Evaluating Organized Breast Cancer Screening Implementation: The Prevention of Late-Stage Disease?

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Abstract

The objective of our study was to evaluate organized breast cancer screening implementation by measuring the association between screening program enrollment and late-stage disease. Our setting was a health plan using mailed mammography reminders to women ages ≥40. We conducted yearly cross-sectional summaries of mammography experience and late-stage (regional or distant Surveillance Epidemiology and End Results Reporting (SEER) stage) breast cancer occurrence for all of the health-plan women ages ≥40 (1986–1998). We estimated the odds of late-stage breast cancer among health-plan and surrounding community women because it was too early to compare changes in mortality. We also estimated the odds of late-stage disease (1995–1998) associated with program enrollment and mammography screening among health-plan women. We found that mammography-within-two-years increased within the health plan from 25.9% to 51.2% among women ages 40–49 and from 32.9% to 74.7% among women ages ≥50. Health-plan late-stage rates were lower than those in the surrounding community [ages 40–49: odds ratio (OR), 0.87; 95% confidence interval (CI), 0.77–0.99; ages 50–79: OR, 0.86; 95% CI, 0.80–0.92] and declined parallel to the community. Among health-plan cancer cases, women ages ≥43 who were enrolled in the screening program and who had at least one program mammogram were less likely to have late-stage disease compared with the women not enrolled in the program (OR, 0.31; 95% CI, 0.16–0.61) but the odds of late-stage was also reduced among program-enrolled women not receiving program mammograms (OR, 0.45; 95% CI, 0.21–0.95). We concluded that enrollment in organized screening is associated with increased likelihood of mammography and reduced odds of late-stage breast cancer. Addressing the concerns of un-enrolled women and those without mammograms offers an opportunity for further late-stage disease reduction.

Introduction

Women, physicians, healthcare organizations, and governments seek evidence that breast cancer screening with mammography is contributing to progress toward breast cancer mortality reductions (1–4). Women have heard the controversy about the quality of breast cancer screening trials and wonder whether they should bother getting a mammogram (5, 6). Primary care physicians face multiple competing demands and must consciously choose to make breast cancer screening referrals (7, 8). Health plans and governments face constrained healthcare resources and must make decisions about continuing organized breast cancer screening programs or investing in screening for other conditions (1–4, 9–12). We undertook this study to evaluate whether offering organized breast cancer screening is associated with indicators of program implementation success, including program enrollment, increased mammography, reduction in late-stage breast cancer, and a reduced odds of late-stage disease among program-enrolled women. The results have relevance to anyone seeking evidence regarding the effectiveness of mammography screening.

Implementation of screening mammography occurs through referral to a radiology facility (opportunistic screening) or through organized programs (organized screening) (13). Opportunistic screening usually occurs at the time of a clinical encounter with a primary care provider for a complete physical examination or women's health visit for cervical cancer screening, but women's self-referral for mammograms also occurs (14, 15). Most organized programs include a centralized administrative structure, screening centers that serve a specific population, direct-mail reminders to women, quality control efforts, and an evaluation component (13). Organized screening exists in some not-for-profit managed care plans in the United States, several European countries, and Canada (16, 17). The proportion of women screened varies from 50 to 89% in countries with organized plans (13, 16). In the United States, where opportunistic screening is the norm, 64.4% of women ages 40–49 and 75.3% of women ages 50–64 had a mammogram within the prior 2 years by 1998 (16, 18). Whether to offer organized screening programs is of interest because relying on the patient-physician interaction may be inadequate, but organizing programs takes resources (13, 19–21).

Health-plan administrators and policymakers need early markers of progress to demonstrate effective screening implementation and to justify continued investment in the face of competing demands. Successful implementation of breast cancer screening programs should result in a high level of program enrollment among the population to whom it is offered and, therefore, a high proportion of women should have regular screening. If both occur, then we expect to see a decreasing rate

Received 7/8/03; revised 10/3/03; accepted 10/8/03.
Grant support: National Cancer Institute Grant CA63731.
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of late-stage breast cancer, a reduced risk of late-stage disease among those who are program enrolled and screened, and a reduced risk of mortality. Although reduced mortality is the desired program effect, achieving that effect takes years so we used late-stage breast cancer as a proxy for mortality. We chose late-stage breast cancer as our outcome measure based on three assumptions: (*a*) mortality reductions are possible through mammography (1, 2, 22, 23); (*b*) late-stage disease rates will fall before mortality reductions occur; and (*c*) late-stage disease is strongly correlated with mortality (24–26). Declining rates of late-stage disease provide evidence of successful screening mammography implementation because cancer stage is established at diagnosis (24–26). Declining rates of late-stage disease also reflect program effects that are independent of treatment and, in this respect, have an advantage over mortality end points for monitoring screening program progress.

