Effect of a community health center intervention on breast cancer screening among Hispanic American women

Jane G. Zapka

University of Massachusetts Medical School

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Effect of a Community Health Center Intervention on Breast Cancer Screening among Hispanic American Women

Jane G. Zapka, Donald R. Harris, David Hosmer, Mary E. Costanza, Edith Mas, and Robin Barth

Objective. A multiple component intervention in a community health center is presented, and its effect on breast cancer screening participation by Hispanic American women between the ages of 45 and 75 years is discussed.

Data Sources/Study Setting. In 1990, data were collected through a retrospective audit (at least as far back as 1987) of community health center medical records, as well as from a client referral log. The health center, located in a small Massachusetts city, primarily serves clients of Latino heritage.

Study Design. The study used a nonexperimental pretest-posttest intervention design to document clients' screening activities. To control for uneven length of enrollment, aging of the population, and sporadic utilization, the unit of analysis chosen for the principle study variables was an "eligible year."

Data Collection. Variables of interest included screening (clinical breast exam and mammography), periodicity of screening, and compliance with referrals.

Principal Findings. Postintervention, considerably greater screening mammography occurred among all age groups, more women had at least one screening mammogram during the period, more clinical breast exams included a mammogram referral, and the compliance rate improved. The rate of clinical breast exam did not significantly improve, showing a downward trend.

Keywords. Mammography screening among Hispanic American women, breast cancer screening, health center intervention

While low utilization of screening measures in general, and breast cancer screening in particular, have been the subject of considerable investigation (NCI Breast Cancer Screening Consortium 1990), the use of preventive services by the poor and minorities is considered particularly critical (Dutton 1978). Indeed, the special access problems of Hispanic
Americans relative to whites and African Americans have been acknowledged (Caplan, Wells, and Haynes 1992; Elder, Castro, deMoor et al. 1991; Anderson, Giachello, and Aday 1986; Zambrana 1987). Although Hispanic American women are not at greater risk for breast cancer development due to ethnicity per se, evidence indicates that they are at an increased risk similar to that of white, non-Latina women for late-stage breast cancer diagnosis (Richardson, Marks, Solis, et al. 1987).

This study evaluates the effect of a community health center–based intervention designed to increase breast cancer screening among Hispanic American women.

STUDY DESIGN OVERVIEW

The study used a nonexperimental pretest-posttest design to document the screening activity of clients before and after the introduction of intervention activities in early 1988. Since grant writing and planning activities had begun at the health center in early 1987, as a conservative measure of effectiveness the postintervention period was considered to have begun in 1987. Data were collected through a medical record audit, as well as a patient referral log. The evaluation plan was designed to determine whether the primary intervention objective of increasing the proportion of women who receive clinical breast exam (CBE) and screening mammography was met. Additionally, several secondary evaluative research questions were addressed:

- Were there differential intervention effects according to age?
- Were there significant increases in the proportion of women who had at least one CBE during the postintervention period?

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Address correspondence and requests for reprints to Jane Zapka, Sc.D., Professor, Preventive and Behavioral Medicine, University of Massachusetts Medical Center, 55 Lake Avenue North, Worcester, MA 01655. Donald R. Harris, Ph.D. is Research Associate and David Hosmer, Ph.D. is Professor of Statistics in the School of Public Health at Amherst. Mary E. Costanza, M.D. is Professor, Department of Medicine, University of Massachusetts, Worcester; Edith Mas, R.N., M.S. is Executive Director of the Greater Lawrence Community Health Center, Lawrence, MA; and Robin Barth, M.S. is Administrator of the Martha Eliot Health Center, Jamaica Plain, MA. This article, submitted to Health Services Research on December 13, 1991, was revised and accepted for publication on September 21, 1992.
• Were there significant increases in the proportion of women who had at least one mammogram during the postintervention period?

• Among women who had a clinical breast exam, did the rate of mammography referral as part of the exam increase during the postintervention period?

• Among women who received a mammogram referral, did compliance with the referral increase during the postintervention period?

