Positive Predictive Value of Screening Mammography by Age and Family History of Breast Cancer

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Objective.—To determine the positive predictive value (PPV) of low-cost screening mammography according to age and family history of breast cancer.

Design.—Cross-sectional.

Setting.—Six counties in northern California.

Participants.—A total of 31 814 women aged 30 years and older referred for mammography to the University of California, San Francisco, Mobile Mammography Screening Program from April 18, 1985, through November 20, 1992.

Measurements.—Breast cancer risk profile, two standard mammographic views per breast, and follow-up of abnormal screening examinations.

Results.—Although women aged 50 years or older constituted only 38.3% of all women who received first-screening mammography, 74% of breast cancers were detected in this group. Ten cancers were diagnosed per 1000 first-screening examinations in women aged 50 years or older, with 14.8 diagnostic procedures per cancer diagnosed compared with two cancers per 1000 screening examinations and 48.3 diagnostic tests per cancer diagnosed in women younger than 50 years. The PPV of first-screening mammography (number of breast cancers detected per abnormal examination) increased with age: .03 for those aged 30 to 39 years; .04 for those aged 40 to 49; .09 for those aged 50 to 59; .17 for those aged 60 to 69; and .19 for those aged 70 years or older (χ^2 for trend, $P<.001$). Women aged 50 to 59 years had a higher PPV for first-screening mammography than women aged 40 to 49 years (.09 vs .04; $P=.004$), and women with a family history of breast cancer had higher PPVs compared with women without history (40 to 49 years of age, .13 vs .04, $P=.01$; and 50 to 59 years of age, .22 vs .09, $P=.01$).

Conclusion.—Five times as many cancers per 1000 first-screening mammographic examinations were diagnosed in women aged 50 years or older compared with women aged less than 50 years. The highest PPVs for mammography were in women aged 50 years or older and in women aged 40 years or older with a family history of breast cancer. Efforts to promote screening mammography should focus on women in these groups, in whom the majority of breast cancers occur and for whom mammography has the highest PPVs.

(*JAMA*. 1993;270:2444-2450)

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Presented in part at the 26th annual meeting of the Society for Epidemiologic Research, Keystone, Colo, June 17, 1993.

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BREAST cancer is the most commonly diagnosed cancer in women and the second leading cause of cancer death.[1] Screening mammography has been shown to reduce mortality from breast cancer by 20% to 39% among women aged 50 years or older,[2] and there is universal agreement among experts that women aged 50 years or older should receive routine screening mammography.[3,4] Among women aged 40 to 49 years, the evidence to support the efficacy of screening mammography is less conclusive. Eight randomized trials have reported no statistically significant reduction in mortality in women aged 40 to 49 years after 7 to 10 years of follow-up,[5-11] and a recent meta-analysis of 7- to 10-year results from these trials showed no reduction in breast cancer mortality.[12] However, after 10 years of follow-up a nonsignificant trend toward reduced mortality ranging from 13% to 23% begins to emerge in several studies.[10,11,13] A recent analysis that combined data from five Swedish trials also reported a nonsignificant 13% reduction in breast cancer mortality after 7 to 10 years of follow-up among women aged 40 to 49 years who underwent screening mammography.[11]

In addition to perhaps being less effective, mammography may also be less accurate in younger women, owing to lower sensitivity[5,12,14] and lower prevalence of breast cancer in younger women. Therefore, screening of younger women may result in a lower positive predictive value (PPV) for mammography, requiring more diagnostic evaluations for each breast cancer detected.

The overall PPV of first-screening mammography has been reported to be 5% to 38%,[5-9,14-30] but there is a paucity of information on the PPV of screening mammography by age or breast cancer risk. In addition, published reports of the accuracy of mammography have not necessarily evaluated a screening population of asymptomatic women, but have included women who would otherwise be recommended for diagnostic mammography such as women with breast symptoms and those with palpable masses.

We determined the PPV of screening mammography in asymptomatic women

under the age of 50 years compared with those aged 50 years or older. In addition, we report the PPV of screening mammography in women with a family history of breast cancer. We also determined the number of tests and diagnostic procedures performed per abnormal screening examination and per cancer diagnosed in younger women compared with older women.