This evaluation has three components that capture the expected changes in a population offered a screening program: (*a*) an evaluation of mammography diffusion among health-plan women (component 1, mammography diffusion); (*b*) an evaluation of the rate of late-stage disease (component 2, late-stage rates) among health-plan and community women; and (*c*) an evaluation of the odds of late-stage disease among health-plan women as a function of program enrollment and screening exposure (component 3, modeling the odds of late-stage disease). We had three major hypotheses: (*a*) that mammography use would increase over time among health-plan women and be higher among women ages ≥50 compared with those ages 40–49; (*b*) that late-stage rates would decrease with time; and (*c*) that the risk of late-stage disease would be reduced with program enrollment and the receipt of program mammograms.

Subjects and Methods

Setting. We conducted this study at Group Health Cooperative (GHC), a not-for-profit health plan with salaried primary care and specialty providers that served more than 350,000 average annual health-plan enrollees during the study period and delivered most services through the health plan facilities. This analysis focused on the 94.5% of the enrollees in the staff model Puget Sound plan who were offered an organized breast cancer screening program (27–30). We excluded the 5.5% of women served through contract-care because of differences in when and how the health plan implemented the screening program for these women. We also evaluated cancer rates in the surrounding community for comparison. However, there is no automated record of mammography exposure in the community; therefore, that comparison was not made.

Group Health Cooperative's Breast Cancer Screening Program (BCSP) began in 1986 to track screening mammography, to mail reminders to women ages ≥40, to provide reports of screening status to primary care physicians, and to oversee implementation in six screening centers (17, 27–30). The program uses a centralized database to manage a risk factor survey and to serve an average annual population of ≥80,000 women over the age of 40 years in the health plan. Eighty-five % of women ages ≥40 complete the survey, and there is no upper age-limit for reminder letters. Classic risk factors (*e.g.,* onset of menses, age when menses end, first- and second-degree family history of breast cancer, previous breast biopsy, atypical hyperplasia on a previous biopsy) are used with age (*i.e.,* ≥50) to identify a high-risk population and to send reminders at 1- or 2-year intervals (27–30). The proportion of the population that is eligible for mammography reminders differs by age categories and includes 65% of women ages 40–49 and all women ages 50 and above. Women ages 40–49 without classic risk factors (35% of women ages 40–49) are not offered reminders until age 50 but may seek screening through their usual care provider. Any woman may be screened at any interval of 1 or more years through their primary care provider.

The program staff monitors monthly automated mailings that include information about the program, the invitation to complete the risk-factor survey and to join the program, and/or reminders to women due for a screening center appointment. During the study period, a screening center appointment included a breast physical examination by a nurse practitioner, instruction in breast self-examination, and a screening mammogram. If a woman had a screening mammogram through her provider during the recommended interval, then she did not get a reminder from the program, and the provider was responsible for any clinical breast examination. Women continued to get reminders until they or their provider requested exclusion. Screening program mammograms and physician-referred mammograms occurred in the same facilities and used the same equipment. Nurses coordinated follow-up of all screened women, regardless of whether the screening occurred within the program or on primary-care referral.

Surveillance Epidemiology and End Results Reporting (SEER) Registry. The Washington State SEER registry includes five counties (King, Snohomish, Thurston, Kitsap, Pierce) that account for most health-plan enrollees. Women from these counties were included in this evaluation. The SEER registry uses national standards to record stage-at-diagnosis and date of diagnosis and provides a report to the health plan of the cancers diagnosed at health-plan facilities. Internal audits at the health plan show that the SEER registry captures 98% of breast cancer cases among health-plan enrollees in the five counties. The other 2% are women who receive diagnoses of breast cancers at contracted facilities but who are not identified as members of the health plan.

Component Definitions, Sample, Measures, and Analysis. Below, we define relevant variables and describe the sample, measures, and analysis for each study component summarized in Table 1. Variables that were used in more than one component are defined where they are first used.

Component 1: Mammography Diffusion

In Component 1, we examined the proportion of women ages ≥40, between 1986 and 1998, who ever had a mammogram and the proportion of women who had a mammogram within a 2-year period.

Definitions. "Health-plan women" included the total population of women ages ≥40 who were enrolled in the health plan in December of each year between 1986 and 1998. "Mammography use" occurred when a health-plan woman received a bilateral (screening or diagnostic) two-view mammogram. We used the date of documented or self-reported mammography occurrence recorded in automated files to establish whether a mammogram occurred in each calendar year.

Measure. "Ever-use of mammography" included all self-reported or automated evidence of having had a mammogram before, and including, the year of interest (1986–1998). "Mammography-within-2-years" measured the proportion of health-plan women who had one mammogram in the previous 2 years from 1986 to 1998.

