Is Screening Mammography Routinely Indicated for Women Between 40 and 50 Years of Age?

An Affirmative View

Gerald D. Dodd, MD
Houston, Texas

Although clinical mammography was described by Warren[1] in 1929, it was not until the mid-1950s that a serious effort was made to screen asymptomatic women for breast cancer. Gershon-Cohen et al published a preliminary report on 2,000 volunteers in 1958[2] and followed with five- and ten-year reports on the same subjects.[3,4] While noting that significant obstacles are encountered in mounting a large-scale screening program, they concluded that periodic roentgenography of the breasts of women over 40 years of age was feasible and should be seriously considered.

In 1961 the breast-screening project of the Health Insurance Plan (HIP) of New York was initiated. Conceived by Shapiro et al,[5] the project was well designed from the statistical standpoint and represents the only large controlled study of mammography ever performed in the United States. All patients in the study group were eligible for physical examination and mammography for four consecutive years. At the end of five years a 52 percent decrease in mortality was found in those who entered the program at the age of 50 years or older. A similar benefit was not demonstrable in those who entered when they were aged between 40 and 49 years; only a 5 percent decrease in mortality occurred in this group.[6]

BREAST CANCER DETECTION AND DEMONSTRATION PROJECT

The impressive results of the HIP program led, in 1973, to the Breast Cancer Detection and Demonstration Project (BCDDP). Jointly organized by the American Cancer Society and the National Cancer Institute, the BCDDP was designed to demonstrate the usefulness of mammography at the community level and was not intended as a further clinical trial of mammography. In retrospect this decision was unfortunate, since the absence of a control population has led to substantial criticism of the BCDDP results.

Initially the BCDDP protocol specified examination of asymptomatic women aged 40 years and older. Both mammography and physical examination were employed, and each woman was eligible for five annual examinations. It is noteworthy that those women aged 40 to 49 years were included even though the then available results of the HIP study did not support screening this segment of the population.

In 1976–77, at the height of the BCDDP program, a controversy arose over the potential carcinogenic effects of radiation. The average midline dose to the breast during mammography was assumed to be 2 rad, and younger women were considered particularly susceptible.[7] This concern, plus the lack of benefit demonstrated by the HIP study, raised serious questions as to the propriety of screening 40- to 49-year-old women, and eventually led to the deletion of mammography for this segment of the BCDDP population.

In the decade that has elapsed since the completion of the BCDDP program, substantial technical advances have occurred in mammography. As a result of the introduction of dedicated machines, improved film-screen systems, better processing control, and the evolution of tube-filter systems, the dose for mammography has dropped while the quality of the images has improved. Depending upon methods employed, the midbreast dose for a two-view examination now varies between 0.08 to 0.8 rad. Recent developments in receptor technology offer a potential for further decrease. It is generally agreed that a properly performed mammogram does not constitute a significant threat from the standpoint of carcinogenesis.

Submitted June 4, 1988.

From the Department of Diagnostic Radiology, M.D. Anderson Hospital, Houston, Texas. Requests for reprints should be addressed to Dr. Gerald D. Dodd, Department of Diagnostic Radiology, M.D. Anderson Hospital, 1515 West Holcombe Blvd, Houston, TX 77030.

The results of the BCDDP program have, despite the criticism of its statistical basis, been of great value and are most impressive from the clinical standpoint. Mammography alone was responsible for 41.6 percent of the 3,557 cancers diagnosed in 280,000 women. The comparable figure in the HIP study was 33.3 percent.

In women aged 40 to 49 years, mammography alone detected 35.4 percent of 762 cancers compared with 19.4 percent in the HIP study. Sixteen and one-half percent of all infiltrating cancers were less than 1 cm in diameter, and 52 percent of these cancers were apparent only by mammography. The comparable figure in the early HIP study was 3.5 percent.[8]

Approximately one third of all cancers diagnosed in the BCDDP occurred in women less than 50 years of age, and the eight-year follow-up shows essentially no difference in the relative survival rates between the two age groups.[9] In short, despite the absence of a control group, there is no substantial difference in the clinical outcome of the histologically proven tumors in women younger than 50 years of age as opposed to the outcome of tumors found in women aged over 50 years. The American Cancer Society has accepted this finding as evidence of the effectiveness of screening mammography in women in the 40- to 49-year age group and continues to recommend its use.