METHODS

Subjects

The University of California, San Francisco, Mobile Mammography Screening Program is a low-cost community-based breast cancer screening program that offers mammography to women of diverse ethnic backgrounds (including non-Hispanic white, Asian, Hispanic, and African-American women) in six counties in northern California, 75% of whom live in San Francisco County. Our study sample included asymptomatic women aged 30 years or older who were screened for the first and second time by the mobile van in all six counties from April 18, 1985, through November 20, 1992. Any additional screening examinations after the second screening were not included in the study sample. In addition, mammographic examinations among women with a history of breast cancer, palpable breast mass by history or physical examination, or mastectomy were excluded.

Measurements

Screening procedures have been described in detail.[31] In brief, mammography is performed in a mobile van staffed by three certified radiologic technologists. For each woman, a breast cancer risk profile and clinical history are obtained, as well as two standard mammographic views per breast on an accredited, dedicated mammography unit (Mamex DC Soredex, Conroe, Tex). The breast cancer risk profile includes questions about personal history of breast cancer, family history of breast cancer, history of breast surgery, age at menopause, age at first menarche, and age at birth of first child.[32] Women were considered to have a family history of breast cancer if they had at least one first-degree relative (mother, sister, or daughter) with breast cancer. Women with a family history of breast cancer were stratified into two groups: (1) women with one first-degree relative diagnosed as having unilateral postmenopausal breast cancer (strong family history), and (2) women with one first-degree relative diagnosed as having either premenopausal breast cancer or bilateral breast cancer, or with more than one first-degree relative with breast cancer (very strong family history). Screening mammography evaluations did not include a complete breast physical examination, but women were questioned regarding breast symptoms and lumps.

Screening examinations are read by board-certified radiologists. Mammographic interpretations are reported as normal or abnormal, with the latter group further divided into the following three subcategories: (1) further imaging tests or aspiration indicated, (2) suspicious for malignancy, biopsy recommended, and (3) malignant by radiological criteria. Tests that may be recommended for evaluation of abnormal mammograms include physical examination, ultrasonography, mammographic magnification views, diagnostic (problem-solving) mammography, early-recall mammography, fine-needle aspiration, or surgical biopsy with needle localization.

Follow-up

Clinical outcomes for all women with screening examinations were determined by contacting the woman's personal physician and searching the University of California, San Francisco, pathology and radiology databases. One month after an abnormal examination, physicians were sent a standardized request for information regarding subsequent diagnostic procedures performed to evaluate abnormal mammograms and the clinical outcome. If physicians did not respond to the mailed request, they were contacted by telephone.

Our monthly computer-generated request for information to physicians resulted in nearly complete follow-up of all abnormal screening examinations.[15,33] Of the 1933 women with abnormal first-screening examinations, 103 (5.3%) were excluded because the women's physicians decided not to perform further diagnostic tests (n=96) or because we could not determine the clinical outcome (n=7). The age distribution and percentage with a family history of breast cancer among these 103 women with incomplete follow-up was similar to that for women with abnormal examinations and complete follow-up.

Women were considered to have breast cancer if biopsy results showed ductal carcinoma in situ (DCIS) or any invasive carcinoma. All breast cancers were classified according to the American Joint Committee on Cancer Staging system.[34]

We also determined which tests were performed to evaluate abnormal screening examinations. This information was obtained by reviewing women's radiology and pathology reports and patient follow-up information supplied by their personal physicians.

Data Analysis

We stratified the data into three groups: (1) first-screening examinations except those in women who had a family history of breast cancer; (2) first-screening examinations in women with a family history of breast cancer; and (3) second-screening examinations in women with two screening examinations whose first screening examination was interpreted as normal. The PPV of screening mammography was calculated as the proportion of women with abnormal screening examinations who were diagnosed as having breast cancer. Since the PPV of mammography is influenced by the criteria used for calling an examination abnormal, we also report the proportion of breast cancers diagnosed per screening examination, a statistic that is not as affected by such criteria. The χ^2 test and Fisher's Exact Test were used for comparison of proportions. The χ^2 test for trend was used to compare proportions stratified by age.

RESULTS

Mammography

From April 18, 1985, through November 20, 1992, a total of 40 532 screening examinations were performed in 31 814 women. We excluded 1976 first-screening examinations (6.6% of all first-screening examinations) and 171 second-screening examinations (2.0% of second-screening examinations) because these women reported a history of breast cancer, had a palpable breast mass by history or physical examination, or had undergone mastectomy. There remained 29 838 first-screening examinations (2973 were in women with a family history of breast cancer) and 8547 second-screening examinations for analysis.

