Is Screening Mammography Effective in Elderly Women?*

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PURPOSE: Screening mammography is effective in reducing breast cancer mortality in women between the ages of 50 and 69 years. We sought to determine whether older women who undergo screening mammography have a decreased risk of metastatic breast cancer.

SUBJECTS AND METHODS: We studied 690,993 women aged 66 to 79 years who were California Medicare beneficiaries from January 1992 to December 1993, and who chose the fee-for-service plan. Health Care Financing Administration part B billing records were used to determine the use of screening mammography. The extent of breast cancer (in situ, local, regional, or metastatic) was ascertained for the 6,767 women who were diagnosed with the disease in 1993, using data from the California State Cancer Registry. For each type (extent) of breast cancer, the relative risk (RR) and 95% confidence (CI) of developing breast cancer was estimated by dividing the risk of its development in screened women by the risk in women who were not screened.

RESULTS: A total of 46% of women had mammography during the 2-year study period. In situ, local, and regional breast cancer were more likely to be detected among women who underwent screening mammography. For example, the relative risk of detecting local breast cancer in screened women was 3.3 (95% CI: 3.1 to 3.5). The risk of detecting metastatic breast cancer, on the other hand, was significantly reduced among women aged 66 to 79 years who underwent screening mammography (RR = 0.57, 95% CI: 0.45 to 0.72).

CONCLUSION: Screening mammography is associated with a decreased risk of detecting metastatic breast cancer among elderly women. Public health recommendations need to weigh the benefit of screening elderly women against the cost and potential harm from screening and treating early lesions that may have no effect on mortality. **Am J Med. 2000;108:112–119.**

Although women aged 65 years and older comprise only 14% of women in the United States, nearly half (47%) of breast cancer cases diagnosed annually and more than half (53%) of breast cancer mortality occurs in this age group (1,2). The decrease in breast cancer mortality observed during the last decade for women aged 50 to 69 years has been less evident in women aged 70 years and older (1–5). In California, for example, women aged 70 to 79 years experienced a 10% decrease in breast cancer mortality from 1989 to 1993, about half that seen in women aged 50 to 69 years (2).

Part of the recent decrease in breast cancer mortality may be attributable to screening mammography. Among women aged 50 to 69 years there has been a decrease in the rate of late stage disease at the same time that there has been an increase in the use of mammography (4,6). Although screening mammography rates have increased for all women during the last decade, women aged 70 to 79 years consistently have lower screening rates than younger women (7–14).

The effectiveness of screening mammography in women aged 70 to 79 years is not known. Of the eight randomized trials of screening mammography, only two included women older than 69 years (15). Both trials showed a small, nonsignificant benefit among women aged 70 to 74 years (16), but lacked statistical power to provide meaningful results. Women aged 75 years and older were not included in any of the trials (15).

We conducted a retrospective cohort study among California women 66 to 79 years of age to evaluate the efficacy of screening mammography. The aim of mammographic screening is not to prevent cancer, but rather to detect it early, when it is potentially curable, and thus prevent the progression to more advanced stages of the disease. We therefore hypothesized that women undergoing

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screening mammography would be more likely to be diagnosed with early stage breast cancer and less likely to be diagnosed with metastatic disease.

MATERIAL AND METHODS

Study Design

Using a retrospective cohort design, we evaluated women who underwent screening mammography during 1992 and 1993 and determined their risk of being diagnosed with early or advanced breast cancer in 1993. We assumed that screening in 1992 and 1993 was a proxy for earlier screening mammography. Thus, we were evaluating whether the use of routine screening mammography in earlier years was associated with the risk of developing early or advanced breast cancer. Because of lead-time bias, survival following the diagnosis of an early stage cancer cannot be used to measure the effectiveness of screening, and there will always be an increase in the diagnosis of early cancers associated with screening. However, the risk of advanced (metastatic) breast cancer should not be confounded by lead-time bias, since most of these women are symptomatic and seek medical care. Thus, if screening is beneficial, the risk of developing metastatic breast cancer should be lower among screened women.