THE CONTROVERSY OVER ROUTINE SCREENING

Opponents of screening in the younger age group base their objections primarily upon the HIP results. Additionally, two other studies carried out in Europe would appear to buttress their position:

Nijmegan study. A case-control study, this program at seven years showed a 52 percent reduction in mortality for women aged over 50 years; women aged under 50 years received no apparent benefit. The study differed from the HIP investigation in that single-view mammography was employed at two-year intervals without physical examination.[10,11]

Swedish study. Begun in 1977, this study utilized single-view mammography at 20- to 36-month intervals. Once again, no physical examination was employed. A 40 percent reduction in mortality was found for those between the ages of 50 and 74 years, but no benefit accrued in those under the age of 50 years.[12,13]

The DOM Project (Netherlands) also demonstrated a positive benefit for the older age group, but included no information for those under the age of 50 years.[14]

Although the initial results of the HIP, Nijmegan, and Swedish studies indicated a lack of effectiveness of mammography in women younger than 50 years, an 18-year follow-up of the HIP subjects has demonstrated a 24.6 percent decrease in mortality.[15] This degree of benefit is most encouraging, but has been questioned on two counts: (1) The number of patients involved is small and may not be statistically significant, and (2) the benefit decreases if calculations are based upon the age at diagnosis rather than age at entry (14 percent).

These questions are valid, but it is indisputable that the results of the HIP study show a trend toward a significant decrease in the mortality rate with the passage of time. The reasons for the delayed benefit are speculative, but it is of interest that the Swedish study, which has now passed the eighth year of follow-up, exhibits a mortality curve for the younger age group that parallels that of the HIP study.

In the opinion of many clinicians the BCDDP data and the most recent HIP analysis amply justify the use of screening mammography in the 40- to 49-year-old group. While this stance does not have statistical purity, it does reflect practical clinical experience and a knowledge of the technical limitations of the HIP study.

The cost of mammography, the outdated equipment reputedly used by many facilities, and the inadequate training of some technologists and radiologists have been cited as negative aspects of screening programs. These questions require examination.

The operational expenses of a breast cancer screening program are substantial, and most investigators concur that the mammogram is the major cost component. The average price is often quoted as $100 to $125, but these figures refer to the examination of symptomatic patients and do not represent a screening situation. There is a measurable difference between the screening mammogram and an examination performed for a clinical abnormality. The screening mammogram involves two standardized views; a physician is not present, and the physical examination, if any, is performed by paramedical personnel. Screen-film mammography is preferred, and the examinations are batched and interpreted at varying intervals, depending upon the schedule of the radiologist. Films are interpreted as suggestive or negative; no attempt is made to formulate a diagnosis from the survey procedure. Patients with questionable findings on mammograms are recalled for further investigation. Depending upon volume, lay screeners may be used to select those cases requiring the attention of the radiologist.

All of the above factors reduce the direct costs of an examination. It has been demonstrated that such cost-cutting efforts work. Bird and others[16,17] have shown the feasibility of producing high-quality screening studies at less than $30 per patient. Similar programs have been reported in which mammography costs $50 or less. While Eddy[18] has calculated the cost of adding a year of life expectancy with screening mammography for women aged between 40 and 50 years to be about $40,000, his calcu-

lations are based upon a combined cost of $105 for mammography and physical examination. When both are performed for under $50, the cost compares favorably with some other detection procedures.

Recently the American College of Radiology has instituted a rigorous accreditation program designed to assure the technical quality of mammography. To date, 80 percent of the facilities applying for accreditation utilize dedicated equipment that has been installed within the past three years; only 5 percent have equipment older than six years. Eighty-eight percent of all facilities use screen-film systems with the average glandular dose substantially below the level recommended by the National Council on Radiation Protection and Measurements.[19] Similarly, in a recent report by Galkin et al,[20] there is virtually total compliance with dose.

The American College of Radiology accreditation procedure has thus far certified 84 percent of hospital facilities and 97 percent of private offices that have applied. Problems, where they exist, are primarily with quality control, a finding that reflects inexperience on the part of some radiologists and technologists. Despite the fact that 60 years have passed since Warren's initial report on mammography, lack of demand has resulted in limited interest on the part of some practicing radiologists. The recent resurgence of the examination has changed this attitude. The American College of Radiology, the American Board of Radiology, and the American Cancer Society have recognized the problem and have mounted effective remedial programs. Experience in mammography is now required as a requisite for certification by the American Board of Radiology, and thousands of radiologists have benefited from postgraduate courses sponsored by the American College of Radiology and the American Cancer Society. In short, some of the perceived deficits of mammography as a screening tool have been or are being addressed. They do not constitute an effective drawback to the establishment of screening mammography programs.