SETTING AND INTERVENTIONS

A demonstration project was undertaken in a community health center located in eastern Massachusetts. The center, which is the major source of bilingual health care in the community, services a population that is predominantly Hispanic and low income. Clients use the health center for comprehensive primary care, and although most visits are initiated for acute care, the staff encourages and incorporates preventive services. The center is staffed primarily by white physicians and nurse practitioners of non-Hispanic American background, most of whom do not speak Spanish. The health center trains Hispanic American women to be nursing assistants; their responsibilities include taking patients’ vital signs, interpreting during the doctor-patient encounter when needed, and providing patient education.

Three intervention components were introduced within the health center in early 1988: client-directed educational strategies, staff training strategies, and management systems intervention strategies (Zapka, Chasen, Barth, et al. 1992). Client education included media and teaching aids such as posters and pamphlets, individual patient counseling, and information programs for community groups. The training and communications component for staff included physician participation in grand rounds (Costanza, Greene, Zapka, et al. 1988), in-service training in enhanced in-reach education, and expanded roles for Hispanic American clinic aides. Management systems strategies included redesign of the referral log to monitor referrals and, during the final year of the project, a mammography appointment reminder mailed to clients to enhance compliance. Additionally, clinic aides routinely “stamped” clinic records when they encouraged screening, and this served as a reminder cue for physicians.
METHODS

MEDICAL RECORD AUDIT

During the summer of 1990, information to assess the effectiveness of interventions was gathered through review of medical records of a sample of the health center's current clients between the ages of 45 and 75. In 1988, a baseline interview survey had been conducted to assist in planning the intervention (Zapka, Stoddard, Barth, et al. 1989). The sampling for the medical record audit was designed to include women surveyed in 1988 who were still clients in 1990 (N = 127), along with a similar number (N = 141) of women not previously surveyed. This was done to enable a possible future validation study to be conducted. The sample of women not previously surveyed was randomly selected from an age-stratified 1990 users list of the center's clients who were clients at least since 1987. Given that the age distribution of the center's clients was skewed toward younger women, a stratified sampling scheme was employed. The first stratum was composed of women aged 47-52 (women 45-50 at the start of the intervention), and the second, women 53 through 67 years of age (women 51-65 at the start); the last stratum included those aged 68 and above (women 66 and older at the start). Due to the paucity of clients 68 years of age and older, the available medical records of all women in this age range were reviewed.

MEASUREMENTS AND ANALYSES

Data were collected by trained auditors using a standardized pre-tested instrument. Information documented included age, date of first clinic appointment, number of visits per year, and insurance information. All clinic notes were reviewed to document dates of complete physical exams, clinical breast exams, mammogram referrals, radiology reports, and follow-up visits.

To evaluate whether or not participation in regular screening had improved, the unit of analysis chosen was an "eligible year." This was defined for each woman as a calendar year in which at least one clinic visit occurred, and therefore the opportunity for some form of screening, to be recommended and/or carried out. For example, a woman with at least one clinic visit in 1981, 1982, 1985, 1987, and 1988 contributed a total of five eligible years. In this example, extended periods in which no clinic visits had taken place (1983, 1984, 1986) were omitted. The algorithm for deriving eligible years also considered the aging of the women and the timing of the intervention. In the example above, the woman could have moved from one age category to another over the course of
these years, thus contributing eligible years to both the pre- and postintervention period.

This approach is similar to the person-years concept used in occupational cohort studies (Breslow and Day 1987). Use of eligible years as the unit of analysis adjusts for the uneven length of enrollment for women during the pretest and posttest periods, and it compensates for women who were not clinic users for contiguous 12-month intervals. For example, some women in this study population return to their country of heritage for extended periods.

Evaluation of other outcome variables was based on other units of analysis. To evaluate changes in the proportion of women who had at least one screening mammogram or one clinical breast exam pre- and postintervention, each woman served as the unit of analysis. This was investigated as a conservative, albeit imprecise, measure of screening participation; that is, if guidelines for regular screening were not being met, we investigated whether or not women were getting minimal exposure to screening services. The statistical approach employed in this case was a matched-pairs analysis relating response in the preperiod to response in the postperiod. Relative risk was estimated as the ratio of post-to pre-usage of screening services. Confidence intervals were based on the log of the relative risk whose variance was calculated using methods for logs of correlated proportions. To evaluate whether or not changes took place in the proportion of clinical breast exams that included a mammogram referral, the clinical breast exam served as the unit of analysis. Last, to evaluate compliance with mammography referral, documented mammogram referrals were employed as the unit of analysis.