Women younger than 50 years underwent 61.7% of first-screening examinations and 59.4% of all screening examinations. The proportion of women aged 50 years or older undergoing first-screening mammography decreased from 44.0% in the first 4 years of screening to 35.1% in the last 4 years of screening (Table 1). Although women aged 50 years or older constituted only 38.3% of all women who received first-screening mammography, 74% of breast cancers detected were diagnosed in this group.

First-Screening Mammography in Women Without a Family History of Breast Cancer

Among the 26 865 women without a family history of breast cancer who had first-screening mammography, the overall frequency of abnormal examinations was 6% (1611 abnormals) and increased

Table 1.—Distribution of First-Screening Mammographic Examinations by Year Screened and Age

Year	Mammographic Examinations, No.	Age, y, %				
		30-39	40-49	50-59	60-69	≥70
1985	2097	21.8	31.1	21.9	18.5	6.7
1986	4072	20.1	32.6	21.0	17.5	8.8
1987	4065	26.6	34.3	17.3	13.8	8.0
1988	4827	29.9	33.8	16.2	12.4	7.7
1989	3576	28.6	33.3	18.4	12.4	7.3
1990	4105	27.5	38.4	17.9	10.2	6.0
1991	3758	29.4	35.4	18.3	11.8	5.1
1992	3338	28.9	38.2	17.0	10.0	5.9

Table 2.—Results of First-Screening Mammography at the University of California, San Francisco, Mobile Mammography Program, Excluding Women With a Family History of Breast Cancer*

Mammographic Interpretation	Age, y				
	30-39	40-49	50-59	60-69	≥70
Normal, No. (%)	6787 (96.0)	8868 (93.7)	4656 (93.4)	3245 (92.2)	1693 (92.7)
Abnormal, No. (%)	282 (4.0)	597 (6.3)	327 (6.6)	276 (7.8)	134 (7.3)
Abnormal reading†					
Further tests needed, No. (%)	270 (95.7)	566 (94.8)	306 (93.6)	241 (87.3)	111 (82.8)
Suspicious for malignancy, No. (%)‡	11 (3.9)	28 (4.7)	16 (4.9)	25 (9.1)	17 (12.7)
Malignant, No. (%)‡	1 (0.4)	3 (0.5)	5 (1.5)	10 (3.6)	6 (4.5)
Breast cancers, No.	9	26	30	46	26
Breast cancers/1000 examinations‡ (95% CI)	1 (1 to 2)	3 (2 to 4)	6 (4 to 8)	13 (9 to 17)	14 (9 to 20)
PPV mammography§ (95% CI)					
All breast cancer‡‖	.03 (.01 to .05)	.04 (.02 to .06)	.09 (.06 to .12)	.17 (.13 to .21)	.19 (.12 to .26)
Invasive breast cancer	.004 (.000 to .023)	.02 (.01 to .04)	.06 (.04 to .09)	.14 (.10 to .19)	.13 (.08 to .20)
PPV abnormal reading					
Further tests needed‡	.02	.02	.06	.09	.10
Suspicious for malignancy¶	.27	.36	.50	.56	.53
Malignant	1.0	1.0	1.0	1.0	1.0

*Excludes women with a history of breast cancer or mastectomy, palpable mass by history or physical examination, or family history of breast cancer. CI indicates confidence interval.
†Further imaging tests or aspiration recommended; suspicous for malignancy, biopsy recommended; malignant by radiological critera.
‡Positive predictive value of mammography (number of breast cancers detected per abnormal screening examination).
§$P<.001$, χ^2 for trend.
‖Includes invasive breast cancer and ductal carcinoma in situ.
¶$P=.04$, χ^2 for trend.

only slightly with age (Table 2). Most abnormal screening examinations (92.5%) were reported as needing further imaging tests or aspiration. The proportions of abnormal screening examinations reported to be suspicious for malignancy and malignant by radiological criteria were low but increased with age (χ^2 for trend, $P<.001$, respectively).

The average number of cancers detected per first-screening examination was five per 1000. The number of cancers detected per screening examination increased with age, with women aged 50 years or older having five times as many cancers diagnosed per 1000 examinations (10 per 1000) as women younger than 50 years (two per 1000).