CONCLUSIONS

While there is general acceptance of the effectiveness of screening in asymptomatic women aged 50 years and older, the potential benefit is statistically less clear for those in the 40- to 49-year age group. The primary difference revolves about the cost-benefit ratio, ie, will the number of cancers found and the number of lives saved offset the number of dollars required to screen younger women. The calculations that support a negative response to this question do not reflect the true costs of screening. Similarly, the estimates of benefit in terms of mortality rates are derived from a study performed with obsolete technology (HIP) and by other studies whose experimental design and follow-up differ significantly from those of the HIP program. Indeed, one of the major strengths of the HIP data is the favorable results that accrued despite the relatively crude technology employed.

The long-term follow-up of the HIP study shows an evolving benefit that, when coupled with the BCDDP findings, would suggest that screening can and does improve the mortality rate in younger women. For those involved in patient care, this reason is sufficient to encourage the formulation of low-cost screening programs for all asymptomatic women who are over the age of 40 years. To date, decreases in costs have been purely voluntary on the part of institutions and radiologists. With reasonable help from third-party carriers, screening mammography could be made available to all. Certainly one of the two most effective cancer detection procedures extant should not be denied to a large segment of women simply because mathematical calculations, based upon assumptions of dubious quality, do not provide a clear benefit in terms of dollars.

References

1. Warren SL: A roentgenographic study of the breast. Am J Roentgenol 1930; 24:113
2. Gershon-Cohen J, Ingleby H, Moore L: Analysis of 2,514 examinations during early phases of an x-ray survey of breast. Surg Gynecol Obstet 1958; 106:478–480
3. Gershon-Cohen J, Hermel MB, Berger SM: Detection of breast cancer by periodic x-ray examinations. JAMA 1961; 176:1113–1116
4. Gershon-Cohen J, Ingleby H, Berger SM, et al: Mammographic screening for breast cancer. Radiology 1967; 88:663–667
5. Shapiro S, Strax P, Venet L: Evaluation of periodic breast cancer screening with mammography: Methodology and early observations. JAMA 1966; 195:731–738
6. Shapiro S: Evidence on screening for breast cancer from a randomized trial. Cancer 1977; 39(suppl):2772–2782
7. Bailar JC III: Mammography. A contrary view. Ann Intern Med 1976; 84:77–84
8. Baker LH: Breast Cancer Detection Demonstration Project: Five-year summary report. CA 1982; 32:194–225
9. Seidman H, Gelb SK, Silverberg E, et al: Survival experience in the breast cancer detection demonstration project. CA 1987; 37: 258–290
10. Verbeek ALM, Holland R, Sturmans F, et al: Reduction of breast cancer mortality through mass screening with modern mammography, first results of the Nijmegan Project. Lancet 1984; 1:1222–1224
11. Verbeek ALM, et al: Mammographic screening and breast cancer mortality: Age-specific effects in Nijmegan Project, letter. Lancet 1 1985; 1:865–866
12. Tabar L, Gad A: Screening for breast cancer. The Swedish trial. Radiology 1981; 138:219–222
13. Tabar L, Gad A, Holmberg LH, et al: Reduction in mortality from breast cancer after mass screening with mammography. Lancet 1985; 1:829–832
14. Collette HMA, Day NE, Rombach JJ, de Waard F: Evaluation of screening for breast cancer in a non-randomized study (the DOM

Project) by means of a case-control study. Lancet 1984; 1:1224–1226
15. Shapiro S, Venet W, Strax P, Venet L (eds): Periodic Screening for Breast Cancer. Baltimore, Johns Hopkins Press, 1988
16. Bird RE: A successful effort to lower costs in screening mammography. Cancer 1987; 60(suppl):1684–1687
17. Dodd GD: The history and present status of radiographic screening for breast carcinoma. Cancer 1987; 60(suppl):1671–1674
18. Eddy D: The value of mammography for women under 50: Report of the Subcommittee on Mammography, National Committee on Cancer Detection. New York, American Cancer Society, 1984, pp 5–17
19. Mammography, A User's Guide. NCRP Report 85, Scientific Committee No. 72. Bethesda, Md, National Council on Radiation Protection and Measurements 1986, pp 40–50
20. Galkin GM, Feig SA, Muir HD: The technical quality of mammography in centers participating in a regional breast cancer awareness program. Radiographics 1988; 8(1):133–146

An Opposing View

Stephen Taplin, MD, MPH
Seattle, Washington

The answer to whether routine mammographic screening should occur in women aged 40 to 49 years is unquestionably No when a careful criteria-based analytic approach to the question is undertaken. While breast cancer is an important condition in this population, it is not necessarily the same condition as that found in women aged 50 years and older; therefore, age-specific evide for the use of mammography should be evaluated before it is routinely recommended. Mammographic screening has not been demonstrated to be effective in this age group despite assertions to the contrary.[1–3] In the absence of demonstrated efficacy, the potential exists to violate fundamental ethical principles in the practice of medicine and misappropriate limited resources in the process.

