Screening Mammography Beginning at Age 40 Years

A Reappraisal of Cost-Effectiveness

C. John Rosenquist, M.D.
Karen K. Lindfors, M.D.

Department of Radiology, University of California, Davis, School of Medicine, Sacramento, California.

BACKGROUND. Several recent studies have added significant information regarding the benefit of screening mammography, especially in the 40–49-years age group. This new information makes it important to reassess the cost-effectiveness of screening.

METHODS. A Markov model was used to study the cost-effectiveness of 4 age-related screening strategies: 1) annually from ages 40–79 years; 2) annually from ages 40–64 years and biennially from ages 65–79 years; 3) annually from ages 40–49 years and biennially from ages 50–79 years; and 4) annually from ages 40–79 years in high risk women (10%) and biennially from ages 40–49 years followed by annually from ages 50–79 years in normal risk women (90%). An additional strategy simulating hormone status and estrogen exposure was evaluated. Cost-effectiveness was expressed as marginal cost per year-life saved (MCYLS).

RESULTS. The MCYLS varied from $18,800 to $16,100. For all strategies this was within the range of other generally acceptable diagnostic and therapeutic medical procedures. There was a 14% decrease in MCYLS from the least cost-effective to the most cost-effective strategy.

CONCLUSIONS. Cost-effectiveness of four age-related mammographic screening strategies was evaluated. The MCYLS for all strategies was within a generally accepted range. With increasing concerns regarding the cost of health care, this information may be useful in health policy decision-making. ***Cancer* 1998;82:2235–40.** *© 1998 American Cancer Society.*

KEYWORDS: mammography, screening, cost-effectiveness, breast, carcinoma.

Several recent investigations have provided additional information regarding the efficacy of screening mammography for the reduction of mortality from breast carcinoma. These studies have helped clarify two controversial issues. First, two separate Swedish trials and a meta-analysis of existing clinical trials have shown statistically significant reductions in breast carcinoma mortality for women ages 40–49 years who undergo screening.[1] Second, for women in their 40s these studies have demonstrated that biennial screening mammography is likely to be significantly less effective than more frequent screening.[2,3] For women age ≥50 years, the difference in efficacy between annual and biennial mammography is not as great. These results have led to revisions in screening guidelines advocated by the American Cancer Society, the American College of Radiology, and most recently the National Cancer Institute. Although all three organizations now agree that routine screening should begin at age 40 years, a consensus has not been reached regarding the frequency of these screenings.

Until recently, most research was directed toward evaluation of the effectiveness of screening mammography, with little attention

Presented at the American Cancer Society Workshop on Guidelines for Breast Cancer Detection, Chicago, Illinois, March 8, 1997.

Address for reprints: C. John Rosenquist, M.D., Department of Radiology, UC Davis, School of Medicine, 2516 Stockton Blvd., Sacramento, CA 95817.

Received August 19, 1997; revision received December 12, 1997; accepted January 16, 1997.

TABLE 1
Probability of Malignancy, by Decade, for Biopsy of Nonpalpable, Mammographically Detected Lesions

Age (yrs)	Probability
40–49	0.22
50–59	0.32
60–69	0.44
70–79	0.52

Compiled from references 9–12.

TABLE 2
Assumed Reductions in Breast Carcinoma Mortality among Screened Women[2]

	Age (yrs)			
	40–49	50–59	60–69	70–79
Annual screening	36%	46%	44%	44%
Biennial screening	13%	39%	39%	39%

TABLE 3
Assumed Cost of Procedures

Procedure (reference)	Cost ($)
Mammography[a]	64
Fine-needle aspiration of palpable mass (community experience)	150
Core biopsy of occult lesion (community experience)	850
Excisional biopsy of occult lesion[23,24]	2800
Excisional biopsy of palpable lesions (community experience)	2400
Definitive treatment for breast carcinoma[25]	6100

[a] Includes prorated costs of breast ultrasound ($150) for 7% of patients and additional mammographic views ($50) for 5% of patients. Base cost of screening mammography is $55.

given to cost or cost-effectiveness. In the current environment of limitation of fiscal resources for medical care in all Western countries, the study of cost-effectiveness of various recommended and proposed mammographic screening programs has become an important consideration. In this investigation we used data from recent studies on the efficacy of screening mammography to reassess the cost-effectiveness of a variety of possible screening strategies.