The overall PPV of first-screening mammography was 8.5% and increased significantly with age from .03 for those aged 30 to 39 years to .19 for those aged 70 years or older (Table 2). Women aged 50 to 59 years had a significantly higher PPV for first-screening mammography than women aged 40 to 49 years (.09 vs .04; $P=.004$) and women aged 60 years or older had the highest PPVs (.17 to .19). The PPVs for invasive breast cancer only were especially low for women less than 50 years of age (.004 to .02) but remained relatively high for women aged 50 years or older (.06 to .14).

The PPVs for screening examinations categorized as "further tests needed" (92.5% of abnormal examinations) increased with age (χ^2 for trend, $P<.001$), but were relatively low for all age groups. Abnormal screening examinations reported as suspicious for malignancy (6% of abnormal examinations) had relatively high PPVs that also increased with age (χ^2 for trend, $P=.04$). Abnormal screening examinations reported as malignant (1.5% of abnormal examinations) had a PPV of 1.0 for all ages.

First-Screening Mammography in Women With a Family History of Breast Cancer

Among the 2973 women with a family history of breast cancer who had first-screening mammography, the overall frequency of abnormal examinations was 7.2%, with the highest frequency occurring in women aged 50 to 59 years (11.9%) (Table 3). The number of breast cancers per 1000 first-screening examinations in women with a family history of breast cancer compared with women without a family history of breast cancer was significantly higher in women aged 40 to 49 years (nine vs three; $P=.008$) and 50 to 59 years (26 vs six; $P=.001$). Women aged 30 to 39, 60 to 69, and 70 years or older with a family history of breast cancer had similar numbers of breast cancers per first-screening examination compared with women without a family history.

The PPV for screening mammography in women with a family history of breast cancer increased with age (Table 3) and was about three times higher compared with women without a family history of breast cancer for those aged 40 to 49 years (.13 vs .04; $P=.01$) and aged 50 to 59 years (.22 vs .09; $P=.01$). Women aged 30 to 39, 60 to 69, and 70 years or older with a family history of breast cancer had similar PPVs for first-screening mammography compared with women without a family history. Since only eight of the 30 breast cancers detected in women with a family history of breast cancer were in women with a very strong family history of breast cancer, we could not calculate separately the PPV for women with a strong and very strong family history of breast cancer.

Second-Screening Mammography

Among 8547 women who had a first-screening examination interpreted as normal, the overall frequency of abnormal second-screening examinations was 2% (Table 4). Compared with first-screening mammography, the number of cancers detected per second-screening examination was lower for all age groups and did not increase with age (χ^2 for trend, $P=.25$). Compared with first-screening mammography, the PPV of second-screening mammography was higher for all age groups except for women aged 60 to 69 years. However, PPVs were not significantly different from those for first-screening mammography in any age group, despite the variation in time between first and second screens.

Diagnostic Evaluations of Abnormal Mammography

Evaluation of the 1461 abnormal first-screening examinations in women aged 30 to 69 years without a family history of

breast cancer required 2816 additional diagnostic procedures. Of the total number of procedures performed to evaluate abnormal examinations, 60% were in women younger than 50 years (Table 5). On average, two procedures were performed to evaluate each abnormal examination, regardless of age, except that women aged 60 years or older required 30% fewer procedures than women younger than 60 years. The number of procedures per cancer diagnosed decreased substantially with age, with women younger than 50 years having a threefold higher number of tests per cancer diagnosed compared with women aged 50 years or older (48.3 vs 14.8 per cancer; $P<.001$).

Breast Biopsies

The frequency of biopsy per screening examination and biopsy per abnormal screening examination increased with age (Table 6). However, women aged 40 to 49 years had approximately the same frequency of biopsy per screening mammography (0.016 vs 0.20; $P=.08$) and biopsy per abnormal screening mammography (0.26 vs 0.31; $P=.09$) as women aged 50 to 59 years.

The overall yield of breast cancer per number of breast biopsies performed was 29%. The yield of cancer diagnosed per number of breast biopsies performed increased with age and was approximately 2.5 times higher in women aged 50 years or older compared with women younger than 50 years (0.40 vs 0.16; $P<.001$).