We began the evaluation of mammography diffusion in 1986 (30). From that time forward, mammogram use was available in automated radiology records and could be supple-

Table 1 Design summary of the three-component evaluation of the effect of offering organized mammography screening 1986–1998 to an annual average of 80,799 female health-plan enrollees ages ≥40 years

Component	Population	Measures
1. Mammography diffusion	Health-plan women enrolled each year 1986–1998 Ages 40–49 or 50+ Residents of five counties of WA[a,b]	Mammography use (screening or diagnostic) at least once before the index year (ever) Receipt of mammography within the previous 2 years
2. Rates of late-stage disease	Community women in five counties of WA Health-plan women in the five counties of WA	Five year age-adjusted late-stage (SEER regional or distant stage) breast cancer rates by age group 40–49 or 50+
3. Modeled odds of late-stage disease	Health-plan women ages 43–79 with invasive breast cancer (SEER regional or distant stage) diagnosed 1995–1998 Health-plan women ages 43–79 with invasive breast cancer (SEER local stage) diagnosed 1995–1998 Health-plan women ages 43–79 frequency-matched to late-stage cases on age and length of health plan enrollment	Odds of late-stage disease as a function of: (*a*) BCSP enrollment and BCSP mammography use (0, 1+) (*b*) Total screening mammography use (0–1, 2+) (*c*) BCSP screening mammography use (0–1, 2+)

[a] Five counties in Washington State: King, Pierce, Snohomish, Thurston, and Kitsap.
[b] WA, Washington State; SEER, Surveillance Epidemiology and End Results Reporting; BCSP, (Group Health Cooperative's) Breast Cancer Screening Program.

mented by self-reported mammography use when women completed the program survey. We graphed the proportion of women, ages 40–49 and ≥50 years, with mammograms and assumed that women without data in a given year had not had a mammogram during that year.

Analysis. For component 1 of this study, we showed the diffusion of mammography over time but did not conduct any statistical tests. On average, there were 33,483 women ages 40–49, and 51,951 women ages ≥50 in each year, but the population size ranged from 18,794 in 1983 to 39,695 in 1998 for women ages 40–49, and from 38,447 to 66,581 for women ages >50.

Component 2: Late-Stage Disease Rates

In component 2, we evaluated whether there was a declining rate of late-stage disease in health plan and surrounding-community women between 1983 and 1998. We started this analysis in 1983 to include comparison late-stage rates from a time-period before the screening program was available within the health plan.

Definitions. We defined "late-stage disease" using the SEER categories of "regional" or "distant" disease because it was consistently available over time. "Regional disease" included invasive breast cancer that extended beyond the limits of the breast directly into surrounding organs or tissues, into regional lymph nodes, or both. "Distant disease" included invasive breast cancer that spread to parts of the body remote from the primary tumor by direct extension or by metastasis (31). Other measures of late-stage disease, such as staging by tumor, node, and metastases (TNM stage), could not be used because they were not available over the entire evaluation time period (1983–1998).

Population. We estimated the total population of community women for each year using the county estimates in 5-year age categories provided by the Washington State Office of Financial Management and subtracting the female age-specific health-plan population (32). The community population included an annual average of 483,101 women (range, 395,068 in 1986 to 610,645 in 1998).

We identified all health-plan women ages ≥40 with invasive breast cancers diagnosed at a late-stage in a health-plan facility between January 1, 1983, and December 31, 1998, regardless of their breast cancer screening program enrollment status.

Measure. We calculated the age-adjusted late-stage disease rate separately for health-plan and community women using the yearly population estimates. We age-adjusted the health-plan and community women rates to the 1970 SEER cancer population to be consistent with SEER policy for cancers diagnosed before 1999.

Analysis. For component 2, we used unconditional logistic regression to examine the association between the occurrence of late-stage disease (yes/no) and time-period.

We grouped data from 1983–1998 into 2-year intervals and modeled time as a group linear variable for each age group (40–49, 50+) while adjusting for age within age group. We used four separate models, one for each population: health-plan women ages 40–49, health-plan women ages 50+, community women ages 40–49, and community women ages 50+. In two additional models, we included all women (health-plan and community) ages 40–49, or all women ages ≥50, and tested for differences in the occurrence of late-stage disease between health plan and the surrounding community by evaluating the main effect of population (health plan *versus* community). We tested whether the rate of decline differed between the health plan and the community by testing for an interaction between the main effects of the population (health plan or community) and time.

Component 3: Modeling the Odds of Late-Stage Disease

In component 3, we evaluated the odds ratio (OR) for late-stage disease in the health-plan population as a function of BCSP program enrollment and screening exposure. This component tested the ecological assumptions underlying any apparent association between the diffusion of mammography and trends in late-stage disease demonstrated in components 1 and 2. Women with late-stage disease should be less likely to have been enrolled in the program and to have received repeated mammography if the screening program enrollment and the use of mammography lead to reduced rates of late-stage disease. If screening takes place independent of the program (*e.g.*, through primary-care referral), then we would not expect BCSP enrollment or BCSP mammograms to be associated with a reduced odds of late-stage disease, even if late-stage disease rates were

falling in the population, because the falling rates could be attributed to screening outside the program.

Definitions. "BCSP enrollment" occurred when health-plan women completed and returned the breast cancer risk-factor questionnaire. A "breast cancer screening program mammogram" was one conducted by radiologists in association with a BCSP Center visit. A "screening mammogram" was any bilateral mammogram designated as "screening" by the radiology facility. These included BCSP mammograms and those referred to radiology by a primary care physician. "Repeated screening mammography" occurred when women received two or more screening mammograms within 5 years. "Index year" was the year of breast cancer diagnosis for each case. "Early-stage breast cancer" included all invasive breast cancers recorded as local stage by SEER.