MATERIALS AND METHODS

Description of Model

A Markov model was used to compare two hypothetic populations of women, one undergoing screening mammography and the other followed clinically without screening. The model has been described and validated previously.[4] It was formulated using a commercially available software program (Smltree, version 2.9; James P. Hollenberg, New York, NY).

In the screening arm of the model, all women had screening mammography during the first cycle (equivalent to 1 year). A decision tree was constructed for all the possible outcomes from screening examinations and subsequent diagnostic workups. A similar tree was developed for those not undergoing screening, and included development of a palpable breast mass with subsequent diagnostic studies. In both the screened and observed groups there were several possible final states of health for each cycle, including continued normal health, successful treatment of breast carcinoma, death from breast carcinoma, or death from some other cause. Data for the probability of each outcome was obtained from published studies (Tables 1–3).[5–8] The benefit for both the screened and observed group was defined as accumulated years of life for each hypothetic population during the years of the screening program.

Each cycle of the model was defined as 1 year for the population being studied. At the end of the chosen number of cycles, accrued costs (U.S. dollars) and effectiveness (years of life saved) were calculated, and the marginal cost-effectiveness was calculated by comparing the screened group with the control group.

The costs included screening mammography, diagnostic workup, short term follow-up mammography, and cost of biopsy and treatment (Table 3). Costs for the observed group included mammography and other breast imaging procedures, fine-needle aspiration, and surgical biopsies for those who developed palpable breast masses, as well as treatment for those with carcinoma.[4]

In the screened group, it was assumed that biopsies would be divided evenly between core needle biopsy technique and needle-localized surgical biopsy. The effectiveness of screening was measured as added years of life that resulted from the reduction in mortality due to the use of screening mammography. Both costs and added years of life were discounted at 3%.

Several modifications and updated assumptions to our previous model[4] were used in this analysis: 1) the assumed cost of screening mammography was reduced from $75.00 to $55.00 to reflect our experience with the more recent average reimbursement in a managed care environment; 2) discounting of 3% was used as the standard; 3) age-related differences in the probability of malignancy for biopsies of clinically occult, mammographically detected lesions were utilized and are shown in Table 1. These estimates were obtained by calculating the mean of positive biopsy rates from four studies;[9–12] and 4) recent data for

TABLE 4
Cost-Effectiveness of Various Mammographic Screening Schedules

Schedule	Marginal cost ($)	Marginal effectiveness (yrs)	MCYLS ($)
Annual, 40–79 yrs	1455	0.0775	18,800
Annual, 40–79 yrs (high risk = 10%) with biennial, 40–49 yrs Annual 50–79 yrs (normal risk = 90%)	1216	0.0669	18,200
Annual, 40–64 yrs Biennial, 65–79 yrs	1333	0.0754	17,700
Annual, 40–49 yrs Biennial, 50–79 yrs	1098	0.0681	16,100

Marginal cost: mean additional cost for women in the screened population compared with the population not screened, marginal effectiveness: mean additional years of life gained for women in the screened population compared with the population not screened, MCYLS: marginal cost per year-life saved (marginal cost/marginal effectiveness).

reductions in breast carcinoma mortality with screening mammography were used, as shown in Table 2.[2]

Cost-Effectiveness Analysis

This analysis was conducted from the societal perspective to represent the public's interest. It included all monetary costs regardless of the payor, and all benefits regardless of the beneficiary. Marginal cost was defined as the difference in total costs between the screened and observed groups. Marginal effectiveness was defined as the difference in years of life saved between the screened and observed groups. Cost-effectiveness was expressed as marginal cost per year-life saved (MCYLS), and was calculated by dividing marginal cost by marginal effectiveness. The formula for MCYLS was: MCYLS = (costs for screened group—costs for observed group)/(years of life accumulated for the screened group—years of life accumulated for observed group).