Breast Cancer Stage and Tumor Size

The majority of breast cancers diagnosed on first-screening mammography were DCIS, or stage I (84%), for all age groups. However, women younger than 50 years more frequently had DCIS (63% of cancers) compared with women aged 50 years or older (26% of cancers) ($P<.001$). Among all age groups, 58% of all tumors were DCIS or 10 mm or less in size and 79% were DCIS or 15 mm or less in size. The proportion of women with invasive cancers greater than 15 mm was similar for women aged 50 years or older (23 [22.5%] of 102) compared with women younger than 50 years (six [17.1%] of 35).

COMMENT

We examined the PPV of screening mammography and the number of breast cancers detected per screening examination by age and family history of breast cancer. For every 1000 women who had first-screening examinations, 6% were abnormal, five cancers were detected, and the overall PPV was .08. Furthermore, there were marked differences

Table 3.—Results of First-Screening Mammography at the University of California, San Francisco, Mobile Mammography Program, in Women With a Family History of Breast Cancer*

Mammographic Interpretation	Age, y				
	30-39	40-49	50-59	60-69	≥70
Normal, No. (%)	906 (94.6)	849 (93.2)	408 (88.1)	352 (92.6)	244 (93.5)
Abnormal, No. (%)	52 (5.4)	62 (6.8)	55 (11.9)	28 (7.4)	17 (6.5)
Abnormal reading†					
Further tests needed, No. (%)	50 (96.2)	55 (88.7)	49 (89.1)	24 (85.7)	13 (76.5)
Suspicious for malignancy, No. (%)	2 (3.8)	5 (8.1)	6 (10.9)	2 (7.1)	0 (0)
Malignant, No. (%)	0 (0)	2 (3.2)	0 (0)	2 (7.1)	4 (23.5)
Breast cancers, No.	2	8	12	4	4
Breast cancers/1000 examinations‡ (95% CI)	2 (0 to 5)	9 (3 to 15)	26 (12 to 40)	10 (0 to 21)	15 (1 to 30)
PPV mammography‡§ (95% CI)	.04 (.00 to .09)	.13 (.05 to .21)	.22 (.11 to .33)	.14 (.01 to .27)	.24 (.04 to .44)

*Excludes women with a history of breast cancer or mastectomy or palpable mass by history or physical examination. Family history is defined as at least one first-degree relative (mother, sister, or daughter) with breast cancer. CI indicates confidence interval.
†Further imaging tests or aspiration recommended; suspicious for malignancy, biopsy recommended; malignant by radiological criteria.
‡$P=.006$, χ^2 for trend.
§Positive predictive value of mammography (number of breast cancers detected [invasive and ductal carcinoma] per abnormal screening examination).

Table 4.—Results of Second-Screening Mammography at the University of California, San Francisco, Mobile Mammography Program*

Mammographic Interpretation	Age, y				
	30-39	40-49	50-59	60-69	≥70
Normal, No. (%)	1357 (97.7)	2951 (98.0)	2005 (98.1)	1415 (98.0)	650 (98.6)
Abnormal, No. (%)	32 (2.3)	61 (2.0)	38 (1.9)	29 (2.0)	9 (1.4)
Breast Cancers, No.	2	4	6	2	2
Breast cancers/1000 examinations (95% CI)	1 (0 to 3)	1 (0 to 3)	3 (1 to 5)	1 (0 to 3)	3 (0 to 7)
PPV mammography† (95% CI)	.06 (.01 to .22)	.07 (.02 to .17)	.16 (.07 to .32)	.07 (.01 to .24)	.22 (.04 to .60)
Months between first and second screen, mean±SD	32.1±12.9	25.7±10.0	18.6±9.4	18.3±9.4	18.6±9.7

*Excludes women with a history of breast cancer or mastectomy, palpable mass by history or physical examination, family history of breast cancer, or abnormal first-screening examination. CI indicates confidence interval.
†Positive predictive value of mammography (number of breast cancers detected [invasive and ductal carcinoma] per abnormal screening examination).