Population. In component 3, we identified all health-plan women ages 43–79 at the time of diagnosis of an invasive breast cancer between January 1, 1995, and December 31, 1998, who had at least 5 years of enrollment before their date of diagnosis of breast cancer. We excluded women less than 43 because they did not have an opportunity to receive two or more mammograms. We also identified a random sample from the "general health-plan population" of women ages 43–79 who did not have late-stage breast cancer, and we frequency-matched them on age and length of health-plan enrollment to the late-stage cases in a ratio of 4:1. These general health-plan controls were selected irrespective of BCSP enrollment, and three had early-stage breast cancer before the index date of their matched case.

Measure. Because a BCSP mammogram rather than program enrollment was what would avoid late-stage disease, we evaluated the two in association. We tested three key measures for their association with late-stage breast cancer: BCSP enrollment and BCSP mammography experience (no, yes+no BCSP mammogram; and yes +1 or more BCSP mammograms); total number of screening mammograms used during the 5 years before diagnosis (0–1, 2+ mammograms); and BCSP screening mammography use (0–1, 2+ BCSP mammograms). We used automated data for all variables for all cases and controls and considered the following variables in addition to mammography use: age, race, family history of breast cancer in a first- or second-degree relative, and length of health-plan enrollment. Mammography use was restricted to examinations documented in the health-plan radiology files during the 5 years before the date of diagnosis.

Analysis. We estimated the OR for late-stage disease as a function of program enrollment, number of mammograms, and screening program mammograms by comparing the experience among women with late-stage disease and that of two separate controls: (*a*) all women with early-stage invasive disease; and (*b*) the age and length-of-enrollment-matched general health-plan population controls.

For the component 3 analysis, we compared the health-plan late-stage breast cancer cases with the two control groups on demographics, breast cancer risk factors, and mammography experience. We used descriptive statistics to compare cases with each set of controls with respect to the variables of interest (age, race, family history, length of health-plan enrollment, BCSP enrollment, and number of screens). We then used unconditional logistic regression to examine separately the effects of program enrollment and its associated BCSP screen, and number of screens in the last 5 years (0–1, 2+). All models adjusted for age at diagnosis in 5-year age categories, index year, and length of enrollment (5–9, 10–14, 15–19, 20+ years). We also tested the above models among women ages 53–79 because all women in this latter age group were eligible for reminders to schedule screening mammograms.

Results

Component 1: Mammography Diffusion. By the end of 1986, 66.4% of all women ages ≥40 who were enrolled in the health plan had self-reported or radiology-based documentation regarding mammograms and the proportion of women with documentation grew to 89% by the end of 1998. On the basis of this documentation among all women ages 40–49, "ever-use" of mammography increased from 36.1% in 1986 to 66.6% in 1998, whereas "use-within-2-years" increased from 25.9% to 51.2% over the same time period (Fig. 1). Among all women ages ≥50, ever-use went from 45.9% in 1986 to 89.1% in 1998, whereas use-within-2-years increased from 32.9% to 74.7% over the same time period.

Component 2: Rates of Late-Stage Disease. Fig. 2 shows rates of late-stage disease among community and health-plan women ages 40–49 and ≥50. Among community women, the OR of late-stage disease was lower in each succeeding time period for both age groups (ages 40–49: OR, 0.98; 95% CI

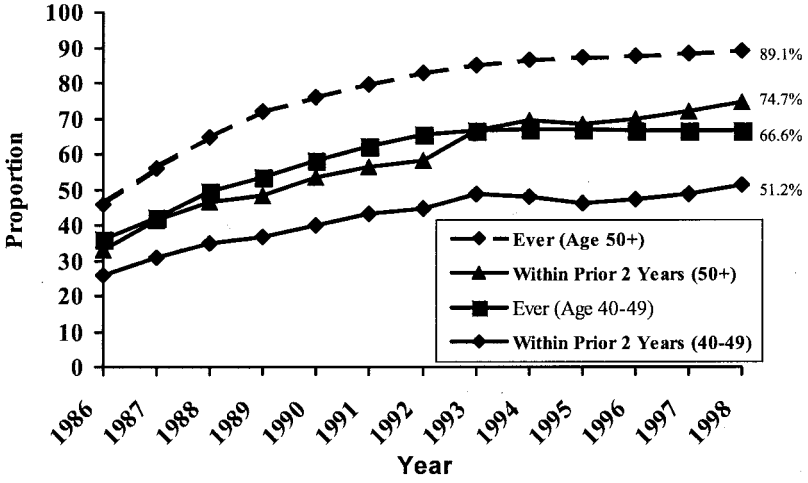

Fig. 1. Mammograph use among health-plan women ages 40–49 and 50+ years.

