammograms increased with age (from 0.56 [95% CI = 0.41 to 0.70] for women aged 40–49 years to 1.07 [95% CI = 0.87 to 1.27] for women aged 70–84 years). Sensitivity of screening mammography in all age groups combined was higher for detecting DCIS (86.0% [95% CI = 83.2% to 88.8%]) than it was for detecting invasive breast cancer (75.1% [95% CI = 73.5% to 76.8%]).** ***Conclusions:*** **Overall, approximately 1 in every 1300 screening mammography examinations leads to a diagnosis of DCIS. Given uncertainty about the natural history of DCIS, the clinical significance of screen-detected DCIS needs further investigation. [J Natl Cancer Inst 2002;94: 1546–54]**

Incidence rates of ductal carcinoma *in situ* (DCIS) of the breast, a noninvasive form of breast cancer, have risen dramatically in the United States and elsewhere since the early 1980s *(1–5).* The increase in DCIS incidence parallels an increase in the use of screening mammography, which makes the detection of DCIS much more likely than in the past. DCIS is a diverse process of the breast epithelium that is, by definition, confined within the breast duct above the basement membrane. The cellular appearance of DCIS varies from low-grade lesions similar to atypical hyperplasia to high-grade or anaplastic lesions. Because DCIS is excised when detected, it is not possible to accurately estimate the fraction of untreated cases that would progress to invasive malignancy. In addition to undergoing surgical treatment (lumpectomy or mastectomy), women with DCIS are frequently treated with radiation or hormone therapy *(1,6,7).* Moreover, in addition to other treatment, axillary lymph node dissection may also be performed for women with DCIS, although this procedure is not standard of care *(6,7).*

It is unlikely that there will ever be definitive studies to demonstrate whether detection of DCIS by mammography has contributed to the reduction in breast cancer mortality associated with screening mammography. However, it seems reasonable to conclude that some women benefit from having DCIS detected through screening mammography, whereas other women do not, depending on whether the disease was likely to progress. Because it is not possible to screen women for invasive breast cancer alone, the detection of DCIS is part of any screening mammography program. A recent survey of 479 women in the United States found that few women had heard about DCIS or were aware that some forms of breast cancer might not progress *(8).* When these women were informed, however, 60% of them wanted to take the possibility of DCIS detection into account when deciding about participating in screening mammography. No information is currently available about the rate of screen-detected DCIS. Therefore, we pooled data from mammography registries across the United States to determine the percentage of DCIS among all screen-detected breast cancers and the rate of screen-detected DCIS per 1000 mammograms performed.

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See "Notes" following "References."

METHODS

Study Population

We obtained patient history and clinical and radiologic assessment data from screening mammography examinations from the mammography registries of the Breast Cancer Surveillance Consortium (BCSC) performed from January 1996 through December 1997. The mammography registries were located in Colorado, New Hampshire, New Mexico, North Carolina, San Francisco (CA), Vermont, and western Washington State. The BCSC, funded by the National Cancer Institute, and its confidentiality procedures are described elsewhere *(9,10).* Each mammography registry had Institutional Review Board approval to collect data from mammography facilities for research purposes. All patient identifiers were removed from the collected data before they were transferred to the BCSC's Statistical Coordinating Center for analysis.

The present analysis is limited to the results of screening mammography examinations for women between 40 and 84 years old who had no self-report of previous breast cancer. To be eligible for inclusion, the woman's mammography examination had to be designated as a screening examination rather than a diagnostic examination by the radiologist. We excluded unilateral screening examinations and examinations that did not have an assessment code indicating whether they had been considered negative or positive for an abnormality indicative of cancer. Assessment codes were based on the American College of Radiology's Breast Imaging Reporting and Data System (BI-RADS) *(11).* We also excluded mammographic examinations if the women had had any breast imaging (including ultrasound or another mammogram) in the preceding 9 months, because imaging within this period may indicate that the screening mammographic examination was not a true screening examination but rather a follow-up examination. We used 9 months rather than a longer time period as the cutoff because women sometimes schedule their annual mammographic examination a month or two early. All screening examinations from the same woman over the 2-year study period were included, subject to the 9-month exclusion rule.

Mammogram Assessment, Categorization, and Cancer Diagnoses

Mammograms were linked to either cancer or pathology registries in the same geographic region as the mammography registry. Not all mammography facilities in a particular geographic region are included in the BCSC for that region, so not all mammograms for that region were ascertained; however, ascertainment of cancers is believed to be almost complete. Statistics by state for each cancer registry are maintained by the North American Association of Central Cancer Registries and show adjusted completion rates based on observed versus expected rates for all cancers in excess of 94.3% in all states included in this study except for Vermont, which did not have statistics available *(12).* Cancer records from the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) Program[1] were used for the three BCSC sites that are located in SEER registry areas—that is, New Mexico, San Francisco, and western Washington State—and a fourth site, Colorado, used a non-SEER cancer registry that uses SEER guidelines for data collection. For the other three sites, where there can be a long delay between cancer diagnosis and appearance of the cancer record in the local cancer registry, pathology registries served as the primary source of case reporting, supplemented by cancer registry data. In this article, we present combined data from all mammography registries participating in the BCSC, recognizing that there may be some variation in cancer ascertainment across registries and, therefore, potential variation in cancer incidence rates.