The obligation to "first do no harm" is the fundamental guiding ethic of medical practice. In 1979 the working group to review the Breast Cancer Detection and Demonstration Project (BCDDP) emphasized the even greater responsibility to follow this ethic when undertaking the search for illness in an asymptomatic population. They proposed the use of specific criteria to analyze whether mammography should be adopted, and concluded that "advice and recommendations for the use of specified examinations or testing techniques for screening purposes are not necessarily the same as those for differential diagnosis."[4] The criteria they adopted were variations on the ones listed below. The following criteria have been advocated since the 1960s and include consideration of the cost implications of a screening program[5–7]:

1. The disease condition is important.
2. It has a recognizable presymptomatic stage.
3. There are reliable tests for this stage that are acceptable in terms of risk, cost, and degree of discomfort to the patient.
4. Treatment in the presymptomatic stages reduces morbidity or mortality more than treatment once symptoms have appeared.
5. Facilities are available for diagnosis and treatment of those persons with positive screening tests.
6. The screening program has been chosen after considerations of other needs competing for the same resource.

These six criteria have been used to review multiple screening issues for a 320,000-member managed health care system in the Northwest, Group Health Cooperative of Puget Sound.[8] Variations of these criteria have been used by Frame[9] in his analysis of the periodic health examination, and the Canadian Task Force, which also reviewed health examinations.[10] The latter group extended the criteria by establishing explicit levels of evidence for whether a test could be judged to be efficacious. Their recommendations have been a cornerstone of primary care and almost exclusively include tests that have been proven effective by randomized trials.[10] The need for evidence of efficacy from a randomized trial has been underscored repeatedly in the case of mammography.[11–13] This article will evaluate the literature that addresses these six criteria and include a discussion of the absence of evidence for the efficacy of mammography in women aged 40 to 49 years.

THE DISEASE AND THE TEST

Breast cancer is a common condition that begins to appear more frequently at age 40 years. There are approximately 13 million women in this age group in the United States today.[14] These women will account for 15 percent of all breast cancers diagnosed in the next year, compared with

7 percent of cases occurring among the 36 million women aged 22 to 40 years. Women aged 40 to 49 years will suffer 11 percent of all breast cancer deaths, while only 4 percent of these deaths will occur in women younger than the age of 40 years.[15] Breast cancer occurs at an average annual rate of 67 cases per 100,000 women aged 40 to 49 years and is the most common cause of death due to malignancy in this age group.[15,16] While this condition is important to women aged 40 to 49 years, women in older age groups are more likely to experience its consequences. The average annual incidence in women aged 50 years and above is 175 per 100,000, and women in this age group account for 85 percent of all breast cancer deaths.[15,16]

Breast cancer in women aged 40 to 49 years is not the same condition as that found in older women. A fundamental biological difference is suggested by its different response to chemotherapy, different cell characteristics, and different growth rate. The National Institutes of Health Adjuvant Chemotherapy Consensus Conference acknowledged this difference in its 1985 report and cited a woman's menopausal status as one key element of this biologic difference.[17] It acknowledged that age less than 50 years was a consistent prognostic variable in determining therapeutic response to tamoxifen and a cytoxan-methotrexate-fluorouracil combination (CMF).[17] Women aged under 50 years are more likely to have estrogen-receptor-negative tumors and not be candidates for tamoxifen.[17,18] In contrast, they are more likely to respond to CMF.[19] These differences in tumor response to therapy suggest fundamental differences in biology. Indeed, examination of screening data from one BCDDP clinic suggests that younger women have more rapidly growing tumors.[1] These screening data demonstrate that the lead time in women aged 40 to 49 years is 1.5 to 2.0 years while it is 3.5 to 4.0 years in women 50 years of age and older.[1] This lead time is the presymptomatic stage that must exist for screening to be justified. Breast cancer in women younger than 50 years of age does have a presymptomatic stage, but it is significantly shorter than the one present in women aged 50 and older. This shorter lead time is further evidence that breast cancer in women aged 40 to 49 years is not the same condition as that present in women aged 50 years and above.