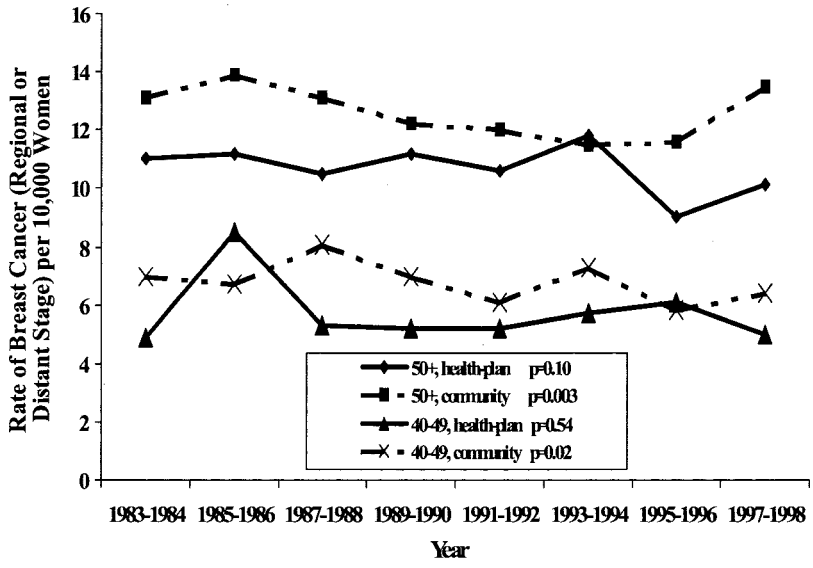

Fig. 2. Rates of late-stage breast cancer among community and health-plan women ages 40–49 and 50+ years.

0.96–0.997; ages 50+: OR, 0.98; 95% CI, 0.97–0.99). Among health-plan women ages ≥50, the odds of late-stage disease was lower in each successive time-period (OR, 0.98; 95% CI, 0.95–1.00), as it was in the surrounding community, although the rate of decline within the health plan was not significant ($P = 0.10$). Among health-plan women, the odds of late-stage disease was reduced in successive time intervals among women ages 40–49 (OR, 0.98; 95% CI, 0.93–1.04), but the reduction was not significant. The peak in the late-stage rate is notable among health-plan women ages 40–49 in 1985–86. When we excluded 1985–1986 and tested the change in late-stage from 1987 onward, the odds of a lower late-stage rate in each successive time period was unchanged (OR, 1.00; 95% CI, 0.93–1.09).

For both age groups, the rates of late-stage disease among health-plan women compared with community women were lower after adjusting for age and year of diagnosis (women ages 40–49: OR, 0.87; 95% CI 0.77–0.99; $P = 0.03$; women ages 50–79: OR, 0.86; 95% CI 0.80–0.92; $P < 0.0001$). A test of the interaction between the main effect of population (health plan *versus* community) and time was not significant for women ages either 40–49 or 50+.

Component 3: Modeling the Odds of Late-stage Disease. Table 2 shows that late-stage cases were similar to the general health-plan population controls. Of note was the slightly younger age of late-stage compared with early-stage cancers (58.4 years *versus* 61.8 years; $P = 0.0005$), and the slightly shorter length of health-plan enrollment.

Table 3 shows the program enrollment and screening exposure of the women identified for the modeling effort (component 3). A higher proportion of late-stage cases (13.1%) was not enrolled in the BCSP compared with women with early-stage cancers (5.4%; $P = 0.001$) and compared with the general health-plan population controls (5.5%; $P = 0.005$). Some women ($n = 34$) enrolled in the BCSP did not have BCSP mammograms but 27% of these late-stage women had at least one mammogram outside the program, and 12% had two or more in the previous 5 years. Among all program-enrolled women, 84% had at least one screening mammogram.

Women with late-stage cancer had a screening pattern that was closer to the general population and reflected less screening than for those with early-stage cancers. A higher proportion of late-stage cases was not screened in the 5 years before diagnosis (26.8%) compared with the early-stage controls (12.4%). The proportion of women with two or more screens was lower among late-stage cases (56.9%) compared with early-stage cancers (65.8%), but similar to the general population (53.4%). The proportion with two or more BCSP screens was lower among late-stage cases (37.9%) compared with early-stage cases (52.6%), but similar to the general health-plan population (42.7%). Ninety-three % (413/445) of the early-stage women, 94% (144/153) of the late-stage women, and 96% (587/614) of the general health-plan population controls received the invitation letters and risk-factor questionnaire recruiting them to the screening program before the date of diagnosis of the cases (data not shown in table).

Late-Stage Cases *versus* Early-Stage Cancer Controls. The odds of late-stage disease was significantly reduced among BCSP enrollees compared with those who were not enrolled and was reduced more among women who had at least one BCSP screen (Table 4). Among the cancer cases, women with two or more BCSP screens were less likely to be late-stage cancers compared with those who had less than two BCSP screens.

Late-Stage Cases *versus* General Health-Plan Population Controls. The OR for late-stage disease was reduced among women enrolled in the BCSP whether or not they had BCSP mammograms. Women with two or more BCSP screens had 20% lower odds of late-stage breast cancer using the general health-plan population control group, although the confidence interval (CI) was wide (OR, 0.80; 95% CI, 0.55–1.17).

Models Restricted to Women Ages 53–79. Results of the separate set of models making the same comparisons as above but restricted to women ages 53–79 are also shown in Table 4. The results did not change our findings, although the protective effect of BCSP enrollment and screening appeared stronger.