For purposes of this investigation, the total number of clinical breast exams and mammograms for each woman were separated into two categories depending on whether the procedure was carried out for screening purposes or as a follow-up for suspicious findings on a previous examination. For example, a clinical breast exam occurring within six months of a previous CBE was considered a follow-up to the prior procedure while one taking place more than six months later was categorized as a screening exam. Similarly, the total number of mammograms was divided into those carried out primarily for breast cancer screening and those conducted as a follow-up to a previous suspect or problematic mammogram. A mammogram occurring less than ten months after another mammogram was considered to be a follow-up procedure, and all others were considered to be screening exams. Failure to consider these alternative scenarios would have led to overestimation of the rates of utilization of these techniques for screening purposes.

Relative-risk estimates were used to compare changes in the utiliza-
tion of specific breast cancer screening technologies within defined age groups before and after intervention. The estimated variances of the log of the relative risk were used to obtain a confidence interval for the log relative risk whose end points were exponentiated to obtain a confidence interval for the relative risk. The relative risk expresses the likelihood that the event of interest will occur in the postintervention period relative to its likelihood of occurring in the preintervention period. For example, a relative risk of 3.0 comparing the rate of utilization of screening mammography in the post- relative to the preintervention period indicates that women were three times more likely to have a screening mammogram performed following the intervention. A relative risk less than 1.0 indicates that the outcome of interest was less likely to occur following the intervention. This relative risk serves as an estimate of the effectiveness of the intervention with respect to the outcomes of interest. The precision of the estimate of effect may be assessed on the basis of the width of the confidence interval estimate. In addition, a confidence interval that does not include the value 1.0 indicates that the post- to preintervention ratio is significant at the 5 percent level. A similar interpretation may be used for the odds ratios used in the matched pre-post analysis.

RESULTS

The study sample consisted of 268 women. The majority were covered by entitlements (58 percent Medicaid, 28.4 percent Medicare at time of audit). The mean number of years since the first clinic visit was 5.6, and the mean number of annual clinic visits was 5.0. The sample sizes for the three age strata were 85 women ages 50 or younger at the beginning of the intervention period, 123 women between 51 and 65, and 60 women at 65 or older. Table 1 presents the eligible-year profile of the study group by each age group between the pre- and postintervention periods. Among women who contributed eligible years, the average was about 1.7 eligible years preintervention and about 2.2 eligible years postintervention. Use of total eligible years per period controls for the fact that the postintervention time period and preintervention period were of different lengths.

Table 2 presents pre- and postintervention data by age groups for both screening procedures. In all age strata, the rates of CBEs per 100 eligible years decreased from pre- to postintervention; this trend was not statistically significant in the oldest group. The average number of CBEs was about 1.2 per eligible woman pre- and postintervention.

With respect to screening mammography, the average number of
Table 1: Eligible-Year Information by Age Group and Study Period

<table>
<thead>
<tr>
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<th>51–65</th>
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<th>≥ 66</th>
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<td></td>
<td>Pre</td>
<td>Post</td>
<td>Pre</td>
<td>Post</td>
<td>Pre</td>
<td>Post</td>
</tr>
<tr>
<td>Eligible years</td>
<td>160</td>
<td>237</td>
<td>153</td>
<td>294</td>
<td>22</td>
<td>113</td>
</tr>
<tr>
<td>Number of women who contributed eligible years (of 268 women)</td>
<td>92</td>
<td>111</td>
<td>80</td>
<td>135</td>
<td>16</td>
<td>50</td>
</tr>
<tr>
<td>Average eligible years</td>
<td>1.7</td>
<td>2.1</td>
<td>1.9</td>
<td>2.2</td>
<td>1.4</td>
<td>2.3</td>
</tr>
</tbody>
</table>

Table 2: Frequencies, Rates, and Relative Risks for the Two Screening Procedures by Age Group and Study Period

