Mammography Diffusion and Trends in Late-Stage Breast Cancer: Evaluating Outcomes in a Population

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Introduction

Despite the evidence for the efficacy of mammographic screening among women 50 years of age and older, it was underutilized in the early 1980s, and mortality remained nearly constant through 1990 (1-5). Failure to achieve expected healthcare outcomes led to the initiation of efforts to establish clinical guidelines and promote the diffusion of mammography (6-14). The National Cancer Institute also funded research sites to measure screening processes in populations covered by cancer registries so that outcomes could be more easily measured (15). The study reported here originates from one of those sites and evaluates the effect of implementing screening guidelines through a formalized screening program offered to enrollees of a staff model managed care plan (12).

Breast cancer screening offers an opportunity to practice prevention but carries a large associated cost (16, 17). Cross-sectional surveys of women suggest they underuse this technology because it is not recommended to them by their physician (14, 18). However, surveys also suggest that mammography occurs more commonly among younger women where controversy exists about its benefits (19, 20). A major challenge in breast cancer control is to insure that recommendations occur regularly and reach the right women, especially those who have not been screened (9).

GHC confronted the challenge of breast cancer screening by using a criteria-based guideline development and program implementation process (21). This process included a structured literature review regarding breast cancer epidemiology, screening efficacy, and the cost-effectiveness of alternative screening strategies (12). The process also involved affected medical providers to encourage subsequent implementation of the developed guideline (12, 21).

GHC began the guideline development process in 1981 and established the BCSP in 1986 (12, 22). The key features of the BCSP between 1986 and 1992 were: (a) the use of risk factor information to vary the mammographic screening interval; (b) direct correspondence with women to remind them when they were due for comprehensive screening; (c) regional centers where women received screening and coordinated follow-up; (d) reliance on primary care for screening breast physical examination and symptomatic cancer detection between screening center visits; and (e) mainframe computer management of the risk factor information, reminder correspondence, and tracking of women’s screening history.

During this evaluation, recommendations in the surrounding community included screening mammography every 1–2 years for women 40 through 49 years of age, and annually thereafter (American Cancer Society), or screening every 1–2...
years among women 50 years of age and older (United States Preventive Services Task Force) (23–25). GHC’s program recommended screening every 1–3 years for all women ≥50 but of women ages 40–49, only the 52% who had commonly recognized breast cancer risk factors (13). Available evidence suggests that few community physicians used automated reminder systems during the study period, and no one had a comparably organized program (26).

To evaluate the progress of screening, we measured mammography diffusion and the incidence rate of late-stage breast cancer. We chose the latter measure as an intermediate outcome of mammography diffusion because more time must elapse before mortality reductions will change significantly in the community. Before mortality reductions will change significantly in the community, 48% were asked to begin at 50 years of age.

Materials and Methods
Setting. During the study period, GHC included more than 398,000 members of the consumer-controlled staff model health maintenance organization who sought care at two hospitals and 28 primary care facilities. These enrollees lived predominantly in four counties (King, Pierce, Snohomish, and Thurston) of western Washington state. GHC enrollees were identified through the CSS, a population-based tumor registry that captures cancer diagnoses among residents of 13 western Washington counties, including the four counties served by GHC. The CSS participates in the National Cancer Institute’s Surveillance, Epidemiology and End Results Registry (SEER) program (31). Previous assessment of case ascertainment has indicated that nearly 100% of all breast cancer cases diagnosed among GHC enrollees are captured by the registry (32).

Data from GHC enrollment files, the radiology systems, the BCSP data system, and the CSS were linked for use as a single analytic data set. GHC women ages 40 years of age and older, regardless of enrollment in the BCSP program.