The MCYLS was calculated for each of the screening strategies that was evaluated. The initial reference case used in the analysis was annual mammography from ages 40–79 years. Other schedules analyzed included: 1) annual mammographic screening from ages 40–49 years, with biennial screening from ages 50–79 years; 2) annual screening from ages 40–64 years, with biennial screening from ages 65–79 years; and 3) annual screening from ages 40–79 years in high risk women (10%) and biennial screening from ages 40–49 years with annual screening from ages 50–79 years in normal risk women (90%). An additional strategy based on hormone status and estrogen exposure also was evaluated. In this analysis hypothetic screening was performed annually from ages 40–64 years and biennially from ages 65–79 years to simulate the group with hormone replacement (30% of total), whereas for women without hormone replacement (70% of total), the schedule was annual screening from ages 40–54 years, and biennial screening from ages 55–79 years.

The assumed breast carcinoma mortality reductions resulting from mammographic screening by decade are shown in Table 2; these assumptions were utilized for the base case for each strategy.[2] Sensitivity testing included evaluation of the effect of a range of costs of mammography, the effect of various reductions of mortality in the 40–49-years age group, and the effect of various discounting rates. A 36% reduction in mortality with annual screening in women ages 40–49 years was used for the reference case;[2] the sensitivity analysis was performed using a 25% reduction to approximate the findings of the most recent meta-analysis of the seven population-based trials[1] and a 45% reduction to simulate recent reports from the Gothenburg Trial.[3]

For the screening protocol that analyzed annual mammography in high risk women and biennial in normal risk women in their 40s, 10% of women were assumed to be at high risk because of a family history of breast carcinoma in a first-degree relative.[13] The relative risk of breast carcinoma was assumed to be 2.4 in the high risk group,[13,14] and the relative risk of breast carcinoma in the normal risk group was appropriately adjusted downward so that the disease burden in the total population of women in their 40s remained constant for each screening scenario.

All results were expressed in U.S. dollars, and were rounded to the nearest $100. For the base case in each strategy, both costs and years of life saved were discounted at a rate of 3%. Each strategy also was analyzed using a 5% discounting rate and without discounting.

RESULTS

The results for the four age-related screening strategies tested are shown in Table 4. The marginal cost, marginal effectiveness, and MCYLS are provided for each hypothetic screening program. The reference case used for the analysis was annual screening from ages 40–79 years; this schedule was the least cost-effective with an MCYLS of $18,800, but had the highest marginal effectiveness. The most cost-effective schedule was annual mammography from ages

TABLE 5
MCYLS for Annual Mammography from Ages 40–79 Years Using Various Assumptions for Mortality Reduction in the 40–49 Years Age Group

Assumed mortality reduction in 40–49 years age group	MCYLS
25%	$20,800
36% (reference case)	$18,800
45%	$17,400

MCYLS: marginal cost per year-life saved.

40–49 years with biennial screening from ages 50–79 years. The MCYLS for this schedule was $16,100. In comparison with the reference case, this schedule resulted in decreases in marginal cost, marginal effectiveness, and MCYLS of 25%, 10%, and 14%, respectively. The schedule that utilized annual screening from ages 40–79 years in high risk patients (10% of total patients) and biennial screening from ages 40–49 years combined with annual screening from ages 50–79 years in normal risk patients (90% of total patients) resulted in a MCYLS of $18,200. This was a 3% reduction when compared with the reference case. The reduction in marginal cost was 16%; however, this schedule also resulted in a 14% reduction in marginal effectiveness.