Cases were categorized as either DCIS or invasive breast cancer based on either cancer registry or pathology registry data. Cases of *in situ* lesions that were specifically coded as lobular carcinoma *in situ* (LCIS) were excluded, but other cases of *in situ* lesions were included (for example, *in situ* lesions that were coded as "not otherwise specified"). Thus, some *in situ* lesions other than DCIS were categorized as DCIS, but the number of these was small. If a cancer case was coded within 60 days of diagnosis as having both invasive and *in situ* components, it was categorized as invasive breast cancer rather than as DCIS. For comparison with the DCIS findings, we also provide some findings for invasive breast cancer; however, the data on invasive breast disease were not examined in detail.

Throughout this article the term "screen-detected" refers to screening mammography and not to other forms of breast cancer detection. We used the initial mammographic assessment category assigned to each screening mammography examination to determine whether cases of DCIS and invasive breast cancer had been screen-detected. We considered cases of DCIS or invasive breast cancer to be screen-detected (i.e., positive) if the patient's most recent eligible screening mammography examination in the 365 days prior to diagnosis resulted in any of the following BI-RADS assessment codes: 0 (needs additional evaluation); 3 (probably benign finding), with a recommendation for immediate work-up; 4 (suspicious abnormality); or 5 (highly suggestive of malignancy). Cases of DCIS or invasive breast cancer were considered non-screen-detected (i.e., negative) if the patient's most recent eligible screening mammography examination in the 365 days prior to diagnosis had resulted in a BI-RADS assessment code of 1 (negative); 2 (benign finding); or 3 (probably benign finding), with no recommendation for immediate work-up or with an unknown recommendation. These case definitions were used to generate the numerators for calculating rates per 1000 mammograms for screen-detected and non-screen-detected DCIS and invasive breast cancer. The denominators used in calculating rates were the number of screening mammography examinations, not the number of women. The follow-up period after a screening examination was 365 days or the next screening examination, whichever came first. This follow-up period ensured that a diagnosis of cancer was allocated to a single screening mammography examination.

Data Analysis

We first determined the sensitivity of screening mammography for detecting DCIS and invasive breast cancer. Sensitivity was defined as the number of cases with a positive mammographic assessment at screening divided by the total number of women. We then calculated the percentage of all screen-detected and non-screen-detected breast cancers that were DCIS, and the rates of screen-detected and non-screen-detected DCIS per 1000 mammograms by age group (40–49 years, 50–59 years, 60–69 years, and 70–84 years) and for all ages combined. The denominator used to calculate the DCIS rate in each category was the total number of screening examinations in that category. We

further cross-classified the percentage and rate variables by previous mammography status as determined by women's self-reported mammography history (screening or diagnostic mammogram). At the time of screening mammography, women were routinely asked if they had had a prior mammographic examination and the date of or approximate time in years since that examination. Women who did not provide complete information about history of previous mammography were categorized as having no previous mammography; 461 129 (71%) women reported a history of a prior mammographic examination and 192 704 (29%) women did not report having a prior mammographic examination.

Data from individual BCSC sites on percentages of cancers that are DCIS and rates of DCIS per 1000 mammograms are not reported, but ranges of these variables over the seven BCSC sites are presented (*see* Tables 3 and 4). Ninety-five percent confidence intervals (CIs) were calculated for sensitivity, for percentage of cancers that are DCIS, and for the rate of DCIS per 1000 mammograms based on the pooled BCSC data and were not corrected for multiple comparisons. We assumed a normal approximation to the binomial distribution for proportions and a Poisson distribution for each cancer rate. Standard chi-square tests were used as statistical tests for proportions, and Poisson regression was used as the statistical test for comparison of cancer rates. Statistical tests were two-sided. We also plotted the distributions of time-to-diagnosis for cases defined as screen-detected and those defined as non-screen-detected.

RESULTS

Demographic and Clinical Variables

Across the seven BCSC sites, data from 653 833 screening mammography examinations (ranging from 43 624 to 150 387 examinations among 540 738 women were available for evaluation (Table 1). Thus, approximately 20% of women contributed more than one screening mammography examination to the analysis. Based on questionnaire data collected at the time of screening, 29% of all mammographic examinations were classified as first ever: 33% for ages 40–49 years, 27% for ages 50–59 years, 28% for ages 60–69 years, and 29% for ages 70–84 years. Race was self-reported for 86% of the women who were screened; of these women, 79% were white, 5% were African-American, 2% were Asian/Pacific Islander, 2% were Native American, and 12% were other/mixed. Of the 81% of women who responded to a question about whether they were of Hispanic origin, 4% reported being Hispanic. Educational level was either not asked for or not reported for 39% of women. Of those women who did report educational level, 34% completed college, 57% completed high school but not college, and 9% did not complete high school. Because this demographic information was not reported for many women, we did not analyze the results of screening mammography data by race or educational level.

Linkage of mammography screening data and cancer case reports resulted in the identification of 3266 cases of breast cancer (2675 invasive and 591 DCIS) occurring within 365 days following screening mammography. The distributions of the number of screening mammography examinations, DCIS cases, and invasive breast cancer cases by age are given in Table 1, where we further distribute by positive (screen-detected) cases.