Screening Correspondence and Exposure. The BCSP mailed one or more reminders to schedule an examination to 64, 89, and 64%, respectively, of the late-stage, early-stage, and general health-plan population controls who had never had a mammogram but were enrolled in the program (data not in

Table 2 Characteristics of study-component-3 women with and without breast cancer, ages 43–79, and health-plan enrolled in 1995–1998

	Late stage[a] ($n = 153$)		Early stage[a] ($n = 445$)		General GHC[b] population[c] ($n = 614$)	
	n	%	*n*	%	*n*	%
Age at diagnosis						
43–49	37	24.2	69	15.5	150	24.4
50–59	55	35.9	122	27.4	220	35.8
60–69	32	20.9	124	27.9	128	20.8
70–79	29	19.0	130	29.2	116	18.9
P vs. late stage				0.003		1.00
Year of diagnosis/index						
1995	26	17.0	91	20.4	101	16.4
1996	38	24.8	106	23.8	156	25.4
1997	38	24.8	117	26.3	154	25.1
1998	51	33.3	131	29.4	203	33.1
P vs. late stage				0.70		1.00
Length of health-plan enrollment						
5–9 yr	16	10.5	73	16.4	67	10.9
10–14 yr	30	19.6	79	17.8	119	19.4
15–19 yr	45	29.4	108	24.3	176	28.7
20+ yr	62	40.5	185	41.6	252	41.0
P vs. late stage				0.25		1.00
Race						
Caucasian	140	91.5	401	90.1	500	92.1
African American	6	3.9	15	3.4	17	3.1
Asian	4	2.6	21	4.7	21	3.9
Other	3	2.0	8	1.8	5	0.9
Missing					71	
P vs. late stage				0.72		0.60
Family history of breast cancer						
First degree	30	21.9	97	22.7	75	12.9
Second degree	24	17.5	91	21.3	95	16.3
None	83	60.6	239	56.0	412	70.8
Missing	16		18		32	
P vs. late stage				0.56		0.02

[a] Late- and early-stage breast cancers diagnosed in 1995–1998.
[b] GHC, Group Health Cooperative.
[c] General GHC population controls frequency-matched to the late-stage cases on age and length of enrollment.

tables). Health-plan women enrolled in the BCSP were more likely to have had a mammogram [84% (957/1134)] compared with women not enrolled in the BCSP [22% (17/78)]. Women enrolled in the BCSP who did not have BCSP mammograms sometimes received them outside the program, but this occurred less frequently among women with late-stage [26% (9/34)] compared with early-stage [48% (35/73)] breast cancer, and similar to the general population controls [28% (44/158); late-stage *versus* early-stage, $P = 0.04$].

Discussion

Our findings demonstrate the challenge of evaluating the implementation of organized screening. We are evaluating progress toward the desired end point of reduced late-stage disease and evaluating whether any progress can be attributed to screening program exposure. We assume a benefit of mammography but recognize it may be small and delayed, relative to program implementation at the population level (1, 22). As expected, we show rising proportions of ever-screened and recently screened women among the health-plan population and a corresponding decrease in late-stage breast cancer, among women ages 50 and above. We do not see a change in the late-stage rate among women ages 40–49. The rate of late-stage cancer is significantly lower at the health plan for both age groups compared with the surrounding community, and the rates of decline do not differ from each other.

A unique strength of this evaluation is that we test the ecological assumption underlying the association between mammography diffusion and decreasing late-stage disease. We use individual-level data and two separate control groups to estimate the OR for late-stage disease among health-plan women. By doing so we demonstrate that enrolling women in organized screening and getting a BCSP mammogram is associated with a 69% reduction in the risk of late-stage disease among the cancer cases. Even more important is a 61% reduction in the OR for late-stage disease with BCSP enrollment and use of BCSP screens when estimated using the general health-plan population controls. The demonstration of reduced risk compared with disease-free controls provides the least biased estimate of the advantage of breast cancer screening program enrollment.

However, the picture is not so simple, because there is also a reduction in the odds of late-stage disease among women enrolled in the program who never receive a BCSP screening mammogram. These findings are consistent with a conclusion that program enrollment is associated with a reduced risk of late-stage disease, but it may not be because of program mammograms. It may reflect the selection bias that women who enroll in the program are most interested in screening. The data show that women enrolled in the program are getting screened, even if some are getting their mammograms outside the screening program. The data also show a point estimate consistent

Table 3 Breast Cancer Screening Program (BCSP) enrollment and screening exposure for health-plan study-component-3 women (1995–1998) used to evaluate the odds of late-stage disease