Not only is the cancer different, but the screening test's reliability may vary in younger women as well. Work by Wolfe[20] to classify mammographic breast patterns demonstrated that as age increased, breast density decreased. Higher density breasts make cancers harder to find. The overall sensitivity of mammography has been shown to be about 68 percent, while the specificity varies between 81 percent and 94 percent.[21,22] In the major randomized trial of mammography performed at the Health Insurance Plan (HIP) of Greater New York, this fact accounted for a 19 percent difference in the proportion of cancers detected by mammography alone in women aged 40 to 49 years compared with those in women aged 50 to 64 years (19 percent vs 38 percent, respectively).[23]

Since the HIP study, mammography has improved. The amount of radiation required has decreased by 10- to 20-fold to a mean glandular dose of between 0.08 and 0.8 rad.[24] Compared with mammography at the time of the HIP trial, a higher proportion of cancers can now be found by mammography alone in younger women.[25] The BCDDP showed that 37 percent of detected cancers were found by mammography alone in women aged 40 to 49 years compared with 43 percent in women aged 50 to 59 years. This 6 percent difference remains substantial, though it is less than the 19 percent difference that occurred in the HIP trial. The actual sensitivity of mammography has been shown to be 62 percent for women aged 40 to 49 years compared with 87 percent for women aged 50 years and above, using the latest techniques and one-year of follow-up after the screening visit.[26]

These differences in the sensitivity of the screening test translate into concerns about the reliability of mammography in this age group. In a randomized trial of single-view mammography in Sweden, 50 percent of the breast cancer deaths in women aged 40 to 49 years occurred among women whose cancers became symptomatic between screening visits.[26] In that study, a two-year interval was used in this age group. Their data, however, also demonstrate that 38 percent of the cancers that would be found in women aged 40 to 49 years over one year would be missed by a screening visit at the beginning of that year. This finding suggests that screening with mammography in this age group remains problematic, even at one-year intervals.

In addition to concerns about the reliability of the test, there have been questions about the risks and costs.[27] Radiation risk is frequently mentioned as a concern by women and physicians but is no longer a scientific concern.[24,28] Using current techniques, the risk of dying from an induced cancer is 1 in 4 million or about the same as the risk of dying from traveling in a car for 15 minutes.[28] More significant are the consequences of false-positive screening results, which lead to biopsies and undue anxiety. From BCDDP results, Eddy et al[29] have estimated that 1 percent of screened women with normal findings on physical examination will require a further evaluation because of a false-positive mammogram. The average cost of the additional views and surgical consultations that may occur are estimated at $900 per person. The psychological consequences of false-positive results are unknown. It is well established, however, that the costs of a screening mammogram are unacceptable.[27] This issue was the principle subject of a recent American Cancer Society conference in which ways of providing a lower cost examination were discussed.[30] At present, the average cost is $100 to $125 for the screening examination alone without a physical examination or additional views.[29]

MAMMOGRAPHIC EFFECTIVENESS AND THE IMPLICATIONS OF ROUTINE CARE

A prospective randomized controlled trial of mammographic efficacy should be the source of policy recommendations and conclusions regarding the use of this test.[10–13] This point has been made repeatedly, since the effect of such recommendations are far-reaching. Only one such study has been designed to address the efficacy of screening in women aged 40 to 49 years, and results are not yet available.[31] Measuring breast cancer mortality differences in populations randomized to a study and control group avoids lead time, length time, and self-selection bias. These biases confuse and confound prospective analyses in any other comparative groupings, as the cancers detected by mammography will differ fundamentally from cancer found in any other way.[32] *Lead time* refers to the asymptomatic period that occurs prior to the time a cancer would have appeared on its own. *Length time* reflects that tumors found by screening are, on average, slower growing than cancers found between screenings. *Self-selection bias* refers to the demonstrated reality that women who seek screening are more likely to have breast cancer present.[23] Comparisons between populations that are screened and any other population are uninterpretable unless prior randomization has removed these biases by allowing comparisons between populations who differ only by the presence or absence of the regular use of mammography.[32]

Retrospective analyses may also be used if a case-control design is undertaken and cases and controls are carefully selected.[11] Least helpful are observational studies when all three biases will be present. While some adjustments can be made for lead time in observational studies, it is impossible to know whether those adjustments were correct or how the fallacies in the adjustments influenced the conclusions. No adjustment can remove length time and self-selection bias.