Sensitivity of Screening Mammography for Detecting DCIS

The sensitivity of screening mammography for detecting DCIS was higher than that for invasive breast cancer. Of all DCIS cases diagnosed during the study period, 86.0% (508/591, 95% CI = 83.2% to 88.8%) were associated with a positive screening mammography assessment (compared with 75.1% (2010/2675, 95% CI = 73.5% to 76.8%) of all invasive breast cancer cases (Table 1). Sensitivity of screening mammography for detecting DCIS did not differ statistically significantly by age ($P = .47$). By comparison, sensitivity for detecting invasive breast cancer increased statistically significantly with age ($P_{trend}<.001$), from 66.9% for women aged 40–49 years to 82.7% for women aged 70–84 years (difference in sensitivity = 15.8%, 95% CI = 10.7% to 21.0%). Sensitivity for detecting both types of cancers combined also increased statistically significantly with age ($P_{trend}<.001$) from 71.7% for women aged 40–49 years to 82.8% for women aged 70–84 years (difference in sensitivity = 11.1%, 95% CI = 6.6% to 15.5%), as might be expected, because the invasive breast cancer cases made up 81.9% of all cases.

Sensitivity of screening mammography for detecting DCIS was slightly higher for women with no previous mammography (88.6%) than it was for those with previous mammography (84.8%), but these values were not statistically significantly different from one another (difference in sensitivity = 3.8%, 95% CI = –2.0% to 9.6%; $P = .25$) (Table 2). The highest sensitivity for detecting DCIS was seen in women aged 40–49 years who

Table 1. Number of screening mammography examinations and the percentage of women with ductal carcinoma *in situ* (DCIS) or invasive breast cancer who had a positive screen (sensitivity), by age*

Age range, y	No. of screening mammography examinations	DCIS		Invasive breast cancer		DCIS and invasive breast cancer combined	
		No. of cases diagnosed	Percentage of cases with positive screen	No. of cases diagnosed	Percentage of cases with positive screen†	Total no. of cases diagnosed	Percentage of cases with positive screen†
40–49	211 551	134	88.1	450	66.9	584	71.7
50–59	200 255	155	88.4	792	72.2	947	74.9
60–69	135 376	165	84.2	709	75.9	874	77.5
70–84	106 651	137	83.2	724	82.7	861	82.8
Total	653 833	591	86.0	2675	75.1	3266	77.1

*Positive screen is a mammography screening examination associated with a positive screening assessment (American College of Radiology's Breast Imaging Reporting and Data System [BI-RADS] assessment code of 0 - needs additional imaging, 3 - probably benign finding with a recommendation for immediate work-up, 4 - suspicious abnormality, or 5 - highly suggestive of malignancy) within 365 days prior to cancer diagnosis. Percentage of cases with a positive screen is sensitivity.

†Proportions using the chi-square (χ^2) test are statistically significantly different across age categories ($P_{trend}<.001$).

Table 2. Percentage of women with ductal carcinoma *in situ* (DCIS) or invasive breast cancer who had a positive screen (sensitivity), by age and previous mammography*

	DCIS				Invasive breast cancer			
	No previous mammogram		Previous mammogram		No previous mammogram		Previous mammogram	
Age range, y	No. of cases	Percentage of cases with positive screen	No. of cases	Percentage of cases with positive screen	No. of cases	Percentage of cases with positive screen†	No. of cases	Percentage of cases with positive screen†
40–49	39	97.4	95	84.2	172	75.6	278	61.5
50–59	46	87.0	109	89.0	254	79.1	538	69.0
60–69	45	84.4	120	84.2	209	83.3	500	72.8
70–84	46	87.0	91	81.3	263	89.0	461	79.2
Total	176	88.6	415	84.8	898	82.3	1777	71.5

*Positive screen is a mammography-screening examination associated with a positive screening assessment (American College of Radiology's Breast Imaging Reporting and Data System [BI-RADS] assessment code of 0 - needs additional imaging, 3 - probably benign finding with a recommendation for immediate work-up, 4 - suspicious abnormality, or 5 - highly suggestive of malignancy) within 365 days prior to cancer diagnosis. Percentage of cases with a positive screen is sensitivity.

†Proportions using the chi-square (χ^2) test are statistically significantly different across age categories (P_{trend}<.01).

reported no previous mammography (97.4%, 95% CI = 85.0% to 100%); however, there was no clear association between sensitivity for detecting DCIS and age when the data were stratified by previous mammography status. For invasive breast cancer, the difference in sensitivity between women with no previous mammography (82.3%) and those with previous mammography (71.5%) was greater than that observed for DCIS (difference in sensitivity = 10.8%, 95% CI = 7.5% to 14.0%; P<.001), and sensitivity increased statistically significantly with age for women without and with previous mammography (P_{trend}<.001 for both).

