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COST-EFFECTIVENESS OF DIGITAL MAMMOGRAPHY BREAST CANCER SCREENING: RESULTS FROM ACRIN DMIST

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Abstract

Background—The Digital Mammography Imaging Screening Trial (DMIST) reported improved breast cancer detection with digital compared with film mammography in select population subgroups, but the economic value of digital relative to film mammography screening has not been assessed.

Objective—To evaluate the cost-effectiveness of digital mammography screening.

Design—Validated discrete-event simulation model.

Data Sources—DMIST data and publicly-available U.S. data.

Target Population—U.S. female population age 40 and older.

Time Horizon—Lifetime.

Perspective—Societal, Medicare.

Interventions—All-film mammography screening; All-digital screening and Targeted digital screening: Age-targeted (digital for women <50) and Age-density-targeted (digital for women <50 or ≥50 with dense breasts).

Outcome Measures—Cost per quality-adjusted life year (QALY) gained.

Results of Base-Case Analysis—All-digital screening cost $331,000 (95%CI: $268,000, $403,000) per QALY gained relative to All-film, but was more costly and less effective than targeted digital screening. Targeted digital screening resulted in more screen-detected cancers, and fewer cancer deaths than either All-film or All-digital screening with cost-effectiveness estimates ranging

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from $26,500 (95%CI: $21,000, $33,000) per QALY gained for Age-targeted digital to $84,500 (95%CI: $75,000, $93,000) per QALY gained for Age-density-targeted digital. In the Medicare population, Density-targeted digital screening cost-effectiveness varied from a base-case estimate of $97,000 (95% CI: $77,000, $131,000) to $257,000 per QALY gained (95%CI: $91,000, $536,000) in the alternative case analyses where assumptions about digital performance in women with non-dense breasts were dampened.

Results of Sensitivity Analysis—Results were sensitive to the cost of digital mammography and to the prevalence of dense breasts.

Limitations—Results dependent on model assumptions and DMIST findings.

Conclusions—Relative to film mammography, All-digital screening is not cost-effective. Age-targeted digital screening appears cost-effective while Density-targeted strategies are more costly and of uncertain value particularly among women age 65 and older.

INTRODUCTION

The Digital Mammographic Imaging Screening Trial (DMIST), a study conducted by the American College of Radiology Imaging Network (ACRIN) that enrolled 49,528 asymptomatic women presenting for screening mammography in the U.S. and Canada, reported no statistically significant difference in diagnostic accuracy between digital and film mammography across the entire study population (1). Nonetheless, the finding that digital mammography was more effective at detecting breast cancer compared to conventional film mammography in women under age 50, pre- and perimenopausal women, and women with dense breasts, without an increase in false positives, has increased demand for digital mammography.

Although breast cancer screening with film mammography is reasonably cost-effective (2-6), the value of the newer digital technology relative to film mammography has not been addressed. The cost-effectiveness of digital mammography is an important policy question because Medicare, which finances mammography screening for women age 65 and older, currently reimburses $50 more per screening exam for digital than for film mammography. To determine whether increased costs of digital mammography screening are warranted by health gains among the millions of women who undergo screening mammography each year in the U.S., we assessed the cost-effectiveness of digital relative to film mammography breast cancer screening from a societal perspective utilizing data collected for this purpose in DMIST.

METHODS

We used a validated computer-based breast cancer natural history model (7) to project the likely impact that breast cancer detection with digital mammography would have on the U.S. female population age 40 and older in 2000. The model incorporated DMIST data on mammography performance characteristics and work-up resource utilization. Strategies considered were: 1) “All-film”: film for all women; 2) “Targeted Digital” including 2a) “Age-targeted”: digital for women age <50 and film for women age ≥50 years; 2b) “Age-density-targeted”: digital for women age <50, or age ≥50 with radiographically dense breasts, and film for others; and 3) “All-digital”: digital for all women (Figure 1). The analysis was repeated for women in the subgroup age 65 and older (the Medicare population) with All-film, “Density-targeted”: digital for women with dense breasts, film for others; and All-digital screening evaluated. To evaluate digital mammography, each digital screening strategy was substituted for All-film screening in the year 2000 and applied to future years until all women age 40 or older in 2000 died. Simulated years beyond 2000 had breast cancer risk, mammography utilization, and adjuvant therapy maintained at year 2000 patterns, because the natural history model was validated based on data available through this time period (7). For each screening strategy, every individual woman's costs and health outcomes were counted from 2000 until her death with a 3% annual discount rate (8). Simulations computing total costs and QALYs using the same time period and population were completed for each screening scenario. Screening strategies were ranked according to increasing mean total costs and incremental costs, then changes in QALYs, and incremental cost-effectiveness ratios were computed for each more costly strategy (8). Mean cost per QALY gained and 95% confidence intervals were computed from 50 independent simulations. The implications of alternative assumptions about modality sensitivity, breast density and digital mammography cost on the cost-effectiveness of the screening strategies were evaluated in sensitivity analyses.