The results of two randomized trials are emphasized here for the reasons cited above. A study in the late 1970s used single-view mammography in 78,085 women aged 40 to 74 years, randomized by community to the study population. The results of the study demonstrated a 31 percent reduction in breast cancer mortality among all study group women compared with controls after seven years.[33] The screening interval was two years in women aged 40 to 49 years, and three years in women aged 50 years and older. Despite the shorter interval for younger women, they did not experience a statistically significant reduction in mortality. In contrast, women aged 50 to 74 years had 40 percent fewer deaths due to breast cancer compared with control group women of the same age.[33] The failure to reduce mortality in women aged 40 to 49 years has been attributed in part to the use of a two-year interval.[26]

Results from the HIP study, begun in New York in the early 1960s, have been cited as evidence that a one-year screening interval can be effective in reducing breast cancer mortality among women aged 40 to 49 years.[1,2,26] This trial randomized 31,000 women aged 40 to 64 years to a study population and offered them a physical examination and mammogram every year for four years.[22,34] A statistically significant 38 percent reduction in breast cancer mortality was demonstrated at five years in the study population compared with controls. Fewer deaths attributable to breast cancer occurred in study women who had breast cancer diagnosed within five years of entry into the study compared with women in the control group even after 18 years of follow-up.[35] Instead of the 38 percent fewer deaths observed at five years, however, the difference has decreased to 23 percent at 18 years.[35] Subanalyses by age groups failed to show a statistically significant difference in breast cancer mortality, at five and ten years of follow-up, in women who were aged 40 to 49 years at entry into the study.[23,34] The most recent report, after 18 years of follow-up, shows a 25 percent reduction in mortality in this age group compared with a 5 percent reduction after five years of follow-up.[34,35]

This late effect is now hailed as evidence from a randomized trial that mammography is efficacious in this age group.[1–3] Such a conclusion is not warranted. The late effect raises many more questions than it answers. First, only 19 percent of the breast cancers found in this age group were found by mammography alone, while 61 percent were found by physical examination alone. Is the late effect evidence for the efficacy of mammography or physical examination? Second, in every other age group the mortality differences between study and control populations decreased with time. Why would they increase with time in women aged 40 to 49 years? Is this a random variation? Is there a fundamental biologic difference that explains this increase, or is there a hidden bias? One such bias might be that more women with breast cancer died of other causes in the control population and their deaths therefore do not appear to be due to breast cancer.[36] This possibility has not been examined. Lastly, there is some debate about whether "age at diagnosis" or "age at entry" should be used in the subanalyses.[13,35] When age at diagnosis is used to subanalyze mortality among women who were aged 40 to 49 years at entry, some confusing results appear. The largest difference in mortality (43 percent) occurs in women aged 50 to 54 years. Women aged 45 to 49 years at diagnosis show a benefit if they were aged 40 to 45 years at entry, but an apparent excess mortality if they were aged 45 to 49 years at entry. The inconsistencies and questions raised by the reported late effect on mortality in women aged 40 to 49 years must be explained before the results become a basis for screening recommendations. This assessment is echoed by the principal investigator on the HIP trial, who concludes his re-

port by stating, "Accordingly, based on the HIP trial, uncertainty exists about the effectiveness of starting to screen under the age of 50. Resolution of this issue is dependent on results from more recent studies based on substantially larger sample sizes."[35]

The results of other studies are available, but the study designs are either retrospective or observational. Two case-control studies showed no protective effect for screening women aged 40 to 49 years despite an overall benefit.[37,38] An observational study of women who sought screening through the BCDDP has claimed that survival in screened women is significantly improved.[2] The assertion that lead time bias has been eliminated by analyzing survival after subtracting the one year of lead time demonstrated in the HIP trial is not convincing. The whole basis for the analysis is that mammography has improved since the HIP trial. If mammography has improved, which it has, then the lead time will have changed as well. Estimates of lead time vary between 0.85 and 3.5 years.[31,39] The sensitivity to lead time assumptions of this survival analysis could be tested, but no amount of adjusting can overcome length and self-selection bias. The BCDDP was designed to demonstrate that mammography could be extended to large populations, and it has successfully accomplished this goal. This project, however, cannot be used to assess the impact of mammography on mortality, since its design limitations do not allow sound conclusions.