Percentage of DCIS Among Screen-Detected and Non-Screen-Detected Breast Cancers

The percentages of screen-detected and non-screen-detected breast cancer cases that were DCIS across all study sites combined varied by age and by prior screening history, as shown in Table 3. The percentage of cancers that were DCIS differed statistically significantly by age overall (P<.001) and for women with positive mammography screens who had previous mammography (P<.001). However, if the women had positive mammography screens and had not had a previous mammogram, or if they had negative screens, the percentage of cancers that were DCIS did not vary statistically significantly by age (P = .19 and P = .07, respectively). For all age groups combined, 20.2% (95% CI = 18.6% to 21.7%) of screen-detected breast cancers were DCIS, with the percentage being higher among women aged 40–49 years (28.2%, 95% CI = 23.9% to 32.5%) than among women in all older age groups (ranging from 16% [95% CI = 13.3% to 18.7%] to 20.5% [95% CI = 17.5% to 23.6%] among women aged 60–84 years). In every age group, a higher percentage of screen-detected breast cancer was DCIS among women with previous mammography than among women with no previous mammography, with the difference being most pronounced for women aged 40–49 years (31.9% versus 22.6%, respectively).

Rates of Screen-Detected DCIS

The association of screen-detected DCIS with age differed depending on whether one was examining the percentage of cases that are DCIS or the rate of DCIS per 1000 mammograms (Fig. 1). The percentage of screen-detected breast cancer that was DCIS decreased with age (Fig. 1, A), whereas the DCIS rate per 1000 mammograms increased statistically significantly with age (Fig. 1, B; P<.001).

Table 3. Percentage of ductal carcinoma *in situ* (DCIS) cases among all breast cancer cases, by age, previous mammography, and whether screening mammography was positive or negative*

	Percentage of DCIS among all breast cancer cases with a positive screen			Percentage of DCIS among all cancer cases with a negative screen	Percentage of DCIS among all breast cancer cases	
Age range, y	No previous mammogram	Previous mammogram	Total (95% CI)†	Total (95% CI)	Total (95% CI)†	Range over BCSC sites
40–49	22.6	31.9	28.2 (23.9 to 32.5)	9.7 (5.2 to 14.2)	22.9 (19.5 to 26.4)	18.3–30.3
50–59	16.6	20.7	19.3 (16.4 to 22.2)	7.6 (4.2 to 10.9)	16.4 (14.0 to 18.7)	11.1–24.7
60–69	17.9	21.7	20.5 (17.5 to 23.6)	13.2 (8.5 to 17.9)	18.9 (16.3 to 21.5)	16.0–23.9
70–84	14.6	16.9	16.0 (13.3 to 18.7)	15.5 (9.7 to 21.4)	15.9 (13.5 to 18.4)	9.1–21.8
Total	17.4	21.7	20.2 (18.6 to 21.7)	11.1 (8.8 to 13.4)	18.1 (16.8 to 19.4)	14.6–23.8

*Mammography screening was considered positive when it was associated with a positive screening assessment (American College of Radiology's Breast Imaging Reporting and Data System [BI-RADS] assessment code of 0 - needs additional imaging, 3 - probably benign finding with a recommendation for immediate work-up, 4 - suspicious abnormality, or 5 - highly suggestive of malignancy) and considered negative when associated with a negative screening assessment (BI-RADS assessment code of 1 - negative finding, 2 - benign finding, or 3 - probably benign finding with no recommendation for immediate work-up or an unknown recommendation) within 365 days prior to cancer diagnosis. CI = confidence interval; BCSC = Breast Cancer Surveillance Consortium.

†Proportions using the chi-square (χ^2) test are statistically significantly different across age categories (P<.001).