Evaluation Overview. We evaluated mammography use and late-stage cancer rates through 1992 for the entire GHC population of women 40 years of age and older. Evaluation definitions and denominators are summarized in Table 1 and are described more fully below. The proportion of women who ever-used mammography was measured each year between 1986 through 1992. The trend in the change of ever-use of mammography (diffusion) was compared within age groups as described below. For women enrolled as of 1992, we evaluated mammography experience to see whether approximately one-third of the mammography had occurred within 1 year, from 1–2 years, or greater than 3 years before. Such a distribution would reflect the program guideline of every 3-year screening for the majority of women. We wanted to know whether the cancer rate was consistent with a program effect on mammography use or some higher rate of use achieved outside the program. The change in late-stage disease incidence between time periods was compared to the surrounding community during successive time periods from before the program began (1983/84) through the latest available time period (1991/92). We made this comparison to evaluate whether the program resulted in a change in rates that exceeded or matched the change in the community. To further evaluate the program implementation, we identified whether GHC women ages ≥40 at the end of the evaluation period had been mailed the risk factor questionnaire and given an opportunity to join the BCSP.

Reported measures are based upon denominators that include all women in the age group enrolled within GHC or living in the surrounding community during the time period. The change in rates reflect differences between the experience of populations at separate time periods rather than the experience of a fixed cohort. For cancer rates, the measures are based upon the entire population of GHC and surrounding county women in the respective age group. For mammography, the rates reflect GHC use recorded on automated sources and self-reported use prior to GHC enrollment.

We established GHC denominators from the enrollment files based on the number of GHC enrollees at the mid-point of each evaluation year. County denominators were estimated by CSS personnel using United States Bureau of Census and

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GHC. After exclusions, there were 1,822 GHC and 11,962 intervals subsequent to full implementation (1986-1992). Odds 673, non-GHC);

Statistical Analysis. analysis and among women 40 years of age and older. non-GHC breast cancer cases diagnosed during the study period (1983-1984), during implementation (1985-1986), and 2-year

For mammography use, we used annual time periods (1986-1992) for mammography use among women ages 40-49 versus ≥50 by testing the significance of the interaction between the main effect of age and year in the logistic model. Similarly, in the late-stage incidence model, we compared the GHC versus non-GHC trend by introducing an interaction term between the main effect of group (GHC and non-GHC) and time period.

Results

Mammography Use. The program reached and enrolled a high proportion of GHC women 40 years of age and older. In 1992, there were 31,401 female GHC enrollees 40-49 years of age, and 46,894 female enrollees 50 years of age and older. Ninety-eight % of these female enrollees had been mailed a BCSP questionnaire. BCSP enrollment among GHC women in the four-county area was 83.7% by 1992. Enrollment was lower among women 40-49 years of age compared to women 50 years of age and older (77.6% versus 87.75%).

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Of the 18,208 women mailed a recommendation to schedule mammography in 1992, 64.6% did so within a year (participated). Previous mammography experience was a strong predictor of mammography use among invited women. Women who had never had a mammogram were much less likely to participate (41%) than women who had 1 or ≥2 prior studies (participation of 70 and 84%, respectively (P < 0.05).

Fig. 1 demonstrates that within each age category, the mammography use among GHC women increased significantly between 1986 and 1992 (P < 0.001, for both trends). The rate of rise in mammography use was more rapid among women 40-49 years of age compared to women ages ≥50 (P < 0.001).

More importantly, the proportion who ever had a mammogram was consistently lower throughout the interval. By 1992, 67.4% of women ages 40-49 and 84.4% of women ages ≥50 had at least one mammogram. The program did not achieve the expected 90% ever-use among older women. Not shown in Fig. 1 are analyses of mammography use among age subgroups. By 1992, the proportion of GHC women who ever had a mammogram was the same (82%) among women 50 through 64 years of age compared to women 65 years of age and older.

We also examined whether women continuously enrolled since 1986 were more likely to have had mammograms, because they had several opportunities to receive program recommendations. Among GHC women continuously enrolled since 1986, the proportion who ever had a mammogram by
1992 was higher than for women enrolled for shorter time periods (72% of continuously enrolled women ages 40–49 years of age versus 67.4% of shorter term enrollees; \( P < 0.05 \), 83% of continuously enrolled women ages ≥50 versus 82.8% of shorter term enrollees \( P < 0.05 \)). Women ages 40–49 were less likely to stay enrolled in GHC throughout the 1986–1992 time period (53% versus 75%).