In the absence of clear evidence for the efficacy of screening, it is tempting to abort any further analyses. Since there will be those who will argue that evidence does exist, however, it is important to look at the impact of a recommendation for regular mammography in women aged 40 to 49 years. Although facilities do exist for screening and evaluation of positive results, Hall[40] has recognized that regular mammography for women aged 40 years and older would mean annual studies for almost 50 percent of adult women, "eight examinations per radiologist per working day." To meet this demand, he states that radiology technicians should be trained to read mammograms, but adequate numbers of such people do not currently exist. Including women aged 40 to 49 years will tax an already limited resource.

A broader analysis of the impact of screening was undertaken by Eddy et al.[29] They mathematically combine the evidence from the literature regarding efficacy and find essentially no effect on mortality. To continue the analysis, however, they focus only on the 18-year results from the HIP trial discussed above. Using these results in a mathematical model with explicit, optimistic assumptions regarding cost (ie, $80 per screening examination), they estimate that adding mammography to a regular physical examination would increase the costs of cancer care by a net of $402 million dollars per year by the year 2000. They conclude that "If any resources to implement a mammography screening policy are limited, priority should be given to activities that would have greater yield."[29]

CONCLUSIONS

At present, a recommendation for regular use of mammography for women between 40 and 49 years of age is unwarranted. Only the first two of the six long-established criteria for analyzing screening policy recommendations can be met, and these two have limitations: (1) Yes, the disease condition is important in women aged 40 to 49 years, but it accounts for only 11 percent of breast cancer mortality. (2) Yes, a presymptomatic stage does exist, but it is short (one year or less). (3) No, mammography is not acceptable with regard to cost, risk, and reliability in women aged 40 to 49 years. (4) No, detection of breast cancer by mammographic screening has not been shown to reduce mortality in this age group. (5) No, there are not adequate facilities to screen these women. (6) No, screening these women should not be chosen above other cancer control priorities. The cost of regular use of mammography in this age group is excessive given the uncertainties regarding its benefits.

Until these six criteria have been met and a true benefit is demonstrated for women aged 40 to 49 years, regular screening mammography should not be undertaken. Doing so not only taxes a limited resource, but threatens a fundamental tenet of screening that is also imbedded in the practice of medicine: first do no harm. The question is not whether to screen women aged 40 to 49 years, but how to reach women aged 50 years and older. Women in the latter age group account for 85 percent of all breast cancer deaths, and the efficacy of screening mammography for these women is unequivocal.

References

1. Moskowitz M: Breast cancer: Age-specific growth rates and screening strategies. Radiology 1986; 161:37–41
2. Seidman H, Gelb SK, Silverberg E, et al: Survival experience in the breast cancer detection and demonstration project. CA 1987; 37:258–289
3. Moskowitz M: Costs of screening for breast cancer. Radiol Clin North Am 1987; 25:1031–1037
4. Beahrs OH, Shapiro S, Smart C: Report of working group to review BCDDP. J Natl Cancer Inst 1979; 62:655–662
5. Wilson JMG, Junger G: Principles and practice of screening for disease. Public Health Papers No. 34, Geneva, World Health Organization, 1968
6. Thorner RM, Remein GR: Principles and procedures in the evaluation of screening for disease. A report of the US Department of Health, Education and Welfare. Public Health Monograph No. 67. PHS No. 616, Government Printing Office, 1961
7. Frankenburg WK, Camp BW: Pediatric Screening Tests. Springfield, Ill, Charles C Thomas, 1973, pp 9–23
8. Thompson RS, Miller JR: Prevention in a health maintenance or-