Subjects

We studied 690,993 California women aged 66 to 79 years who were Medicare beneficiaries in fee-for-service plans in 1992 and 1993. Women enrolled in health maintenance organizations (HMOs), approximately 34% of California's Medicare population, were not included because the Health Care Financing Administration (HCFA) does not receive bills for specific services, such as mammography, provided under managed care contracts. Analysis was limited to women aged 66 years and older to allow at least 1 year of Medicare eligibility during which a 65-year-old woman could have obtained mammography before a breast cancer diagnosis. Race was recorded as white, African-American, and other. The study was approved by the University of California, San Francisco, Committee on Human Research.

Definition of Screening Mammography

We used HCFA part B billing records and enrollment files to assess mammography utilization between January 1, 1992, and December 31, 1993 (Figure). Medicare uses three separate billing codes for mammography: screening, diagnostic, and unilateral. Although most mammographic examinations are for screening purposes, they are usually billed as diagnostic tests because of greater reimbursement. Therefore, we considered any mammographic examination in a woman who did not have a subsequent diagnosis of breast cancer to be a screening examination (n = 315,536) regardless of the billing code (Physician Current Procedural Terminology [CPT] billing codes 76090, 76091, and 76092) (17). Women without cancer who did not have at least one mammographic examination during 1992 or 1993 were considered as not screened (n = 368,690).

Because diagnostic mammography is used to evaluate women with suspicious clinical findings, as well as to evaluate abnormalities found on screening mammography, a substantial proportion of women with breast cancer have had mammography. Thus, among women with breast cancer, we could not assume that all mammographic examinations were for screening purposes. Instead, complete part B billing records were used to differentiate screening from diagnostic examinations in the 6,767 women with breast cancer (Figure). We assumed that diagnostic examinations were those that were billed as a unilateral examination (billing code 76090, n = 136). We also assumed that diagnostic examinations were those that occurred following a breast diagnostic procedure such as a breast biopsy, breast fine needle aspiration, breast ultrasound or galactogram (CPT billing codes 76086, 76088, 76645, 76942, 19000, 19001, 19020, 19030, 19020; n = 265); or coincident with or following a hospital admission for a lumpectomy, excisional biopsy, or mastectomy (billing codes 76096, 76097, 76098, 19100, 19101, 19110, 19112, 19100, 19120, 19125 19110, 19112, 19120, 19290, 19291; n = 588.) These 989 women with breast cancer, along with the 1110 women with breast cancer who did not have at least one mammographic examination during 1992 or 1993, were considered as not screened. All other women with breast cancer who had a mammographic examination were classified as having been screened.

Classification of Breast Tumors

Breast cancer cases among women diagnosed in 1993 were ascertained by linkage of the Medicare enrollment files with the California Cancer Registry, which collects information on all primary breast cancers, including patient age and race, date of detection, and extent of disease. Four patient identifiers (name, social security number, age, and unique HCFA patient number) were used to link the Medicare files to the cancer registry (18). Five percent of women failed to match and were excluded. The extent of disease at detection was categorized as in situ, local, regional, and metastatic using the Surveillance, Epidemiology, and End Results (SEER) summary stage system (18). The extent of disease was ascertained for 97% of the women included in our analysis; women with unknown extent of disease were excluded (58 screened women and 136 women who were not screened).

Statistical Analysis

We calculated the biennial mammography rate by dividing the number of women who were screened from January 1, 1992, through December 31, 1993, by the total