Table 2 demonstrates the number of years since last-mammogram among GHC women 40 years of age and older enrolled in 1992. The table reflects mammography experience at the beginning of the year. The proportion of women who never had a mammogram is higher than for Fig. 1, because the latter reflects mammography use by the end of 1992, rather than the beginning. The proportion of women with mammograms within 1 year, between 1 and 2 years, and greater than 2 years before 1992, reflects the screening guidelines. In accordance with the guideline, each year the program recommended mammography to about 38% of women 50 years of age and older. Because 65% of women obtained the screening mammogram when it was recommended, it would be expected that about 25% (0.65 × 0.38) of the population had screening mammograms in each year of a 3-year cycle (i.e., mammograms are recommended at least every 3 years to all women 50 years of age and older). Among women 40–49 years of age, 19% were recommended for mammography each year. Close to 20% received mammograms. After the expected proportion is adjusted for participation (0.65 × 0.19 = 0.12%), the actual proportion reflects some 7% of the women in this age group receiving mammograms outside the program.

Reduction in Late-Stage Disease Incidence. Among the 1,822 GHC and 11,962 non-GHC women 40 years of age and older with breast cancer diagnosed from 1983 through 1992, 380 and 2,780, respectively, had tumors ≥3 cm at the time of diagnosis. Table 3 shows the annual age-adjusted incidence (per 10,000 women) of tumors ≥3 cm in diameter among GHC and non-GHC women for 1983 through 1992. A significant reduction in late-stage disease incidence did not occur among either GHC or non-GHC women 40–49 years of age, although the rate dropped in both populations. In contrast, there was a reduction in the incidence of large tumors among GHC women 50 years of age and older \( (P < 0.001) \). Among non-GHC women, the incidence of large tumors also dropped significantly \( (P < 0.001) \).

By 1992, the proportion of invasive breast cancers that could be classified as TNM stages I and II among women 40–49 years of age was 83% (44 of 53) for GHC women and 83% (200 of 242) for non-GHC women. Among women 50 years of age and older, the proportion of breast cancer cases classified as TNM stages I and II was 83% (163 of 196) for GHC women and 84% (879 of 1047) for non-GHC women.

Discussion
There is a growing call for organized approaches to healthcare in populations, the promotion of prevention, and the measurement of results (6, 7, 36). Breast cancer screening is a good example of the challenge of such an approach. Wider use of mammography should benefit women by reducing mortality, but it results in increased health care costs (5, 16, 17, 37). The goal is to optimize outcomes, within realistic cost constraints. This requires establishing which groups will benefit at what screening frequency, and then encouraging regular mammography among them (5, 7, 17, 19, 38).

In an effort to optimize breast cancer outcomes within cost constraints, GHC established a policy of recommending screening to high-risk women ages 40–49 years and risk-dependent screening intervals of 1–3 years among women ages ≥50 years (27). This policy was linked to a program implementation plan that included regional screening centers and mailed reminders to women when they were due for screening. The analyses presented here were intended to evaluate GHC’s program implementation and demonstrate mammography use consistent with its guidelines. Fewer GHC women ages 40–49 had mammograms than among women ages 50 and above. By 1992, mammography experience was distributed evenly over the previous 3 years among women ages 50 and above, as would be expected from the recommendations. About 25% of women 50 years of age and older had mammograms in each of three time periods prior to 1992 (<1 year, 1–<2 years, and ≥2 years). Overall, 84% of GHC women 50 years of age and older had ever had a mammogram by 1992. This meets one national Healthy People 2000 goal for this age group 8 years ahead of schedule (8), but it does not achieve the 90% ever-use expected at the evaluation’s onset.