	Late stage[a] (n = 153)		Early stage[a] (n = 445)		General GHC[b] population[c] (n = 614)	
	n	%	*n*	%	*n*	%
BCSP enrollment						
No	20	13.1	24	5.4	34	5.5
Yes, no BCSP screening mammogram	34	22.2	73	16.4	158	25.7
Yes, at least one BCSP screening mammogram	99	64.7	348	78.2	422	68.7
P vs. late stage				0.001		0.005
Screening mammogram within 26 mo prior to index date						
No	56	36.6	95	21.3	220	35.8
Yes	97	63.4	350	78.7	394	64.2
P vs. late stage				0.0002		0.86
Total no. of screening mammograms in 5 yr prior to index date						
0	41	26.8	55	12.4	142	23.1
1	25	16.3	97	21.8	144	23.5
2+	87	56.9	293	65.8	328	53.4
P vs. late stage				0.0001		0.15
No. of BCSP screening mammograms in 5 yr prior to index date						
0	54	35.3	97	21.8	192	31.3
1	41	26.8	114	25.6	160	26.1
2+	58	37.9	234	52.6	262	42.7
P vs. late stage				0.001		0.52

[a] Late- and early-stage breast cancer diagnosed in 1995–1998.
[b] GHC, Group Health Cooperative.
[c] General GHC population controls frequency-matched to the late-stage cases on age and length of enrollment.

with reduced risk of late-stage disease among women with two or more BCSP mammograms, although the CIs around the estimate are wide (Table 4). Although the point estimate is consistent with results from randomized trials using mortality end points, it would be a simpler story if we that knew the estimate was significantly reduced (22).

Another ambiguity is that the declining rate of late-stage breast cancer among health-plan women ages ≥50 has not yet attained statistical significance. Although the target population for mammography screening is more than 80,000 women, cancers are diagnosed infrequently, and cancers are diagnosed at a late stage even more infrequently. Consequently, it is difficult to attain numbers of cases that allow tests of significance with adequate precision. However, despite the lack of significance, the odds of late-stage disease is reduced over time, similarly to the reduction of odds in the surrounding community for women ages ≥50, and the cancer rate is lower than in the surrounding community. Both facts suggest that the risk-based approach at the health plan is doing no harm compared with the approach taken in the community, and that both populations are showing expected progress toward a mortality reduction by achieving low rates of late-stage disease.

Although the rate of late-stage disease is falling in the surrounding community, data regarding the screening experience of individuals are not available. Without individual level data regarding screening exposure, we cannot evaluate the amount of mammography the community was using to achieve their significant decline in late-stage disease. However, community level estimates from the Behavioral Risk Factor Surveillance Survey for 1998 show that a higher proportion of community women ages 40–49 were screened within the prior 2 years (68.8%) compared with the health-plan population (51.2%) and a lower proportion (66%) of community women ages ≥50 have had a mammogram within 2 years compared with health-plan women (74.7%; Ref. 33). Self-reported mammography somewhat overestimates the proportion of those who receive a mammogram within a given time frame, but it would appear that the health plan screened a smaller proportion of younger women and reached a higher proportion of women ages ≥50. Although reaching a wider population is one important measure of implementation, it is also important to know how frequently women are screened. Because the community may be more likely than the BCSP to be screening annually, there could be substantial differences in the resources used to achieve the late-stage rates reported here. More should be done to link the data from tumor registries with data on population-based mammography to further evaluate the impact of mammography screening in the general United States population.

The association between BCSP enrollment and the reduced odds of late-stage disease seems like a convincing argument for encouraging program enrollment. Program enrollment leads to reminders that do not depend on a visit to a health center. The higher proportion of general-population women with a mammogram among those enrolled in the BCSP suggests that the reminders lead to mammograms, but it may also reflect the selection bias that women who are interested in mammograms are the ones who enroll in the program.

What may be more important is that this organized screening effort creates the opportunity to identify women at increased risk of late-stage disease, including those who are not enrolled in the program, and those who are enrolled but not getting mammograms. As many as 10% of the women ages ≥50 in the entire population had never had a mammogram and 25% had not had one within the previous 2 years. The process of enrollment in the program affords an opportunity to identify women who do not complete the process and, therefore, are at increased risk of late-stage disease as shown in this analysis. Women who do not enroll in the screening program could be approached to solicit and address their concerns.

But some women in the program are also not getting mammograms. Our results show that women without mammograms had documentation of mailed recommendations remind-

Table 4 Model results for the odds of late-stage disease, 1995–1998[a]

	Late stage *vs.* early stage			Late stage *vs.* general GHC pop.[c]		
	OR[b]	95% CI	Overall *P*	OR	95% CI	Overall *P*
Ages 43–79						
BCSP enrollment						
No	1.00			1.00		
Yes, no BCSP screening mammogram	0.45	0.21–0.95		0.36	0.18–0.71	
Yes, at least one BCSP screening mammogram	0.31	0.16–0.61	0.002	0.39	0.21–0.71	0.006
Screening mammograms within 26 mo prior to index date						
No	1.00			1.00		
Yes	0.47	0.31–0.71	0.0004	0.96	0.66–1.41	0.85
Total no. of screening mammograms in 5 yr prior to index date						
0–1	1.00			1.00		
2+	0.72	0.49–1.08	0.11	1.17	0.80–1.70	0.42
No. of BCSP screening mammograms in 5 yr prior to index date						
0–1	1.00			1.00		
2+	0.57	0.38–0.85	0.006	0.80	0.55–1.17	0.25
Ages 53–79						
BCSP enrollment						
No	1.00			1.00		
Yes, no BCSP screening mammogram	0.34	0.13–0.87		0.28	0.11–0.68	
Yes, at least one BCSP screening mammogram	0.25	0.11–0.55	0.003	0.28	0.13–0.60	0.004
Screening mammogram within 26 mo prior to index date						
No	1.00			1.00		
Yes	0.48	0.28–0.81	0.006	1.00	0.62–1.63	0.99
Total no. of screening mammograms in 5 yr prior to index date						
0–1	1.00			1.00		
2+	0.61	0.37–1.01	0.054	0.99	0.62–1.58	0.96
No. of BCSP screening mammograms in 5 yr prior to index date						
0–1	1.00			1.00		
2+	0.58	0.36–0.92	0.02	0.76	0.49–1.20	0.24