ganization. In Barker WH (ed): Teaching Preventive Medicine in Primary Care, New York, Springer Publishing, 1983
9. Frame PS: A critical review of adult health maintenance. Part 1: Prevention of atherosclerotic diseases. J Fam Pract 1986; 22: 341–346
10. Canadian Task Force on the Periodic Health Examination: The periodic health examination. Can Med Assoc J 1979; 121:1194–1254
11. Cole P, Morrison AS: Basic issues in population screening for cancer. J Natl Cancer Inst 1980; 64:1263–1272
12. Prorok PC, Connor RJ: Screening for the early detection of cancer. Cancer Invest 1986; 4:225–238
13. Miller AB: Screening for cancer: Issues and future directions. J Chronic Dis 1986; 39:1067–1077
14. Bureau of the Census: Statistical Abstract of the United States 1987, ed. 107. US Department of Commerce, 1986
15. Seidman H, Mushinski MH: Breast cancer: Incidence, mortality, survival, and prognosis. In Feig SA, McLelland R (eds): Breast Carcinoma, Chicago, Year Book Medical, 1983, pp 9–46
16. Horn JW, Asire JA, Young JL, Pollack ES: Cancer incidence and mortality in the United States. SEER, 1973–1981 NIH Publication No. 85-1837. Government Printing Office. November 1984, p 53
17. Adjuvant chemotherapy for breast cancer. NIH consensus conference. JAMA 1985; 254:3461–3463
18. Ballard-Barbash R, Griffin MR, Fisher LD, et al: Estrogen receptors in breast cancer. Am J Epidemiol 1986; 124:77–84
19. Forrest APM: Advances in the management of carcinoma of the breast. Surg Gynecol Obstet 1986; 163:89–100
20. Wolfe JN: The prominent duct pattern as an indicator of cancer risk. Oncology 1969; 23:149–158
21. Gohagan JK, Rodes ND, Blackwell CW, et al: Individual and combined effectiveness of palpation, thermography and mammography in breast cancer screening. Prev Med 1980; 9:713–721
22. Baines CJ, Miller AB, Wall C, et al: Sensitivity and specificity of first screen mammography in the Canadian national breast screening study: A preliminary report from five centers. Radiology 1986; 160:295–298
23. Shapiro S: Evidence on screening for breast cancer from a randomized trial. Cancer 1977; 39(suppl):2772–2782
24. Dodd GD: The major issues in screening: Mammography. The history and present status of radiographic screening for breast carcinoma. Cancer 1987; 60:1671–1674
25. Baker LH: Breast Cancer Detection and Demonstration Project: Five-year summary report. CA 1982; 32:194–225
26. Tabar L, Faberberg G, Day NE, Holmberg L: What is the optimum interval between mammographic screening examinations? An analysis based on the latest results of the Swedish two-county breast cancer screening trial. Br J Cancer 1987; 55:547–551
27. Gold RH, Bassett LN, Fox SA: Mammography screening: Successes and problems in implementing widespread use in the United States. Radiol Clin North Am 1987; 25:1039–1046
28. Feig SA: Low-dose mammography: Assessment of theoretical risk. In Feig SA, McLelland R (eds): Breast Carcinoma, Chicago, Year Book Medical, 1983, pp 69–76
29. Eddy DM, Hasselblad V, McGivney W, Hendee W: The value of mammography screening in women under 50 years of age. JAMA 1988; 259:1512–1519
30. Dodd GD, Fink DJ, Bertram DA: Mammography. Addressing the needs and solutions to increase the use of low-cost screening mammography. Cancer 1987; 60:1669–1670
31. Miller AB, Howe GR, Wall GC: The national study of breast cancer screening. Protocol for a Canadian randomized controlled trial of screening for breast cancer in women. Clin Invest Med 1981; 4: 233–246
32. Prorok PC, Hankey BF, Bundy BN: Concepts and problems in the evaluation of screening programs. J Chronic Dis 1981; 34: 159–171
33. Tabar L, Gad A, Holmberg LH, et al: Reduction in mortality from breast cancer after mass screening with mammography. Lancet 1985; 1:829–832
34. Shapiro S, Venet W, Strax P, et al: Ten-to-fourteen-year effect of screening on breast cancer mortality. J Natl Cancer Inst 1982; 69:349–355
35. Shapiro S, Venet W, Strax P, Venet L: Current results of the breast cancer screening randomized trial: The health insurance plan (HIP) of greater New York study. Presented at the UICC Workshop on Evaluation of Screening for Breast Cancer, Helsinki, Finland, April 5–7, 1986
36. Aaron JL, Prorok PC: An analysis of the mortality effect in a breast cancer screening study. Int J Epidemiol 1986; 15:36–43
37. Palli D, Del Turco MR, Buiatti E, et al: A case-control study of the efficacy of a nonrandomized breast cancer screening program in Florence (Italy). Int J Cancer 1986; 38:501–504
38. Verbeek ALM, Holland R, Sturmans F, et al: Reduction of breast cancer mortality through mass screening with modern mammography, first results of the Nijmegan project. Lancet 1984; 2:1222–1224
39. Walter S, Day N: Estimation of the duration of a pre-clinical disease state using screening data. Am J Epidemiol 1983; 118:865–886
40. Hall FM: Screening mammography: Potential problems on the horizon. N Engl J Med 1986; 314:53–55

Submitted March 29, 1988.

From the Department of Preventive Care Research, Group Health Cooperative of Puget Sound, Seattle, Washington. Requests for reprints should be addressed to Dr. Stephen Taplin, Preventive Care Research, Center for Health Studies, Group Health Cooperative of Puget Sound, 521 Wall St, Seattle, WA 98121.