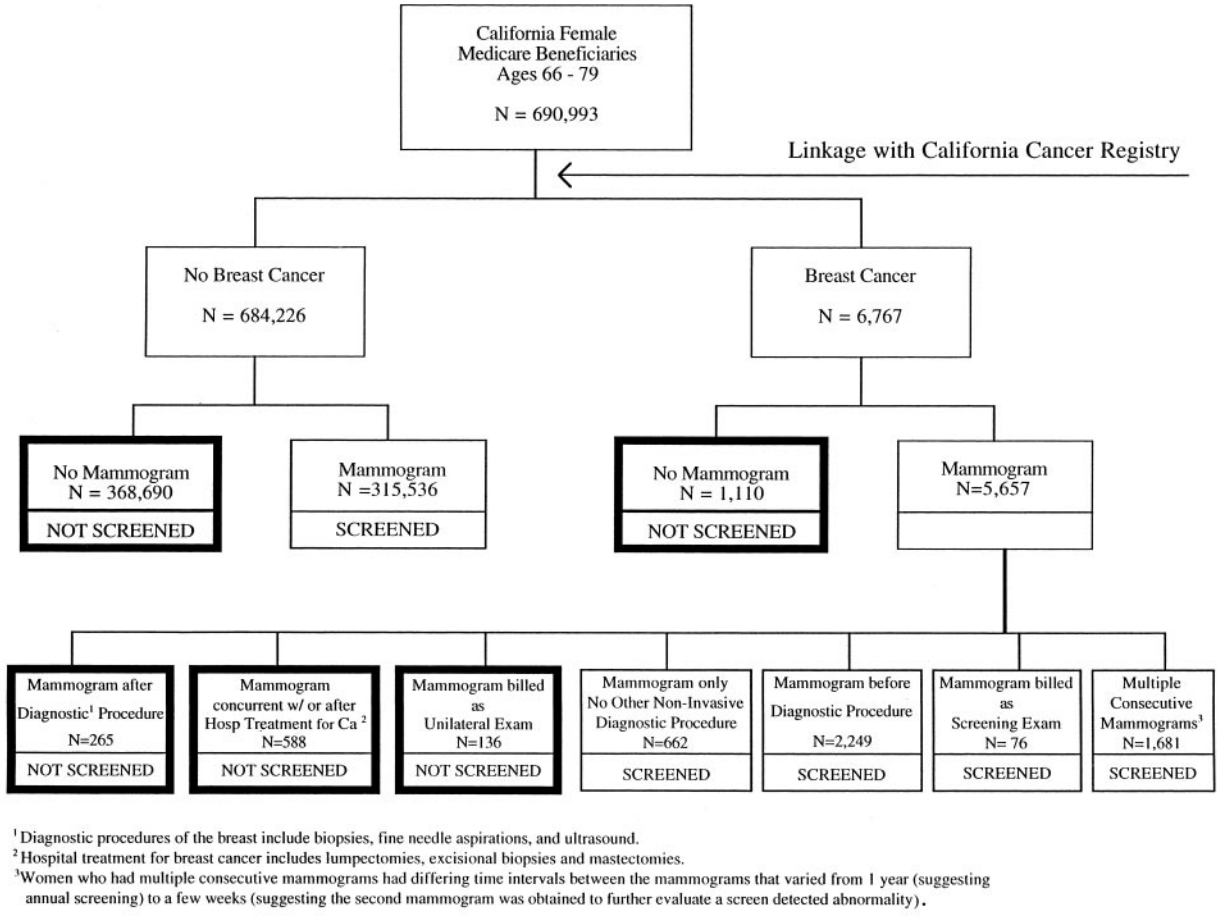

Figure. Method of classification of California female Medicare beneficiaries as having been screened or not screened with mammography using Medicare part B claims data, 1992 to 1993.

number of female Medicare beneficiaries (n = 690,993). We calculated the risk of developing breast cancer by dividing the number of women who were diagnosed with breast cancer in 1993 by the number of Medicare beneficiaries. Risks were calculated separately by race (white, African-American), 5-year age intervals, extent of disease, and screening status. We were not able to distinguish other racial or ethnic groups (n = 48,748); these women were included in the overall results. The relative risk (RR) of developing breast cancer (with 95% confidence intervals [CI]) was estimated as the risk in screened women divided by the risk in women who were not screened. Two-tailed Fisher's exact tests were used to test for statistical significance. We tested for the consistency of effects among age strata using a chi-square test for homogeneity.