Table 5.—Diagnostic Procedures Following Abnormal First-Screening Examinations

	Age, y			
	30-39	40-49	50-59	60-69
Mammographic examinations, No.*	7066	9454	4978	3519
Abnormal mammographic examinations, No.	279	586	322	274
Diagnostic procedures, No. (%)				
Physical examination only	24 (4.4)	37 (3.2)	35 (5.3)	19 (4.1)
Additional mammography†	320 (58.2)	640 (56.1)	363 (55.3)	236 (50.3)
Ultrasonography	59 (10.7)	124 (10.9)	72 (11.0)	38 (8.1)
Fine-needle aspiration	20 (3.6)	66 (5.8)	21 (3.2)	16 (3.4)
Excisional biopsy	68 (12.4)	149 (13.0)	95 (14.5)	92 (19.6)
Needle localization	59 (10.7)	125 (11.0)	70 (10.7)	68 (14.5)
Total‡	**550**	**1141**	**656**	**469**
Procedures/screening examination	0.08	0.12	0.13	0.13
Procedures/abnormal screening examination	2.0	1.9	2.0	1.7
No. of breast cancers	9	26	30	46
Procedures/breast cancer diagnosed (95% CI§)	61.1 (54.1 to 68.0)	43.9 (40.4 to 47.4)	21.9 (19.9 to 23.9)	10.2 (8.9 to 11.5)

*Values may differ from Table 2 owing to missing data.
†Includes magnification views, diagnostic (problem-solving) mammographic examinations, and early-recall mammography.
‡Does not sum to the number of abnormal mammographic examinations since a woman could have more than one procedure.
§CI indicates confidence interval.

Table 6.—Results of Breast Biopsies in Women With First-Screening Mammography*

	Age, y				
	30-39	40-49	50-59	60-69	≥70
Breast biopsy/screening examination†	.009	.016	.020	.028	.030
Breast biopsy/abnormal screening examination† (95% CI)	.22 (.18 to .25)	.26 (.23 to .28)	.31 (.27 to .34)	.36 (.32 to .40)	.41 (.35 to .46)
Breast biopsy interpretation, No. (%)					
Benign‡	52 (85.2)	127 (83.0)	71 (70.3)	54 (54.0)	29 (52.7)
Malignant	**9** (14.8)	**26** (17.0)	**30** (29.7)	**46** (46.0)	**26** (47.3)
Invasive	1 (11.1)	12 (46.2)	20 (66.7)	38 (82.6)	17 (65.4)
DCIS§	8 (88.9)	14 (53.8)	10 (33.3)	8 (17.4)	9 (34.6)
Breast cancer/biopsy† (95% CI)	.15 (.06 to .24)	.17 (.11 to .23)	.30 (.21 to .39)	.46 (.36 to .56)	.47 (.34 to .60)

*Excludes women with a history of breast cancer or mastectomy, palpable mass by history or physical examination, or family history of breast cancer. CI indicates confidence interval.
†$P<.001$, χ^2 for trend.
‡Includes biopsies classified as epithelia hyperplasia with cellular atypia and lobular carcinoma in situ.
§Ductal carcinoma in situ.

by age. For every 1000 women younger than 50 years, 5.3% of first-screening examinations were abnormal, two cancers were found, and the PPV of mammography was .03 to .04. In comparison, for every 1000 women aged 50 years or older, 7.1% of first-screening examinations were abnormal, 10 cancers were found, and the PPV of mammography was .09 to .19.

Other studies report that approximately 5% of first-screening mammographic examinations are abnormal,[18-19,24,35] five to eight cancers are detected per 1000 screening examinations,[5-6,8,14,20,24,30,36-38] and the PPV of first-screening mammography is .05 to .38.[5-9,14-30] The wide range of PPVs reported for screening mammography are due to differences in the definitions of an abnormal screening examination, what constitutes a screening examination, and differences in the age and breast cancer risk profile in women included in the screened population. In addition, many reports of screening mammography wrongly define the PPV as the number of cancers diagnosed per number of biopsies performed.[14,20,25-29] We defined the PPV of mammography as the proportion of women with abnormal mammograpy who actually had breast cancer. This approach takes into account all diagnostic procedures that result from abnormal screening examinations including, but not limited to, excisional biopsy and the accompanying anxiety associated with being informed of an abnormal examination.[39]