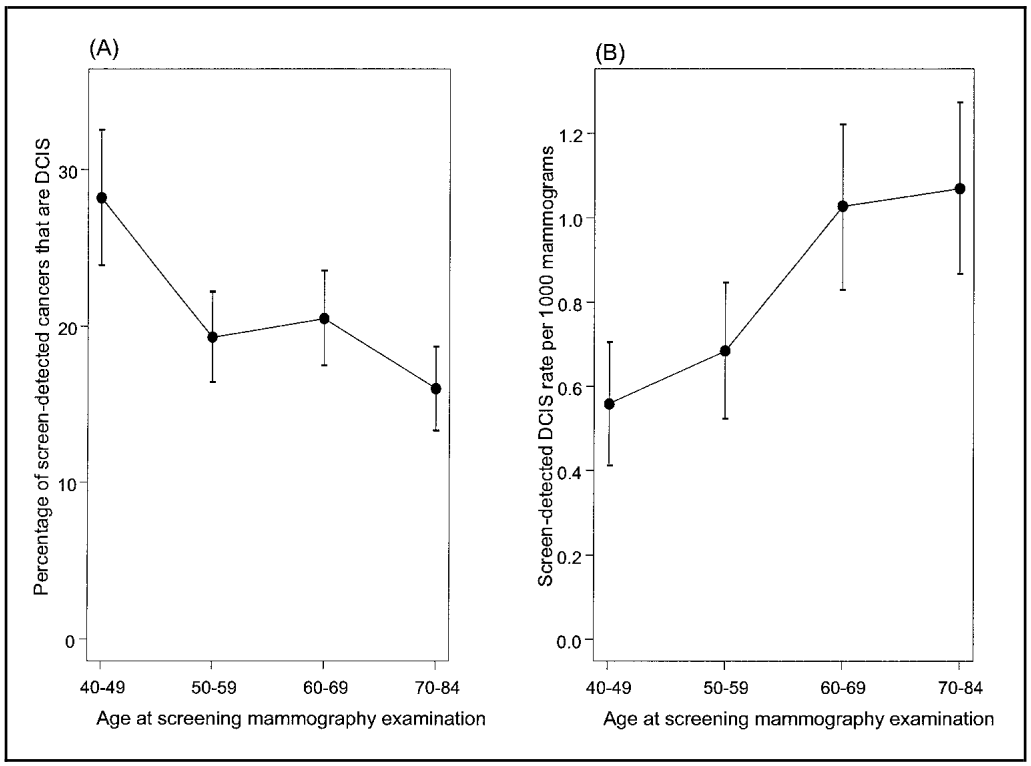

Fig. 1. Percentage of ductal carcinoma *in situ* (DCIS) cases among all screen-detected breast cancers and screen-detected DCIS rates per 1000 mammograms. **A**) Percentage of all screen-detected breast cancers that were diagnosed as DCIS stratified by age group. **B**) Rate of screen-detected DCIS per 1000 mammograms stratified by age group. Cancers were considered screen-detected if they were associated with a positive screening mammography examination according to the American College of Radiology's Breast Imaging Reporting and Data System [BI-RADS] assessment codes of 0 (needs additional evaluation), 3 (probably benign finding, with a recommendation for immediate work-up); 4 (suspicious abnormality), or 5 (highly suggestive of malignancy) within 365 days prior to cancer diagnosis. The data in **A** are in Table 3, and the data in **B** are in Table 4.

Table 4. Screen-detected and non-screen-detected ductal carcinoma *in situ* (DCIS) rates per 1000 mammograms, by age and previous mammography*

	Screen-detected DCIS rate			Non-screen-detected DCIS rate	DCIS rates, all cases	
Age range, y	No previous mammogram†	Previous mammogram†	Total (95% CI)†	Total (95% CI)†	Total (95% CI)†	Range over BCSC sites
40–49	0.54	0.57	0.56 (0.41 to 0.70)	0.08 (0.02 to 0.13)	0.63 (0.48 to 0.79)	0.44–1.10
50–59	0.74	0.66	0.68 (0.52 to 0.85)	0.09 (0.03 to 0.15)	0.77 (0.60 to 0.95)	0.51–1.38
60–69	1.00	1.04	1.03 (0.83 to 1.23)	0.19 (0.11 to 0.28)	1.22 (1.00 to 1.44)	1.00–2.26
70–84	1.31	0.97	1.07 (0.87 to 1.27)	0.22 (0.13 to 0.31)	1.28 (1.06 to 1.51)	0.50–1.75
Total	0.81	0.76	0.78 (0.60 to 0.95)	0.13 (0.05 to 0.20)	0.90 (0.72 to 1.09)	0.72–1.42

*Screen-detected = cases of DCIS associated with a positive mammography-screening assessment (American College of Radiology's Breast Imaging Reporting and Data System [BI-RADS] assessment code of 0 - needs additional imaging, 3 - probably benign finding with a recommendation for immediate work-up, 4 - suspicious abnormality, or 5 - highly suggestive of malignancy) within 365 days prior to diagnosis. Non-screen-detected = cases of DCIS associated with a negative mammography-screening assessment (BI-RADS assessment code of 1 - negative finding, 2 - benign finding, or 3 - probably benign finding with no recommendation for immediate work-up or an unknown recommendation) within 365 days prior to cancer diagnosis. CI = confidence interval.

†Proportions using chi-square (χ^2) test are statistically significantly different across age categories ($P<.001$).

Table 4 shows the rate of screen-detected and non-screen-detected DCIS (for all sites combined) and the ranges of the rates across sites for all DCIS cases. The rate of screen-detected DCIS was 0.56 (95% CI = 0.41 to 0.70) per 1000 mammograms among women aged 40–49 years and increased to 1.07 (95% CI = 0.87 to 1.27) per 1000 mammograms among women aged 70–84 years. The overall rate (i.e., for all age groups combined) of non-screen-detected DCIS (0.13 [95% CI = 0.05 to 0.20] per 1000 mammograms) was only approximately one sixth that of screen-detected DCIS (0.78 [95% CI = 0.60 to 0.95] per 1000 mammograms). Similar to screen-detected DCIS, the rate of non-screen-detected DCIS increased with age from 0.08 (95% CI = 0.02 to 0.13) per 1000 mammograms among women aged 40–49 years to 0.22 (95% CI = 0.13 to 0.31) per 1000 mammograms among women aged 70–84 years ($P<.001$). Differences in screen-detected DCIS rates between women with and without previous mammography were small, with no consistent direction across age groups.

The rate of screen-detected cancers increased more markedly with age for invasive breast cancer than for DCIS, from 1.42 (95% CI = 1.19 to 1.66) per 1000 mammograms among women aged 40–49 years to 5.62 (95% CI = 5.15 to 6.08) per 1000 mammograms among women aged 70–84 years (data not shown). In addition, although in every age group the rates of non-screen-detected invasive breast cancer were lower than those of screen-detected cancers, the rate of non-screen-detected invasive breast cancer was approximately one half that of screen-detected invasive breast cancer among women aged 40–49 years (0.70, 95% CI = 0.54 to 0.87 per 1000 mammograms) and approximately one fifth that of screen-detected invasive breast cancer among women aged 70–84 years (1.17, 95% CI = 0.96 to 1.38 per 1000 mammograms) (data not shown).