<table>
<thead>
<tr>
<th></th>
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<th>≥ 66</th>
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<tr>
<td></td>
<td>Pre</td>
<td>Post</td>
<td>Pre</td>
<td>Post</td>
<td>Pre</td>
<td>Post</td>
</tr>
<tr>
<td>Screening CBEs*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total screening CBEs</td>
<td>106</td>
<td>133</td>
<td>120</td>
<td>165</td>
<td>15</td>
<td>59</td>
</tr>
<tr>
<td>Average number CBEs per eligible woman</td>
<td>1.2</td>
<td>1.2</td>
<td>1.5</td>
<td>1.2</td>
<td>0.9</td>
<td>1.2</td>
</tr>
<tr>
<td>CBE rate per 100 eligible years</td>
<td>66.3</td>
<td>56.1</td>
<td>78.4</td>
<td>56.1</td>
<td>68.2</td>
<td>52.2</td>
</tr>
<tr>
<td>Relative risk (95% CIE)</td>
<td>0.85</td>
<td></td>
<td>0.72</td>
<td></td>
<td>0.77</td>
<td></td>
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<tr>
<td>(0.72, 0.99)</td>
<td></td>
<td></td>
<td>(0.63, 0.82)</td>
<td></td>
<td>(0.59, 1.07)</td>
<td></td>
</tr>
<tr>
<td>Screening Mammograms</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total screening mammograms</td>
<td>20</td>
<td>105</td>
<td>29</td>
<td>177</td>
<td>3</td>
<td>63</td>
</tr>
<tr>
<td>Average number mammograms per eligible woman</td>
<td>0.2</td>
<td>0.9</td>
<td>0.4</td>
<td>1.3</td>
<td>0.2</td>
<td>1.3</td>
</tr>
<tr>
<td>Screening mammogram rate/100 eligible years</td>
<td>12.5</td>
<td>44.3</td>
<td>19.0</td>
<td>60.2</td>
<td>13.6</td>
<td>55.8</td>
</tr>
<tr>
<td>Relative risk (95% CIE)</td>
<td>3.54</td>
<td></td>
<td>3.18</td>
<td></td>
<td>4.09</td>
<td></td>
</tr>
<tr>
<td>(2.30, 5.47)</td>
<td></td>
<td></td>
<td>(2.26, 4.47)</td>
<td></td>
<td>(1.41, 11.85)</td>
<td></td>
</tr>
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</table>

Overall relative risk (95% CIE)
CBE = 0.77 (0.70, 0.85)
Mammography = 3.45 (2.66, 4.48)

*CBE = clinical breast exam.
†CIE = confidence interval estimate.
Table 3: Matched Pairs-Based Relative Risks and 95% Confidence Interval Estimates (CIE) Evaluating the Change over Time in the Proportion of Women Ever Using Specific Breast Cancer Screening Technologies

<table>
<thead>
<tr>
<th>Screening Technology</th>
<th>Crude Overall Risk Ratio</th>
<th>Age-Stratified Odds Ratios and 95% CIE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>≤50</td>
</tr>
<tr>
<td>Clinical breast exam</td>
<td>1.41</td>
<td>1.47</td>
</tr>
<tr>
<td></td>
<td>(1.25, 1.58)</td>
<td>(1.15, 1.87)</td>
</tr>
<tr>
<td>Screening mammography</td>
<td>4.49</td>
<td>7.63</td>
</tr>
<tr>
<td></td>
<td>(3.51, 5.74)</td>
<td>(4.27, 13.63)</td>
</tr>
</tbody>
</table>

screening mammograms was 0.3 and 1.2 pre- and postintervention, respectively. The rate of mammography screening per 100 eligible years increased in each age stratum; the relative risk was significantly greater than 1.0 in all age strata. The crude overall relative risk for screening mammograms per eligible year was 3.5 times greater following initiation of the intervention. The eldest age group was about four times more likely to have had a mammogram in each eligible year during the postintervention period compared to the preintervention period.

We also investigated whether or not women were getting minimal exposure to screening services by determining the proportion of women who had had at least one screening mammogram and the proportion having at least one CBE pre- and postintervention, and comparing these proportions to those calculated postintervention. As reported in Table 3, women were significantly more likely (about 1.4 times) to have had at least one clinical breast exam posttest than pretest. They were also significantly more likely to have had a screening mammogram (approximately four to eight times as likely).

Table 4 reports the number of screening CBEs, the number of CBEs that included a mammogram referral, and the percentage of CBEs with mammography referral. Table 4 also reports the estimated relative risks. While the rate of clinical breast exam by eligible year has decreased, the proportion of clinical breast exam visits that include a mammogram referral has significantly increased for the two younger age groups. The proportion also increased in the eldest age group, but the degree of improvement was not statistically significant.