Sensitivity testing was performed for several variables. When the cost of screening mammography was varied from $35 to $75, there was a progressive increase in MCYLS for each schedule, but this did not change the relative cost-effectiveness of the schedules. Because the percentage reduction in mortality resulting from screening mammography in the 40–49-years age group remains somewhat uncertain, sensitivity testing also was performed for various assumed reductions in mortality resulting from screening mammography in the this age group (Table 5). For annual mammography from ages 40–79 years with an assumed mortality reduction in the 40–49-years age group of 36% (reference case), the MCYLS was $18,800. If the reduction in mortality was assumed to be 45%, MCYLS was reduced to $17,400, and if the reduction in mortality was assumed to be 25%, MCYLS was increased to $20,800.

The screening schedule that simulated a population of women with (30%) or without (70%) hormone replacement after menopause had a MCYLS of $16,900. This schedule was more cost-effective than annual mammography from ages 40–79 years, and was within the range of the other schedules analyzed.

In our model, discounting of costs and benefits has a significant effect on MCYLS of a mammographic screening program. For the reference case (annual mammography from ages 40–79 years), with no discounting, MCYLS was $11,400; with 3% discounting, the MCYLS increased to $18,800; and with 5% discounting, MCYLS was $26,600. Similar decreases in cost-effectiveness with discounting were observed with the other schedules (Table 6).

DISCUSSION

Recently reported data regarding the effectiveness and sensitivity of mammographic screening have resulted in a need to reevaluate the cost-effectiveness of this procedure. This especially is important for screening between the ages of 40–49 years because of increasing evidence for the effectiveness of screening in this age group. Reappraisal of cost-effectiveness also is of interest because various professional societies and governmental agencies have revised their recommendations for screening mammography. In March 1997, the American Cancer Society revised its guidelines for screening mammography and now recommends annual mammography beginning at age 40 years.[15] Concerns regarding cost-effectiveness, especially in younger women, were a part of the discussions that preceded this recommendation. Shortly thereafter the National Cancer Institute revised its recommendations to include screening mammography every 1–2 years beginning at age 40 years. They also recommended that women at high risk of developing breast carcinoma should consult with their physicians regarding possible mammography before age 40 years, and more frequent examinations thereafter. The American College of Radiology supports the recommendation of the American Cancer Society. The U.S. Preventative Services Task Force recommends screening every 1 to 2 years for women from ages 50–69 years.[16] This organization makes no recommendation for or against screening mammography for women ages 40–49 years or greater than age 70 years.

Studies have shown that the cost-effectiveness for screening mammography is similar to other generally accepted medical procedures.[17] Our previous analyses of the cost-effectiveness of different screening strategies also showed that several commonly used schedules were within this acceptable range. In the current investigation the screening schedules analyzed were similar to those previously reported. The MCYLS differ for all schedules because of changes in several of the assumptions used in the model. First, the cost of screening was reduced from $75.00 to $55.00. This

TABLE 6
Effect of Discounting on MCYLS

Schedule	Discount rate 0%	3%	5%
Annual, 40–79 yrs	$11,400	$18,800	$26,600
Annual, 40–79 yrs (high risk = 10%) with Biennial, 40–49 yrs Annual, 50–79 yrs (normal risk = 90%)	$11,211	$18,200	$25,739
Annual, 40–64 yrs Biennial, 65–79 yrs	$10,100	$17,700	$25,700
Annual, 40–49 yrs Biennial, 50–79 yrs	$9900	$16,100	$24,100

MCYLS: marginal cost per year-life saved.

lower cost more accurately reflects the current reimbursement for screening mammography. Second, discounting of 3% was used for all evaluations because this now generally is accepted as a standard for cost-effectiveness studies.[18] Third, more recent data for estimation of reduction in breast carcinoma with screening mammography were used. Finally, age-related differences in positive biopsy rates for clinically occult lesions were utilized. When compared with our previous studies, these changes resulted in greater cost-effectiveness for all schedules. In comparison with our previous study, for the reference case of annual screening from ages 40–79 years, the MCYLS was reduced from $27,100 to $18,800.[19]