Time to Diagnosis of DCIS

The time to DCIS diagnosis following screening mammography was generally much shorter for women with a positive

mammography screen than for women with a negative screen (Fig. 2). Whereas 91% of DCIS cases associated with a positive screen were diagnosed within 3 months after screening, the distribution of DCIS cases diagnosed following a negative screen was spread throughout the subsequent year. The distribution of time to diagnosis following a negative screen had distinct peaks at around 1, 6–7, and 12 months. This distribution is consistent with the occurrence of further follow-up mammograms and subsequent diagnostic evaluation immediately following the screening mammography examination (perhaps due to clinical findings, such as a breast mass, even though the indication for the examination was routine screening), at the 6-month short-interval follow-up and at the repeat annual screening mammography examination occurring just prior to 12 months.

DISCUSSION

Our study of nearly 654 000 mammography screening examinations among nearly 541 000 women aged 40–84 years from seven mammography registries throughout the United States showed that approximately 20% of all screen-detected breast cancers were DCIS and that the overall rate of DCIS detection by screening mammography was 0.78 per 1000 mammograms; this rate increased with age. Our results suggest that one case of DCIS is detected for approximately every 1300 screening mammography examinations performed. This rate varies by age, ranging from approximately 1 in every 1800 mammograms among women aged 40–49 years to 1 in every 935 mammograms among women aged 70–84 years.

Several reports regarding the occurrence of *in situ* lesions have been published that were based on data from population-based cancer registries in the United States *(1,2,4,13)* and elsewhere *(3,5).* Data from cancer registries, however, do not permit determination of the incidence of screen-detected disease specifically, because cancer registries do not routinely collect information on screening mammography practices either for individual cancer cases or for the populations they cover. To the extent that non-screened women are included in cancer registry statistics, estimates of DCIS incidence based on cancer data from population-based cancer registries will underestimate the incidence of DCIS among screened women because DCIS is primarily detected by mammography. Reports from individual mammography programs and from case series have provided additional estimates of the percentage of all breast cancers or of nonpalpable breast cancers that are DCIS *(14–16).*

There are, however, several reports of the occurrence of *in situ* lesions among women participating in large, organized screening mammography programs. The Breast Cancer Detection Demonstration Project, conducted in the 1970s, reported that 18% of breast cancers detected at initial screening mammography in study participants were intraductal and *in situ* cases, with a smaller percentage of DCIS being detected in subsequent screenings *(17).* In the early 1990s, community-based screening mammography programs in New Mexico and British Columbia found that approximately 20% of all breast cancers detected were *in situ (18,19).* The U.S. National Breast and Cervical Cancer Early Detection Project reported in 1998 *(20,21)* that 25.3% of all breast cancers detected on the first round of screening mammography and 32.8% of those detected on subsequent rounds of screening were *in situ.* DCIS detection rates in this study were approximately 1.5 cases per 1000 first-round mammograms and 0.9 cases per 1000 subsequent mammograms. Several international studies *(22–24)* have also found that the proportion of screen-detected cancers that were *in situ* ranged from 15% to 22%. Precise comparisons of either the percentage