Our evaluation is limited because of the absence of equivalent data about mammography use in the surrounding community. The Behavioral Risk Factor telephone survey conducted by the Center for Health Statistics, Washington State Department of Health, provides some information about secular trends in the surrounding community, although survey data...
of stages I and II cancers in all age groups and populations was diffusion without a system of automated reminders. There does not appear to be an adverse effect of selective younger women. The selective approach to screening used at advocated screening every 1-2 years for all women ages 40-49 recommendations of the American Cancer Society, which ad-
dulations with similar mammography use. However, the effect of significant among women ages 50 years of age and older but not among women ages 50 and above. Ever-use of mammography increased from 43.5% (95% CI, 63.7–93.1) in 1992 among women ages 40–49 in the four-county area surrounding GHC. The high rate of ever-use among women ages 40–49 may reflect implementation in accord with the more aggressive recommendations of the American Cancer Society, which ad-
ducation screening every 1–2 years for all women ages 40–49 (23). Among women ages 50 and above, the ever-use rate increased from 52.6% (95% CI, 38.0–67.2) in 1987 to 84.5% (95% CI, 73.0–96.0) in 1992 (as prepared by the Washington State Department of Health, Center for Health Statistics). These results suggest that the surrounding community had also achieved the prevalence of mammography use cited in the Healthy People 2000 goal.

With increased use of mammography among GHC women, we demonstrate a falling rate of breast cancers ≥3 cm in diameter at diagnosis. This drop achieved statistical significance among women 50 years of age and older but not among younger women. The selective approach to screening used at GHC achieved the same or somewhat higher rate of reduction in late-stage disease incidence as the surrounding community. There does not appear to be an adverse effect of selective screening, but the rate of decline in late-stage disease among GHC women was no better than the surrounding community, suggesting that secular trends have achieved mammography diffusion without a system of automated reminders.

As expected, the decline in late-stage disease is associated with high rates of early-stage disease. By 1992, the proportion of stages I and II cancers in all age groups and populations was greater than 80%. It seems very likely that similar findings could be demonstrated in other populations with comparable levels of mammography diffusion. We feel that the conclusions regarding the late-stage disease decline at GHC, and in the surrounding community, are credibly generalized to other populations with similar mammography use. However, the effect of mammography diffusion on late-stage disease needs evaluation in more ethnically diverse populations.

The decrease in late-stage incidence among GHC women ages ≥50 was achieved using broader intervals than those recommended by other guidelines. Optimal intervals for screening women 50 years of age and older remain uncertain and vary between 1 and 3 years (3, 4, 9). Despite the fact that a large proportion of GHC women were screened every 2–3 years, the magnitude of the decrease in incidence at GHC was larger (35%) than in the surrounding community (25%). The addition of annual mammography compared to mammography every 3 years is currently being evaluated in a randomized trial in Europe (38). Our results demonstrate that regular mammography achieves a reduction in late-stage disease, even when regular is not synonymous with annual. However, breast self-examination was encouraged as part of this program, we cannot say that the effect of the program on late-stage disease is due to mammography alone.

The late-stage disease rate findings among GHC and surrounding community women 40–49 years of age are consistent with the current debate about the benefits of screening for this age group (9, 41, 42). The percentage of reduction in late-stage disease was comparable among non-GHC women ages 40–49 (25%) compared to the decline in the rate among non-GHC women ages ≥50 (26%). The late-stage disease rate is dropping, but not significantly. Either there is no benefit, a longer period of observation is necessary to show the benefit, ineffective intervals were used for screening among women ages 40–49, or a larger population is needed to show a significant effect (43, 44). During the recent consensus conference review of the literature from randomized trials, they drew the same conclusions about the effect of mammography on mortality among women ages 40–49 (20). Like these trials, this observational study is finding outcomes in this age group that may take a long period of time to evolve.

Like others, we have implemented a compromise (selective screening) policy for women ages 40–49, which is not completely supported by the literature from randomized trials. The data presented here support the conclusion that it is not having an adverse effect compared to the community. The evidence for a screening benefit for all women has not been forthcoming, therefore, the recommendation has not been extended to all women in this age group (20). However, women in this age group can be referred by their physician, and the total use of mammography reflects these referrals.