In a separate analysis to determine if there was an association between mammography use in a single year with its use in subsequent years, we examined the relation between mammography utilization in 1992 (the first time period) and mammography utilization in 1993 to 1994 (the second time period) among women without breast cancer. We determined the proportion of women who had mammography during 1992 and during 1993 to 1994 or who did not have any mammography from 1992 to 1994, as well as the proportions who had mammography during only one of the periods. A kappa statistic was used to determine the strength of the association.

RESULTS

Overall, 46% of women underwent as least one screening mammogram during 1992 or 1993. The rate of screening mammography declined with age, from 50% in women aged 66 to 69 years to 40% in women aged 75 to 79 (Table 1). Screening was substantially more common in white women of all ages. Mammography use during 1992 predicted mammography use during 1993 to 1994; 72% of women had concordance in their mammography utilization (kappa = 0.44).

Relative Risk of Breast Cancer by Age and Race

The risks of in situ, local, and regional breast cancer were greater among women who underwent screening mam-

Table 1. Numbers of Medicare Beneficiaries and Percentages of Women Receiving at Least One Mammogram by Age and Race, 1992 to 1993

Age (Years)	White		African-American		Other Races		All Races	
	N	Screened	N	Screened	N	Screened	N	Screened
66–69	200,822	53%	11,138	35%	19,408	36%	231,368	50%
70–74	228,239	50%	12,260	34%	17,589	33%	258,088	48%
75–79	179,947	42%	9,839	30%	11,751	26%	201,537	40%
All ages	609,008	48%	33,237	33%	48,748	33%	690,993	46%

mography (Table 2). For example, in women aged 66 to 79 years, screened women were 3.5 times more likely to be diagnosed with in situ cancer as women who were not screened. The relative risks of being diagnosed with in situ, local, and regional breast cancer among screened women compared with women who were not screened increased with age (Table 2). As the severity of disease increased from in situ to regional disease, the relative risk of detecting disease decreased. Among all women, the relative risk of in situ disease was 3.5, whereas the relative risk of regional disease was 2.2 (Table 2).

Overall, the risk of metastatic disease was 43% lower among women who were screened ($P < 0.0001$, Table 2). The relative risk of metastatic disease did not differ by age ($P = 0.60$). Age-stratified results for white women were similar to the overall findings (Table 3). We did not find clear evidence of benefit among African-American women, although the confidence intervals were wide (Table 4).

The risk of detecting breast cancer was greatest among screened women; 73% of breast cancers were diagnosed in the 46% of women who had been screened (Tables 3 and 4). For example, among white women of all ages, the risk of detecting breast cancer was 136 per 10,000 screened women, compared with 51 per 10,000 women who were not screened (Table 3). For each 10,000 white women who were screened, an additional 86 cases of breast cancer were detected, including 11 in situ cancers, 61 local cancers, and 14 regional cancers, whereas 3 fewer cases of metastatic breast cancer were detected.

African-American women had greater risks of regional and metastatic breast cancer, and correspondingly lower risks of in situ and local breast cancer, than white women (Tables 3 and 4). This was true for women who were screened as well as those who were not screened. Among women who had screening mammography, for example, the risk of regional cancer was 37 per 10,000 in African-American women compared with 27 per 10,000 in white women. Similarly, the risk of metastatic disease was greater in African-American women (8 per 10,000) compared with white women (3 per 10,000).

Effects of Possible Misclassification

There may have been misclassification in the way women were characterized as screened or not screened, particularly among the 662 women who had a mammogram and no other noninvasive diagnostic procedures (Figure). These women may have been symptomatic and had a diagnostic, rather than a screening, mammogram. To evaluate the effect of possible misclassification, we considered all of these 662 women as not screened. The relative risk for in situ (RR = 2.7, 95% CI: 2.2 to 3.3), local (RR = 2.2, 95% CI: 1.9 to 2.5), and metastatic disease (RR = 0.25, 95% CI: 0.18 to 0.34) were similar to those in Table 2. The relative risk for regional disease was lower (RR = 1.2, 95% CI: 1.0 to 1.4).