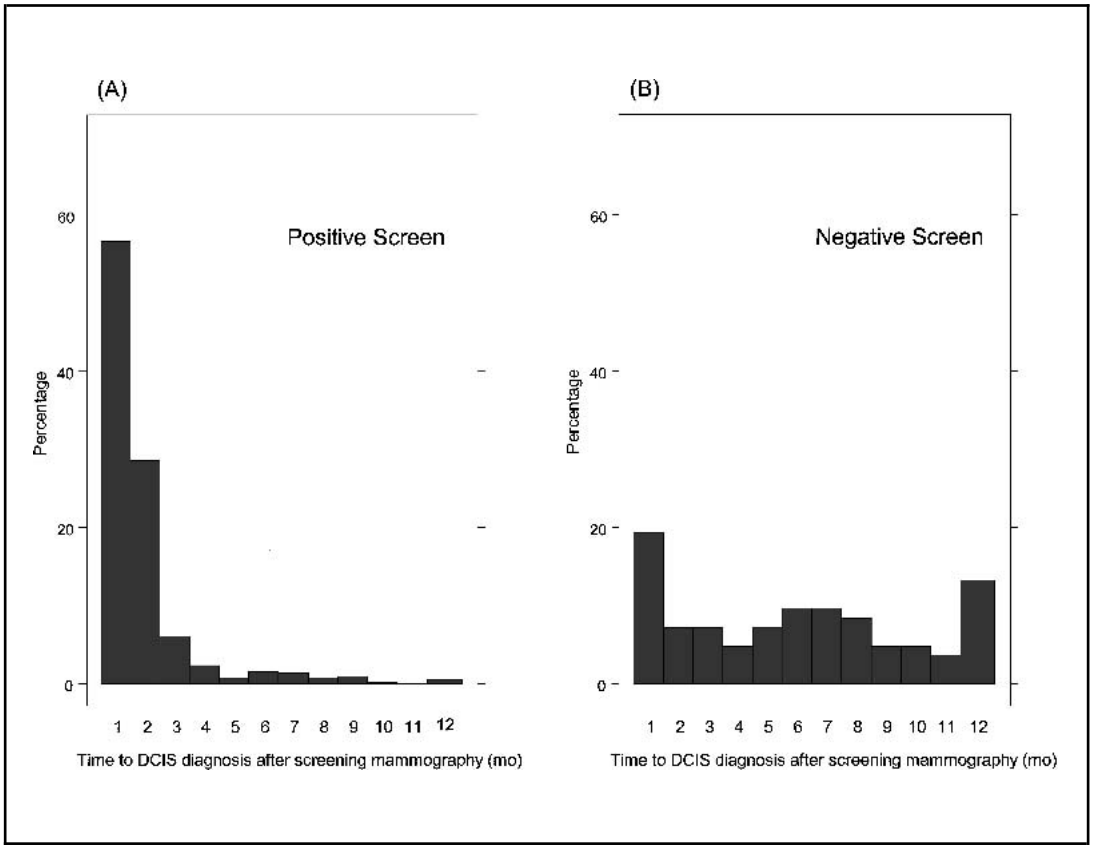

Fig. 2. Distribution of ductal carcinoma *in situ* (DCIS) cases by time from screening mammography examination to DCIS diagnosis. **A**) Cases of DCIS diagnosed after a positive screen. DCIS cases were considered screen-detected if they were associated with a positive screening mammographic examination according to the American College of Radiology's Breast Imaging Reporting and Data System (BI-RADS) assessment codes of 0 (needs additional evaluation); 3 (probably benign finding, with a recommendation for immediate work-up); 4 (suspicious abnormality); or 5 (highly suggestive of malignancy) within the 365 days prior to DCIS diagnosis. **B**) Cases of DCIS diagnosed after a negative screen. DCIS cases were considered non-screen-detected if they were associated with a negative screening mammographic examination (BI-RADS assessment codes of 1 [negative], 2 [benign finding], or 3 [probably benign finding with no recommendation for immediate work-up or unknown recommendation]) within 365 days prior to DCIS diagnosis.

of screen-detected cancers that are DCIS or of the rates of DCIS per 1000 screening mammograms across screened populations are not possible because of differences in calendar period, age distributions, racial/ethnic composition, socioeconomic status, recommended screening intervals, definitions of screen-detected cancer and prior mammography, and type of *in situ* cases included. Nevertheless, the rates we estimated in this study are similar to those reported elsewhere.

In this study, we found that the percentage of all screen-detected breast cancer that was DCIS decreased with increasing age. That is, if a woman had screen-detected breast cancer, it was less likely to be DCIS if she was older. Other investigators *(25,26)* with similar findings have misinterpreted the percentages of DCIS in their studies as meaning that the incidence of DCIS is higher in younger women than it is in older women. However, as was the case for invasive breast cancer, we found that the rate of DCIS detection actually increased with age, from 0.56 per 1000 mammograms among women aged 40–49 years to 1.07 per 1000 mammograms among women aged 70–84 years. Other studies *(20,22,23)* have confirmed that the percentage of DCIS among all screen-detected breast cancers does generally decrease with age, but those studies did not always show a consistent increase in the rate of detection of DCIS with age.

Similar to another report *(27)*, we found that screening mammography was more sensitive for detecting DCIS (86%) than it was for detecting invasive breast cancer (75%). Invasive carcinoma is usually associated with a mass or density found on mammography, whereas DCIS is usually associated with microcalcifications *(25).* Missed DCIS is much less likely than missed invasive breast cancer to be diagnosed subsequently as a palpable mass, and it may never become clinically apparent. This phenomenon has the potential effect of overestimating the ability of screening mammography to detect *in situ* disease, so that sensitivity for detecting DCIS would be biased upward. Furthermore, in dense or heterogeneously dense breast tissue, microcalcifications are easier to detect on mammography than are masses.

In our study, sensitivity of screening mammography for detecting both DCIS and invasive breast cancer was higher among women for whom no previous mammography was recorded than it was for women with previous mammography. Earlier work has also shown that the sensitivity of mammography is higher for women without a known previous mammogram, presumably because the cancers available for screen detection include prevalent cases that may be larger and/or slower growing than cancers among women undergoing regular screening *(28).* Although we found that sensitivity for detecting invasive breast cancer increased with age, both for women with previous mammography and for women with no previous mammography, there was no clear relationship between sensitivity for detecting DCIS and age. Among women with no previous mammography, however, sensitivity for detecting DCIS was higher in women younger than 50 years of age than for older women. Thus, the proportion of DCIS cases in different study populations, as well as age and previous mammography status of the women, will influence reported overall sensitivities of screening mammography for detecting breast cancer.

Surprisingly, given the general understanding that DCIS is readily detected by screening mammography, we found that 14% of DCIS cases (83/591) were among women whose most recent screening mammography examination had a negative assessment. It should be noted that the screening examinations of 21 of the 83 non-screen-detected DCIS cases had an assessment code of 3 with a recommendation for short interval follow-up (i.e. a follow-up generally occurring within 3–6 months from a screening mammography examination), which indicates that the radiologist had some concern about the result even though an immediate work-up was not recommended. Over 90% of DCIS diagnoses for women with positive screens occurred within 3 months of mammography, whereas DCIS diagnoses for women with negative screens were spread throughout the year following mammography, suggesting that many of these DCIS cases were detected by other means. We do not know, however, whether these non-screen-detected DCIS cases represent cases that were present but missed at the time of screening mammography or were new (i.e., interval) occurrences of DCIS detected by means other than mammography. For example, some studies *(29,30)* indicate that some DCIS cases can be detected by clinical breast examination.