The optimal measure of screening effectiveness is a decline in mortality, but a decrease in the incidence of late-stage disease is a necessary precursor (45). Day and others (27, 29, 45, 46), therefore, advocate evaluating late-stage disease as an intermediate measure of program success, because its use avoids the lead-time bias associated with survival analyses and minimizes length-time bias associated with the evaluation of screen-detected breast cases. We defined late-stage disease as tumors ≥3 cm in diameter because that was a consistently collected measurement. This appears to be a reasonable intermediate outcome for this evaluation of the effect of mammography because reductions mirror the findings in randomized
Fig 2. GHC versus non-GHC trends in the incidence of breast cancers with tumor size ≥3 cm at diagnosis. a, \( P = 0.27 \) for GHC versus four-county trend. b, \( P = 0.26 \) for GHC versus four-county trend.

trials: significant reductions among women ages ≥50, and downward trends, although not significant, among women ages 40–49. During the evaluation period, national staging practices and terminology changed. Rates of axillary node dissection also differed between GHC and the surrounding community. Use of summary staging like “distant” disease or TNM stage IV, therefore, presented potentially biased comparisons or limited comparisons over time.

As with any study, there are limitations that temper our conclusions. The lack of equivalent mammography use data for the community limits the interpretations of the comparable reduction in late-stage disease. It is intriguing to consider whether GHC’s program achieved similar results with less frequent mammography use, but we cannot say because we do not know the frequency of mammography in the community. We also cannot be certain whether our operationalization of late-stage disease is a valid intermediate measure along the path to a mortality reduction. With the implementation of TNM staging, we may now have a better measure, but it will need validation.

Our results reflect implementation within a health maintenance organization population that was slightly more educated and less likely to be in the highest and lowest income brackets than women in the surrounding community (30). Generalizing to non-health maintenance organization populations raises some questions. However, because education and higher economic status have been shown to be associated with increased use of mammography, it is at least safe to say that getting mammography use rates above 85% may be difficult for any population.

This limitation in screening mammography implementation has implications for everyone concerned with breast cancer control. Cross-sectional studies suggest that women without mammograms have not had a recommendation, but this is not the case at GHC (14, 47). The program insures that 87% of women 40–49 years of age with risk factors either receive a mammogram or a mailed recommendation. Among women 50 years of age and older, nearly all (91%) received either a mammogram or recommendation in the three years before 1992. Given the absence of cost barriers and higher educational level of the population in this managed care setting, it is surprising that mammography usage subsequent to a clear recommendation is only 65%. This is the same rate reported in the Health Insurance Plan of New York randomized trial of the 1960s (48). Participation in the first screening examination remains especially problematic, even for the GHC program. Results from two randomized trials of interventions to increase screening participation suggest that getting women who have never had mammograms into a screening program, in this era of aggressive screening, requires more than reminders and physician involvement (49, 50).

Conclusion. The BCSP at GHC developed from a participatory policy development process (21). That process continues, and in 1993, a new set of guidelines were implemented. These guidelines were based on more recent evidence from randomized trials and resulted in the shortening of mammography intervals to no more than 2 years.

As new information appears, the guidelines will change again. Part of the information needed is measurable outcomes in the population being served. This evaluation shows that increased mammography use can be associated with measurable cancer outcomes if adequate monitoring systems are in place. Comparisons will be improved by having similar systems for entire regions and diverse populations throughout the country. This work is now beginning (15).

GHC breast cancer screening implementation between 1986 and 1992, emphasized the use of an organized program of automated reminders to concentrate mammography among those at greatest risk. Although the guidelines themselves varied from others that have been developed, the results presented here show similar outcomes in GHC and the surrounding community. The results also show that reductions in late-stage disease occurred when regular mammography was not synonymous with annual.

Finally, we have shown that implementing a system of automated reminders may be an insufficient approach to maximizing mammography use in a population. More must be done to encourage participation once a reminder is given (47, 49, 50).

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