DISCUSSION

Although breast cancer is the second leading cause of cancer death in women 65 years of age and older, there has been little research addressing whether mammography is effective in decreasing breast cancer mortality in these women (19–22). Conflicting recommendations by vari-

Table 2. Relative Risk of Breast Cancer by Age and Extent of Tumor, Comparing Women Who Had Screening Mammography with Those Who Did Not

Age (Years)	Number of Women	Number of Cancer Cases	All Cancer	In Situ	Local	Regional	Metastatic
			Relative Risk (95% Confidence Interval)*				
66–69	231,368	2109	1.9 (1.7–2.1)	2.5 (1.9–3.3)	2.2 (2.0–2.5)	1.5 (1.2–1.8)	0.54 (0.36–0.81)
70–74	258,088	2577	2.9 (2.7–3.2)	3.7 (2.8–4.9)	3.8 (3.4–4.3)	2.3 (1.9–2.7)	0.53 (0.37–0.76)
75–79	201,537	2081	3.6 (3.3–4.0)	4.9 (3.5–6.9)	4.4 (3.9–5.0)	3.1 (2.5–3.7)	0.69 (0.46–1.0)
All ages	690,993	6767	2.7 (2.5–2.8)	3.5 (3.0–4.2)	3.3 (3.1–3.5)	2.2 (1.9–2.4)	0.57 (0.45–0.72)

* Chi-square test for homogeneity of relative risks across age strata, $P = 0.60$.

Table 3. Annual Risk of Breast Cancer for White Women by Age and Extent of Tumor*

Age (Years)	Number of Women	Number of Cancer Cases	In Situ	Local	Regional	Metastatic
			Risk per 10,000 Women (95% Confidence Interval)†			
66–69						
Not screened	95,049	57 (53–63)	6 (5–8)	32 (29–36)	14 (12–17)	5 (4–6)
Screened	105,773	109 (103–115)	15 (12–17)	70 (65–75)	22 (19–25)	3 (2–4)
Relative risk (95% CI)		1.9 (1.7–2.1)	2.4 (1.8–3.2)	2.2 (1.9–2.5)	1.5 (1.2–1.9)	0.60 (0.38–0.95)
70–74						
Not screened	115,169	48 (44–52)	4 (3–6)	25 (22–28)	12 (10–15)	6 (5–8)
Screened	113,070	139 (132–146)	16 (14–18)	93 (88–99)	27 (24–30)	3 (2–4)
Relative risk (95% CI)		2.9 (2.6–3.2)	3.6 (2.6–4.9)	3.8 (3.3–4.3)	2.2 (1.8–2.7)	0.50 (0.33–0.75)
75–79						
Not screened	104,603	48 (44–52)	4 (3–5)	27 (24–30)	12 (10–14)	6 (4–7)
Screened	75,344	168 (159–177)	18 (15–21)	112 (104–119)	35 (31–39)	4 (3–6)
Relative risk (95% CI)		3.5 (3.2–4.0)	4.8 (3.4–6.9)	4.2 (3.7–4.8)	2.9 (2.3–3.5)	0.72 (0.46–1.1)
All ages						
Not screened	314,821	51 (48–53)	5 (4–6)	28 (26–29)	12 (12–14)	6 (5–6)
Screened	294,187	136 (132–140)	16 (15–18)	89 (86–93)	27 (25–29)	3 (3–4)
Relative risk (95% CI)		2.7 (2.5–2.8)	3.5 (2.9–4.2)	3.3 (3.0–3.5)	2.1 (1.9–2.4)	0.58 (0.46–0.75)

* Totals may not sum because of rounding.
† Chi-square test for homogeneity across age strata, $P = 0.48$.
CI = Confidence interval.

ous organizations about the age to stop mammographic screening reflect the uncertainty about the benefits of screening mammography in older women (23–27). We found that metastatic breast cancer was reduced by 43% in screened women aged 66 to 79 years, a reduction similar in magnitude to the reduction in breast cancer mortality seen in randomized trials of screening mammography among women aged 50 to 69 years (15,16,28).