In this study only one screening schedule included biennial screening from ages 40–49 years. This was the program that used annual screening from ages 40–49 years for high risk patients (10%) and biennial screening from ages 40–49 years combined with annual screening from ages 50–79 years for normal risk patients (90%). In comparison with the reference case, this schedule reduced marginal cost by 16%; however, MCYLS was reduced by only 3%. This occurred primarily because assumed mortality reduction for biennial screening from ages 40–49 years is 13%, whereas annual screening in this age group is estimated to reduce mortality by 36%. The marginal effectiveness of this schedule is the lowest of those analyzed. Because the percentage reduction in cost is nearly the same as the reduction in effectiveness when biennial screening is substituted for annual screening in the 40–49-years age group, any schedule that includes biennial rather than annual screening from ages 40–49 years would be an unlikely choice for clinical use.

The MCYLS was calculated for screening from ages 40–79 years for the 4 schedules that were analyzed. Previous studies have shown that the MCYLS is greater for the 40–49 years age group, decreases from ages 50–69 years, and increases again in the 70–79-years age group.[19] Similar results by decade would be expected for the schedules used in the current study. These differences by decade occur because of the lower incidence of breast carcinoma in younger women, and the decrease in potential years of life to be saved in older women.

For the measurement of effectiveness in this study we chose to use ''years of life saved'' rather than ''quality adjusted life years.'' This decision was made for several reasons. First, there are limited data and no generally accepted standard of how participation in a mammography screening program affects quality of life.[20–22] Second, most adjustments for quality of life relate to chronic problems that result from a particular intervention. It is much more difficult to make quality-of-life adjustments resulting from annual screening mammography. Finally, it is difficult to assess the possible positive impact of screening mammography on quality of life (e.g., the knowledge that no tumor is seen on mammography, or the establishment of better health habits resulting from annual checkups). For these reasons it was decided that comparison of studies of cost-effectiveness of mammography would be more reliable and useful if the additional variable of quality-of-life adjustment was not used.

Although several recent studies have added considerable new information regarding the effectiveness of screening mammography, agreement regarding the optimal screening schedule has not been achieved. Questions concerning cost-effectiveness have become an important issue as attempts are made to develop a consensus regarding the appropriate age and intervals for screening. Therefore, it is important to reassess cost-effectiveness using the recently published data regarding effectiveness, especially as it relates to screening in the 40–49-years age group.

In this study we found that the cost-effectiveness of all analyzed screening mammography schedules was within the range that generally is accepted for medical programs. However, it is important to note that the cost-effectiveness of the least cost-effective program was 17% greater than the most cost-effective program. In a time of increasing competition for funds for medical care, information of this type may be useful to health policy planners when making decisions regarding how best to use available resources.