Our study has several limitations. First, we relied on self-reported questionnaire data to classify women as to whether they had had a previous screening mammography examination, and if there was no information provided on the questionnaire about previous mammography, we assumed that the screening mammogram was the woman's first ever. To the extent that misclassification occurred, "true" differences between women with and without previous mammography would be diminished. Second, we used the initial mammographic assessment category assigned to each screening mammogram to determine whether the finding was positive or negative. Subsequent imaging mammograms of the study participants may have resulted in a reappraisal of the BI-RADS assessment code and its associated recommendation. However, estimates of sensitivity for detecting cancer are most commonly based on the initial assessment, so we chose to use the initial mammographic assessment to allow comparison to existing literature.

Given that the likelihood of detecting DCIS among women undergoing screening mammography has increased and is not small at 20% of all screen-detected breast cancer cases, is there evidence to suggest that detecting DCIS prevents deaths from breast cancer? The rationale for early detection and treatment of DCIS is based on several lines of evidence. First, a small series of untreated women with DCIS diagnosed in the premammography era had higher than expected subsequent occurrences of invasive breast cancer *(31,32).* In addition, larger, more recent series of women treated for DCIS have also been shown to be at increased risk of recurrence of both *in situ* and invasive breast cancer *(33).* The estimates of recurrence rates range fairly broadly across studies and are influenced by patient and tumor characteristics, such as age and tumor grade, and by treatment *(34–36).* In a large clinical trial, after a mean follow-up of 90 months, the incidence of ipsilateral invasive breast cancer among women with DCIS who had been treated with lumpectomy alone was 13.4% *(37).* Thus, DCIS can recur as invasive breast cancer. Findings from randomized clinical trials that have shown that the addition of radiation therapy and tamoxifen to lumpectomy treatment of DCIS reduces the chance of future invasive disease recurrence compared with lumpectomy alone also bolster the case for treatment of DCIS *(37–39).* Finally, data are accumulating to suggest that there are both epidemiologic and genetic similarities between DCIS and invasive breast cancers, further suggesting that treatment for DCIS may yield ben-

efits similar to those of treatment for invasive breast cancer *(40–46)*.

In contrast, some lines of evidence temper enthusiasm for detecting DCIS. For example, autopsy studies have shown that DCIS is not uncommon among women who died of causes unrelated to breast cancer; across seven autopsy studies, median prevalence of DCIS was 8.9% (range = 0% to 14.7%), although, presumably, not all such cases of DCIS would have been detectable by mammography *(47)*. This finding suggests that some cases of DCIS do not progress to clinically significant lesions and may never require treatment in the patient's lifetime. In addition, although their risk of subsequent invasive disease is elevated, most women treated for DCIS do not experience an invasive recurrence, at least within 10–15 years after DCIS diagnosis. Follow-up data from population-based registries show that only about 2% of women who have been diagnosed with and treated for DCIS since the time when screening mammography was widely introduced in the early 1990s died of breast cancer within 10 years following DCIS diagnosis *(48,49)*. These favorable outcomes presumably reflect both the effectiveness of current treatment regimens and the relatively benign nature of most mammographically detected DCIS. Finally, even though over four times as many *in situ* cases were found among women in the Canadian National Breast Screening Study-2 who had received mammography plus clinical breast examination as were found among women who had received clinical breast examination alone, there was no overall difference in breast cancer mortality between the two groups of women after 13 years of follow-up *(30)*.

The use of screening mammography has become widespread. Based on 1998 nationally representative data from the National Health Interview Survey, the estimated number of U.S. women aged 40 years and older who had mammography in the previous year was more than 28.4 million (Breen N, National Cancer Institute: personal communication). Our data suggest that approximately 1 in every 1300 screening mammography examinations results in a DCIS diagnosis. If early detection and treatment of DCIS have contributed to the recent decline in U.S. breast cancer mortality *(50)*, independent of effects attributable to early detection and treatment of invasive disease and independent of recent advances in breast cancer treatment, then some women who have been treated for screen-detected DCIS have benefited. The pathology of DCIS is heterogeneous, and presumably, the likelihood of benefit from treatment is greater for women with larger, higher grade, or multifocal lesions than for those with very small low-grade lesions. The BCSC affords the opportunity to explore both the distribution of grade of DCIS in a population-based mammography program and the long-term sequelae of DCIS identification. More research is needed to understand the biology and clinical significance of DCIS to identify disease that is likely to progress and to better tailor treatment decisions.

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NOTES

[1]*Editor's note:* SEER is a set of geographically defined, population-based, central cancer registries in the United States, operated by local nonprofit organizations under contract to the National Cancer Institute (NCI). Registry data are submitted electronically without personal identifiers to the NCI on a biannual basis, and the NCI makes the data available to the public for scientific research.

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