Only one other study has reported the PPVs for screening mammography by age, and it too showed an increase in the PPV of screening mammography with increasing age, with the highest PPVs in women aged 60 years or older.[19] The PPVs in that study were lower than those reported here (in women aged 40 to 49 years, .007; 50 to 59, .03; and 60 to 70, .08), probably because women with dense breasts but no other findings on their mammograms were considered to have abnormal examinations. The observed increase in PPV with increasing age is most likely due to the lower prevalence of breast cancer in younger women. The incidence of breast cancer increases by approximately 1.5-fold every 10 years, starting at the age of 40, to the age of 70 years.[40] Our results reflect this increasing incidence, as the number of breast cancers detected per first-screening examination approximately doubled with each 10-year increase in age up to 70 years (Table 2), a finding consistent with other reports.[5]

However, the observed increase in PPV of screening mammography with increasing age could, in part, be due to a lower sensitivity of mammography in younger women. The sensitivity of screening mammography in younger women has been reported to be 60% to 84% compared with 86% to 95% in older women.[5,12,14] This is probably because their breasts have a lower fat content and consequently are less radiolucent than those of older women. However, this difference in the sensitivity of mammography in younger compared with older women probably does not affect the PPV of screening mammography as much as the prevalence of breast cancer.

In addition to age, a family history of breast cancer has a major impact on breast cancer prevalence. Since the relative risk of breast cancer is two to three times higher in women with a family history of breast cancer,[41,42] the prevalence of breast cancer is increased approximately twofold to threefold in these women. For every 1000 women in our study aged 40 years or older with a family history of breast cancer, 80 first-screening examinations were abnormal, 14 cancers were found, and the PPV of mammography was .17. Thus, the higher PPV of screening mammography we report for women with a family history of breast cancer compared with women without a family history of breast cancer is probably because of a higher prevalence of breast cancer in these women.

We attempted to calculate the PPV for mammography in women with a very strong family history (one first-degree relative diagnosed as having either premenopausal breast cancer or bilateral breast cancer, or with more than one first-degree relative with breast cancer) separately from those with a strong family history (one first-degree relative with postmenopausal breast cancer). However, since only eight of 30 breast cancers among women with a family history of breast cancer were detected in women with a very strong family history, the numbers were inadequate to allow meaningful results. Nevertheless, since the relative risk of breast cancer is higher in women with a first-degree relative with premenopausal breast cancer or with more than one first-degree relative with breast cancer compared with women with one first-degree relative with postmenopausal breast cancer,[42] the prevalence of breast cancer will also be higher in these women. Consequently, it is reasonable to assume that the PPV of mammography will be as high or higher in women with a first-degree relative with premenopausal breast cancer compared with women with a first-degree relative with postmenopausal breast cancer.

We also calculated the PPVs in women with early menarche (aged 12 years or younger), late menopause (aged 55 years or older), and age at first birth (aged 30 years or older or nulliparous). The PPVs in women with these risk factors were slightly higher for each age group, but not clinically significantly different than in women without these risk factors. It may be possible to combine these risk factors and identify women in whom the PPV of mammography is as high as in those with a family history of breast cancer. However, there were too few women with multiple risk factors in our cohort in whom breast cancer was detected to allow calculation of PPVs.

The PPV of mammography is also affected by the percentage of the population being screened for the first time.[43] Although the number of breast cancers detected per examination decreases with subsequent screening examinations, the PPV tends to increase since fewer examinations are interpreted as abnormal when prior films are available for comparison. Our data and the data of others

Table 7.—Comparison of First-Screening Mammography, Stratified by Age 50

	<50 y	≥50 y
No. of women screened	1000	1000
No. of abnormal examinations	53	71
No. of diagnostic procedures*	102	132
No. of biopsies	13	25
No. of invasive cancers	1	7.5
No. of DCIS†	1	2.5

*Includes all procedures listed in Table 5.
†Ductal carcinomas in situ.

support these conclusions.[5,9,15,22,44] Of note, however, the PPV for second-screening mammography for women younger than 50 years is still low and less than the PPV of second-screening mammography for women aged 50 years or older (.06 vs .13), and the PPV of first-screening mammography for women aged 50 to 59 years (.06 vs .09).