REFERENCES

1. Hendrick RE, Smith RA, Rutledge JH, Smart CR. Benefit of screening mammography in women aged 40–49 years. A new meta-analysis of randomized controlled trials. *Monogr Natl Cancer Inst* 1997;22:87–92.
2. Report of the organizing committee and collaborators, Falun Meeting. Falun, Sweden. March 21–22, 1996. Breast cancer screening with mammography in women aged 40–49 years. *Int J Cancer* 1996;68:693–9.
3. Bjurstam N, Bjorneld L, Duffy SW, Smith TC, Cahlin E, Erikson O. The Gothenburg Breast Cancer Screening Trial: preliminary results on breast cancer mortality for women aged 39–49. *Monogr Natl Cancer Inst* 1997;22:53–5.
4. Lindfors KK, Rosenquist CJ. Needle core biopsy guided with mammography: a study of cost-effectiveness. *Radiology* 1994;190:217–22.
5. Bassett LW, Liu TH, Giuliano AE, Gold RH. The prevalence of carcinoma in palpable vs. impalpable, mammographically detected lesions. *AJR Am J Roentgenol* 1991;157:21–4.
6. Baker LH. Breast cancer detection demonstration project: five-year summary report. *CA Cancer J Clin* 1982;32:194–225.
7. Sickles EA. Periodic mammographic follow-up of probably benign lesions: results in 3,184 consecutive cases. *Radiology* 1991;179:463–8.
8. Costanza ME. Breast cancer screening in older women. *Cancer* 1992;69(Suppl):1925–31.
9. Kerlikowske K, Grady D, Barclay J, Sickles EA, Ernster V. Likelihood ratios for modern screening mammography: risk of breast cancer based on age and mammographic interpretation. *JAMA* 1996;276:39–43.
10. Kerlikowske K, Grady D, Barclay J, Sickles EA, Eaton A, Ernster V. Positive predictive value of screening mammography by age and family history of breast cancer. *JAMA* 1993;270:2444–50.
11. Kopans DB, Moore RH, McCarthy KA, Hall DA, Hulka CA, Whitman GJ, et al. Positive predictive value of breast biopsy performed as a result of mammography: there is no abrupt change at age 50 years. *Radiology* 1996;200:357–60.
12. Linver M. Screening pre and post menopausal women: outcome data from New Mexico. American Cancer Society workshop on guidelines for breast cancer detection. Atlanta: American Cancer Society, 1997.
13. Colditz GA, Willett WC, Hunter DJ, Stampfer MJ, Manson JE, Hennekens CH, et al. Family history, age, and risk of breast cancer: prospective data from the nurses' health study. *JAMA* 1993;270:338–43.
14. Slattery ML, Kerber RA. A comprehensive evaluation of family history and breast cancer risk: the Utah population database. *JAMA* 1993;270:1563–8.
15. Leitch AM, Dodd GD, Costanza M, Linver M, Pressman P, McGinnis L, et al. American Cancer Society guidelines for the early detection of breast cancer: update 1997. *CA Cancer J Clin* 1997;47:150–3.
16. U.S. Preventive Services Task Force. Guide to clinical preventive services. 2nd edition. Baltimore: Williams and Wilkins, 1996:73.
17. Tengs TO, Adams ME, Pliskin JS, Safran DG, Siegel JE, Weinstein MC, et al. Five-hundred life saving interventions and their cost-effectiveness. *Risk Anal* 1995;15:369–90.
18. Weinstein MC, Siegel JE, Gold MR, Kamlet MS, Russell LB. Recommendations of the panel on cost-effectiveness in health and medicine. *JAMA* 1996;276:1253–8.
19. Rosenquist CJ, Lindfors KK. Screening mammography in women aged 40–49 years: analysis of cost-effectiveness. *Radiology* 1994;191:647–50.
20. DeKoning HJ, van Ineveld BM, van Oortmarssen GJ, de Haes JC, Hubertine JA, Hendriks JH. Breast cancer screening and cost-effectiveness: policy alternatives, quality of life considerations and the possible impact of uncertain factors. *Int J Cancer* 1991;49:531–7.
21. Hall J, Gerard K, Salkeld G, Richardson J. A cost utility analysis of mammography screening in Australia. *Soc Sci Med* 1992;34:993–1004.
22. Forrest P. Breast cancer screening: report to the health ministers of England, Wales, Scotland and Northern Ireland. London: Department of Health and Social Security, 1986.
23. Parker SH, Lovin JD, Jobe WE, Luethke JM, Hopper KD, Yakes WF, et al. Stereotactic breast biopsy with a biopsy gun. *Radiology* 1990;176:741–7.
24. Schmidt R, Morrow M, Bibbo M, Cox S. Benefits of stereotactic aspiration cytology. *Admin Radiol* 1990;9:35–42.
25. Eddy DM, Hasselmad V, McGivney W, Hendu W. The value of mammography screening in women under age 50 years. *JAMA* 1988;259:1512–9.