[a] All models include age group (5-year intervals), length of enrollment (5–9, 10–14, 15–19, 20+ yrs), and index year (1995,. . ., 1998) as covariates.
[b] OR, odds ratio; CI, confidence interval; GHC pop., Group Health Cooperative population; BCSP, Breast Cancer Screening Program.
[c] Frequency-matched on length of enrollment and age.

ing them to schedule screening mammograms. However, reminders alone may not be adequate because 12% (107/903) of health-plan women ages ≥50 who were enrolled in BCSP had not had a mammogram in the last 5 years. Of these women, 73% (78/107) had been sent two or more reminders. Randomized trial results in this population suggest that telephone contact is a more effective approach to women who do not schedule appointments after mailed reminders (34). However, these telephone reminders require personnel and an investment that may not be justified (35). It seems prudent to encourage further program enrollment so that reminders are sent. Whether to invest in further recruitment efforts raises the question of who is responsible for achieving screening, women who receive reminders or the health plan that sends them?

Our finding of reductions in late-stage disease with rising mammography use are consistent with findings from the United Kingdom and Sweden who have organized programs and also use screening intervals of 2 or more years for women ages ≥50 (1, 36). These programs report reductions in late-stage disease (37) and reductions in mortality (1); therefore, it is reasonable to expect mortality reduction in our population as well, given adequate time. Aside from mortality, however, there is evidence that surgical morbidity is reduced when late-stage is avoided (38). Our program results in the United States should provide reassurance that we can see progress toward a benefit when screening is implemented and reaches the population.

This study has several strengths. To our knowledge, it is the first report of population-based mammography screening and outcomes to evaluate the impact of screening during the active period of mammography diffusion in the United States. As such, it provides comprehensive population and individual-based information on mammography use and late-stage breast cancer. The recorded findings reflect the experience of an entire population and are not subject to sampling error. Furthermore, all of the cancers have been staged using SEER methodology and, as such, represent a uniform standard in breast cancer staging. We also have comprehensive mammography exposure data including self-report and actual use in our facilities. Together, these factors make this a unique opportunity to look at the impact of screening at the population level (components 1 and 2) and test whether what we see for the population makes sense at the individual level (component 3). Mammography does diffuse during the observation period, and the rate of late stage-disease drops. Component 3 suggests that the drop in late-stage disease would be explained by mammography exposure. Women enrolled in the program are more likely to have mammograms, although not necessarily in the BCSP.

Another strength is access to an entire population of cancers, careful selection of the study populations for each component, and the use of two controls when we estimated the odds of late-stage disease for individuals (component 3). We excluded women under age 43 from component 3 to allow adequate time to have two previous mammograms before the diagnosis of the cancer, but, otherwise, all women enrollees are included. We chose 1995 as the first year for inclusion of individual cases in component 3 because it is the first year that repeated screening occurred at 2-year intervals (27–30). We frequency-matched late-stage breast cancer cases and the gen-

eral health-plan population on age and length of health-plan enrollment because both factors could influence the likelihood of getting mammograms.

The different controls provide different insights into the program and mammography screening effect but each has its limitation. The limitation of using the general population as a comparison group is that the risk of breast cancer is higher among women who get screened compared with those who do not, and, therefore, the incidence of breast cancer will be expected to be higher among screened women (39). This higher breast cancer incidence (of all stages) would mask some of the effect of screening on reducing the odds of late-stage disease. Alternatively, use of the early-stage breast cancer cases as the comparison group resolves this problem, because all of those women have cancer, but the ORs for estimating the association with screening exposure could be biased toward showing a stronger than true effect if mammography leads to over-diagnosis of early-stage invasive breast cancer instead of, or as well as, a decrease in late-stage diagnosis.

Some may say that a limitation is that these results come from a managed care plan, but it is likely that similar levels of implementation would achieve similar outcomes in other populations. There is no reason to believe that breast cancer operates differently among these managed care enrollees. However, the rate of late-stage disease in the surrounding community may be higher because some members of the community do not have access to care (40). The question these findings raise is whether an organized screening approach has advantages. One answer is yes, because it identifies women at increased risk of poor outcomes because they either do not enroll in the program, or they do not get mammograms when reminded. The question that needs to be raised is whether pursuing these women would further reduce late-stage disease. Organized screening offers that opportunity.

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