The majority of breast cancers diagnosed on first-screening mammography were stage I, or DCIS. Of the cancers detected in women younger than 50 years, 64% were DCIS compared with 26% of those detected in women aged 50 years or older, and the proportion of cancers that were DCIS decreased with age. The significance of DCIS lesions is not fully understood and there is controversy about whether all of these lesions are precursors of invasive cancer.[45] In two retrospective studies, both with information on 25 patients with DCIS lesions and more than 16 years of follow-up, the incidence of subsequent invasive cancer was 28%[46] and 25%[47] in those treated with excisional biopsy alone. More recent prospective studies of mammographically identified DCIS lesions show an even lower incidence of subsequent invasive breast cancer after excisional biopsy alone (12% to 13%), but the median follow-up for these studies was only 5 years.[48,49] The reported low incidence of subsequent invasive cancer in all these studies[46-49] may reflect complete removal of DCIS by adequate excisional biopsy, and thus cure of DCIS.

Our data suggest that if 1000 women under the age of 50 years undergo first-screening mammography, approximately 50 will have an abnormal finding requiring some additional procedure (including 13 excisional biopsies); two will have cancer, one of which will be DCIS (Table 7). In comparison, if 1000 women aged 50 years or older undergo first-screening mammography, approximately 70 women will have an abnormal finding requiring some additional procedure (including 25 excisional biopsies); 10 will have cancer, 7.5 of which will be invasive and 2.5, DCIS. Thus, women younger than 50 years will have approximately 2.5 times as many biopsies and three times as many diagnostic procedures for every cancer diagnosed compared with women aged 50 years or older (Tables 5 and 6).

Our results and those of others show that the majority (62%) of screening-mammography participants are under the age of 50 years.[23,50-54] However, in the six northern California counties served by our screening-mammography program, the majority of women (65%) are under the age of 50 years.[55] Therefore, the larger proportion of women under the age of 50 years undergoing mammography screening reflects the relatively young age of the six northern California counties. Nevertheless, because the majority of screened women are young and the PPV of screening mammography is low, women under the age of 50 years will undergo the majority of diagnostic procedures (60%) to find fewer cancers than in older women (two vs 10 per 1000 screening examinations).

Our study is limited by incomplete follow-up of all abnormal screening examinations. Nevertheless, it is unlikely that we underestimated the PPV of first-screening mammography in younger women relative to older women since the proportion of younger women with abnormal examinations and unknown follow-up is low (5%) and similar to that in older women. Moreover, the number of cancers detected per first-screening examination by age in our study is similar to that found in other studies.[5,9,20,22] Another limitation is that the study population may not be representative. Women who undergo screening mammography might be healthier than those who do not, have a lower prevalence of breast cancer, and lower PPVs for screening mammography. On the other hand, women at increased risk for breast cancer may be more likely to undergo screening mammography, have a higher prevalence of breast cancer, and higher PPVs for screening mammography. Finally, we do not know the ethnicity of the women screened in our study. Consequently, we do not know how the PPV of screening mammography may be modified by race.

Our results suggest that screening women aged 40 to 49 years with a family history of breast cancer will identify similar numbers of cancers per screening examination and cancers per abnormal screening examination as in women aged 50 years or older without a family history of breast cancer. In women aged 50 years or older, screening mammography has the highest PPV, breast biopsies yield the highest proportion of cancers, and clinical trials clearly demonstrate a significant reduction in breast cancer mortality.[5-8,10-12,30] Based on these data, we recommend that efforts to promote mammography screening be concentrated on all women aged 50 years or older, and on women aged 40 to 49 years with a family history of breast cancer or otherwise at high risk for breast cancer. Furthermore, asymptomatic women who request or are offered screening mammography should be told the likely outcomes of screening.[56] Women younger than 50 years without a family history of breast cancer should be informed that if 1000 women undergo screening mammography, about 50 will require further diagnostic procedures. Of these 50 women, one is likely to have invasive breast cancer and one is likely to have DCIS, a breast tumor that does not always become invasive. In addition, women younger than 50 years of age should be informed that while there is some inferential evidence that mammography may be beneficial, randomized trials to date have not demonstrated that screening mammography in women younger than 50 years of age reduces breast cancer mortality. Women aged 50 years or older should be informed that for every 1000 women screened, further diagnostic procedures will be required in about 70, that 10 breast cancers will be detected in those 70 women (7.5 cases of invasive cancers and 2.5 cases of DCIS), and that screening mammography in their age group has been shown to reduce significantly the death rate from breast cancer.

This study was supported in part by the Breast Cancer SPORE (Specialized Program of Research Excellence), from the National Institutes of Health, Bethesda, Md, and a Merck/Society for Epidemiologic Research Clinical Epidemiology Fellowship Program (Dr Grady).

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