We could not determine whether mammographic screening affects mortality. Metastatic breast cancer, however, is a close surrogate for breast cancer mortality; in postmenopausal women with metastatic breast cancer, the 5-year survival is $< 20\%$ (1,2). Metastatic breast cancer often represents a failure to detect disease while it is potentially curable, and the effectiveness of a screening program can be evaluated by how much metastatic disease is prevented. Importantly, the risk of metastatic breast cancer should not be confounded by lead-time bias, since most women who have metastatic breast cancer are symptomatic.

Not surprisingly, we found an increase in the risk of detecting in situ and local breast cancer among screened women. The aim of a breast cancer screening program is to detect cancer early when it is potentially curable, and thus prevent the progression to a more advanced stage and death. However, the risk of in situ cancer was fivefold greater, and the risk of local cancer was 28-fold greater than the risk of metastatic cancer among screened white women. Thus, 24 early breast cancers were diagnosed for each case of metastatic breast cancer prevented. Mammography is benefiting some of these women through the detection of early breast cancers. However, some of the in situ lesions and small invasive cancers may not have become clinically evident. This is particularly true for ductal carcinoma in situ (DCIS) lesions, only 15% to 25% of which progress to invasive cancer during 5 to 10 years (29–33). It is not possible, however, to distinguish which lesions will progress, and therefore would benefit from early detection (34). Thus, surgical treatment is required for the vast majority of women with these early lesions.

We were unable to demonstrate a benefit among African-American women, perhaps because there were few African-American women with metastatic breast cancer. The wide confidence intervals for the relative risks in African-American women reflect the lack of precision. Alternatively, mammography may not be as effective in African-American women. Indeed, the recent reduction in breast cancer mortality observed among white women in the United States has not been observed among African-American women (3). We found, as have other investigators, that the risk of advanced breast cancer was greater among African-American than white women (1–3). Some have hypothesized that this is largely the result of socioeconomic factors such as poverty, inadequate access to health care, and lower rates of mammography use (8,9,

Table 4. Annual Risk of Breast Cancer for African-American Women by Age and Extent of Tumor*

Age (Years)	Number of Women	Number of Cancer Cases	In Situ	Local	Regional	Metastatic
			Risk per 10,000 Women (95% Confidence Interval)			
66–69						
Not screened	7,223	53 (38–73)	8 (3–19)	17 (9–30)	18 (10–32)	10 (4–21)
Screened	3,915	110 (81–149)	10 (3–28)	59 (38–90)	36 (20–62)	5 (1–21)
Relative risk (95% CI)		2 (1–3)	1 (0.4–4)	4 (2–7)	2 (1–4)	0.50 (0.1–3)
70–74						
Not screened	8,065	47 (34–65)	5 (2–14)	22 (14–37)	12 (6–24)	7 (3–17)
Screened	4,195	145 (112–188)	24 (12–450)	72 (42–103)	38 (23–63)	12 (4–30)
Relative risk (95% CI)		3 (2–5)	5 (2–15)	3 (2–6)	3 (1–7)	1.6 (0.5–5)
75–79						
Not screened	6,921	33 (22–51)	3 (1–12)	17 (9–31)	4 (1–14)	9 (4–20)
Screened	2,918	120 (85–168)	17 (6–42)	58 (35–95)	38 (20–70)	7 (1–28)
Relative risk (95% CI)		4 (2–6)	6 (1–31)	3 (2–7)	9 (2–31)	0.8 (0.2–4)
All ages						
Not screened	22,209	45 (36–55)	5 (3–10)	19 (14–26)	12 (8–17)	9 (5–14)
Screened	11,028	126 (106–149)	17 (11–27)	64 (50–81)	37 (27–51)	8 (4–16)
Relative risk (95% CI)		3 (2–4)	3 (2–7)	3 (2–5)	3 (2–5)	1.0 (0.4–2)

* Totals may not sum because of rounding.
CI = Confidence interval.