Table 4 also reports on patient compliance with mammography referral, pre- and postintervention. Although the rates for the youngest and oldest age strata improved substantially, the differences were not statistically significant, in part due to small sample sizes.
DISCUSSION

Clearly, much greater breast cancer screening activity is going on at the health center during the postintervention period compared to the preintervention period. Increased screening mammography is occurring per eligible year, more women are having at least one screening mammogram, more CBEs now include a mammogram referral, and the client compliance rate is improving following intervention. The improvement in screening participation of the eldest group is particularly notable given other documented reports of less screening among the elderly (NCI Breast Cancer Screening Consortium 1990; Harris, Fletcher, Gonzalez, et al. 1990). An earlier client survey conducted in this health center found that 54 percent of women 65 years of age or older had ever had a mammogram as compared to 67 percent of women ages 55–64,

Table 4: Frequencies, Percentages, and Relative Risks of Mammography Referral with Clinical Breast Exams (CBE) and Patient Compliance with Mammography Referral, by Age Group and Study Period

<table>
<thead>
<tr>
<th></th>
<th>≤50</th>
<th>51–65</th>
<th>≥66</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Pre</td>
<td>Post</td>
<td>Pre</td>
</tr>
<tr>
<td>Total screening CBEs* with mammogram referral</td>
<td>16</td>
<td>50</td>
<td>26</td>
</tr>
<tr>
<td>Total screening CBEs</td>
<td>106</td>
<td>133</td>
<td>120</td>
</tr>
<tr>
<td>Percent of CBEs with mammogram referral</td>
<td>15.1</td>
<td>37.6</td>
<td>21.7</td>
</tr>
<tr>
<td>Relative risk (95% CIE)†</td>
<td>2.49</td>
<td>(1.51, 4.11)</td>
<td>2.38</td>
</tr>
<tr>
<td>Total patients complying with mammogram referral</td>
<td>18</td>
<td>112</td>
<td>31</td>
</tr>
<tr>
<td>Total mammogram referrals</td>
<td>26</td>
<td>140</td>
<td>39</td>
</tr>
<tr>
<td>Percent patient compliance with mammogram referral</td>
<td>69.2</td>
<td>80.0</td>
<td>79.5</td>
</tr>
<tr>
<td>Relative risk (95% CIE)</td>
<td>1.16</td>
<td>(0.88, 1.51)</td>
<td>0.99</td>
</tr>
</tbody>
</table>

Overall relative risk (95% CIE)
CBE = 2.29 (1.74, 3.03)
Mammography = 1.09 (0.94, 1.26)

*CBE = clinical breast exam.
†CIE = confidence interval estimate.
although there was no difference in the proportion having a mammogram in the past year (Zapka, Stoddard, Barth, et al. 1989). It should be noted that screening experience within this center was notably better even before the intervention than other reports of poor minority experience (Centers for Disease Control 1991; Caplan, Wells, and Haynes 1992). We had hypothesized that this reflects Dutton's (1978, 1986) theory concerning the importance of the adequacy of the delivery system used by the poor. Financial coverage factors are important, but access and sensitivity of practitioners, both to cultural issues and prevention orientation, are also of fundamental importance. This finding of the potential for improved screening among women of lower income and of minority status, was recently supported by the work of Lane, Polednak, and Burg (1992). Despite significantly lower socioeconomic levels, a higher proportion of minority women receiving care in community health centers in New York had higher screening rates than community women.

Due to the limitations of the study design, it is impossible to attribute this screening improvement solely to the intervention activities; there was no control group, and a strong secular trend in increasing participation in screening has been documented (Centers for Disease Control 1990). Additional limitations of this study are similar to those faced by other researchers collecting data from a retrospective review of medical records—including the limitations of the medical record as a data source (Romm and Putnam 1981). Another potential source of error is the validity of the outcome measures, notably the estimation of screening versus diagnostic and follow-up mammograms or clinical breast exams. We reason that we have minimized this potential limitation by undertaking the procedures described in the methods section. Another general limitation of the study is that women may be obtaining screening elsewhere, and the health center clinician may or may not know this. We consider this situation to be uncommon in this setting, however, as other data indicate that the vast majority of women report that they receive comprehensive care at the center (Zapka, Stoddard, Barth, et al. 1989). Additionally, this limitation would not result in an overestimation of screening improvements as a result of the center interventions.