11,35–41). Others have hypothesized that breast cancer is more aggressive in African-American women (42–45).

We were conservative in our classification of women with breast cancer as having not been screened. Women were considered not screened if Medicare had never been billed for mammography. This included 16% of the women with breast cancer, a proportion that is similar to that reported by others (40). Women were also considered not screened if they had mammography only following a diagnostic or surgical procedure for breast cancer. Women who obtained mammography and no other diagnostic procedure were considered screened, even if mammography had been ordered because of a palpable mass. Therefore, some women who presented with a breast lump on clinical breast examination who subsequently had diagnostic mammography were incorrectly categorized in the screening mammography group. Classifying these women as screened biased our results against finding a reduction in metastatic disease from screening mammography. When we considered women who had a mammogram without an additional diagnostic procedure as not screened, mammography was associated with a 75% reduction in metastatic breast cancer, compared with the 43% that we reported. Thus, our conservative assumptions regarding screening history tended to underestimate the benefit of early detection by mammography and overestimate the relative risks of regional disease associated with screening.

We categorized all mammography in women without breast cancer as screening mammography. Women without breast cancer who presented with a palpable mass or breast symptom who underwent diagnostic mammography were misclassified as having had screening mammography. This will make screening appear more beneficial for metastatic cancer. (Because the actual number of screened women is less than the estimated number, the actual risk of disease in screened women is greater; the reverse is true among women who are not screened.) While this misclassification may be responsible for some of the decreased risk of metastatic disease among screened women, diagnostic mammography would have to account for 30% or more of all mammography among women without breast cancer to nullify the association we found.

Although we could not validate our algorithm (Figure) by chart review or patient interview, we believe that it correctly classified women according to whether they had screening or diagnostic mammography. The risk of DCIS, which is primarily detected mammographically, was similar in our study and in a large screening population (46). Additionally, in clinical practice, most mammograms ordered by physicians are screening examinations: A 10% random sample of community mammography practices in the United States found that screening accounted for 87% of all examinations performed (47).

We did not expect to find an increased risk of regional

breast cancer among screened women. The apparent increased risk of regional breast cancer might be attributable to our classification of women with breast cancer as screened when they had a mammogram proceeding a diagnostic biopsy. When we used the less conservative definition of a screening mammogram, there was no longer an increased risk of regional disease associated with screening (RR = 1.2, 95% CI: 1.0 to 1.4).

We evaluated mammography use in the 1- to 2-year period before a breast cancer diagnosis as an indirect measure of earlier mammography utilization. Our analysis of the patterns of mammography use suggests that there is a moderate association between mammography use in a year with its use in subsequent years (48). Thus, while we could not directly evaluate each woman's history of mammography use before 1992, it is likely that her mammography utilization in 1992 and 1993 is an adequate marker for earlier use.

This study is not a randomized trial, and thus we do not know why the women in our study chose to have mammography. In general, women who are screened are wealthier, better educated, and have better access to medical care than women who are not screened (8–14). If women who make healthy lifestyle choices are more likely to undergo mammography and less likely to develop advanced breast cancer, this could result in an overestimate of the benefit of mammography. On the other hand, if women with a greater risk of breast cancer, such as those with a family history of breast cancer, are more likely to be screened and more likely to develop advanced breast cancer, this could result in an underestimate of the benefit of mammography reported here. Overall, the effects of confounding may be balanced, and were likely offset by the conservative definition that we used to define the screened population, which tended to underestimate the benefit of screening mammography.

In conclusion, we found that screening mammography was associated with a decreased risk of detecting metastatic breast cancer among women aged 66 to 79 years. These results support the view that routine mammography may be effective in elderly women. However, early cancers were detected 3 times as often among screened women. Screening may benefit some of these women with early breast cancer—those whose disease would have progressed—but may not be beneficial in others, whose lesions may not have been clinically important. Public health recommendations will need to weigh the benefit of screening elderly women with mammography against the increased costs of screening and treating early lesions that may have no effect on mortality.

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