Even with these limitations, the rather dramatic increases in the rates of screening mammograms per eligible year and in the proportion of women who have had at least one screening mammogram provide support for an intervention effect, particularly when considered in the light of other process evaluation data available from clinic staff.

Clinic aides were to initiate discussion about breast cancer screening and stamp the medical record indicating that particular procedures had
been discussed. This also was to serve as a reminder to the clinician to suggest screening. During the record audit, it was found that 66 percent of the charts were indeed stamped. The health center schedule is a very busy one, and during the course of the demonstration project several medical staff vacancies occurred. Even in view of these difficulties the aides managed to undertake some discussion with a substantial number of clients.

One year before the start of the breast cancer demonstration project, the medical and nursing staff had agreed to begin using a prevention services checklist that consisted of a fold-out insert to the medical record on which to document implementation of preventive services. Although supportive of the move, the medical director was worried that the intensity of work needed to complete the initial histories would limit the effectiveness of that strategy. This concern was proved to be well founded: only 40 percent of the charts held a completed form. Yet clinic aide discussion was undertaken and subsequent referrals were made.

Staff members have also reported a high level of client satisfaction with the mammography intervention experience. Client feedback about mammograms to staff that “it wasn’t so bad” or “it was really interesting” appeared to reinforce the staff’s educational efforts and to motivate them further.

The rate of patient compliance with mammography referral did increase (Table 4), although the changes were not statistically significant. During the early phases of the intervention, the waiting time for a mammogram at local hospitals increased dramatically. Consequently, health center patients were referred to another hospital facility, located outside their neighborhood, that was unfamiliar to the women. Anecdotal evidence suggests that this factor could have resulted in an even higher no-show rate. Since the reminder system was added in the later phases of the intervention, its potential impact is probably not reflected in the post-test compliance rates, and the constant rate of compliance may actually reflect success of the reminder system.

The documented decrease in the rates of CBE per eligible year is curious. It might be due, in part, to poor record documentation during a period of staff shortages. Alternatively, clinicians could have put emphasis on mammography given awareness of the project as well as awareness of changing secular trends. Lane, Polednak, and Burg (1991) reported that as a result of a physician education intervention, referrals for mammography increased while CBE did not. A more likely explanation, however, relates to the fact that during the staff vacancies, no new clients were accepted at the health center. Complete physical exams, which include CBE, almost universally happen when a new client is enrolled. Given the sampling strategy used for the medical record audit, only the screening
participation of existing patients was monitored. All complete entry physical exams would therefore be "assigned" to the preintervention period, contributing to a lower rate per eligible year in the post-test period.

In addition, the extended appointments required for a complete physical exam were less available because of the staff shortage during the post-test period. This perhaps contributed to a lower CBE rate per eligible year because it took longer to get an appointment for a "complete physical"—the context, at this center, for completing many clinical breast exams. At any rate, the issue of quality screening—CBE coupled with mammography—deserves further attention since randomized trials suggest that CBE produces incremental benefits over and above the benefits of mammography (Shapiro et al. 1987). Even with the documented increase in screening, the goal of regular screening remains a challenge for the health center staff, as few women over 50 participate in annual screening. Continued attention to client education and reinforcement, as well as provider prompts are indicated.

An encouraging feature of the intervention has been that many of the activities continue in place, even since formal termination of the evaluated project. The staff’s enthusiasm and support has also transferred to other issues. For example, clinicians have recently been concerned about the levels of anemia in clients, and after considerable discussion of possible strategies the staff is implementing a program that includes special-stamping of medical records as a cue to clinician action.

ACKNOWLEDGMENTS

We gratefully acknowledge the assistance of the staff of the Greater Lawrence Community Health Center in the implementation of this demonstration project, particularly Denise Rajotte, Juan Rodriguez, and Patricia Mirisola. We thank Vicki Gaw and Diane Davis-Whitham for their assistance with data collection. We also thank Dr. Jane McCusker and Dr. Harris Pastides for their helpful review of the manuscript.

REFERENCES