Model

Developed at the University of Wisconsin as part of the National Cancer Institute's Cancer Intervention and Surveillance Modeling Network (7), the U.S. population-based model simulates life histories of women utilizing four interacting processes: 1) breast cancer natural history, 2) breast cancer detection, 3) breast cancer treatment, and 4) competing cause mortality. Described in detail elsewhere (7), the simulation incorporates actual age-specific U.S. screening patterns (9), observed secular trends in cancer risk (10), and dissemination of adjuvant treatment (11-14) from 1975-2000 and assumes that a fraction of all early-stage breast cancers are clinically irrelevant (i.e., they do not lead to breast cancer mortality if left undetected). The model has been shown to replicate changes in annual age- and stage-specific breast cancer incidence in the U.S. population. The model was recently used to assess the role of breast cancer screening and adjuvant therapy on breast cancer mortality (15) and to evaluate cost-effectiveness of a range of film mammography screening policies (6).

Mammography Performance Characteristics

Performance characteristics were estimated from DMIST separately for film and digital mammography for each strategy-relevant age and breast-density subgroup (Table 1, detail by subgroup in Appendix). Most DMIST participants had both film and digital exams; radiologists independently read mammograms and recorded recommendations for additional work-up based on each modality (16). Mammograms were considered positive in the present analysis if the radiologist recommended additional evaluation or assigned a score 0 (incomplete data), 4 (suspicious appearing abnormality) or 5 (findings highly suggestive of cancer) based on the American College of Radiology Breast Imaging Reporting and Data System® (BI-RADS®) classification (17) . This definition was used because of its tangible meaning in clinical practice and differs from more academic mammogram positivity definitions used in the primary DMIST report (1) and a follow-up paper that makes a thorough statistical investigation of subgroups using receiver operating characteristic (ROC) curve analysis (18). For the present analysis, true cancer status was defined as positive or negative by whether or not breast cancer was diagnosed within 455 days of the screening mammogram, the definition used in the primary ROC analysis (1). Note that sensitivity and specificity estimates in the primary DMIST report used a 365, rather than a 455, day window (see Appendix).

DMIST performance characteristics were incorporated into the simulation via model calibration because sensitivity is a model output rather than a direct input. Breast cancer detection is modeled as an age-specific increasing function of tumor size and calendar year. These detection probability functions were adjusted until the overall average simulated sensitivity in year 2000 approximated DMIST results for relevant subgroups as shown in Table 1.

The base-case analysis, which was undertaken for both women age 40 and older (U.S. population) and women age 65 and older (Medicare population), intentionally assumed comparable sensitivity for digital and film mammography because analyses did not identify statistically significant overall differences between modalities (1) or for age-density-specific subgroups (18). An “alternative-case” analysis was undertaken as a sensitivity analysis to examine the impact that higher film sensitivity would have on the cost-effectiveness of digital mammography among older women (age 65 and older). The alternative-case was motivated both by observed DMIST point estimates of sensitivity (1,18) and previous studies (19-21). The primary difference between the base- and alternative-case assumptions is in the sensitivity of All-film screening. Under alternative-case assumptions the sensitivity of “All-Film” was increased to 0.59 (vs. 0.54 in base-case), while the sensitivity for “All-digital” was lowered to 0.51(vs. 0.54 in base-case). For the alternative-case density-targeted strategy, the sensitivity for digital mammography among women with dense breasts was modeled as 0.58 (vs. 0.55 in base-case) while the sensitivity for film among women without dense breasts was modeled as 0.62 (vs. 0.59 in base-case). Averaging across women with dense and non-dense breast, the sensitivity for density-targeted strategies under the Alternative-case was 0.60 (vs. 0.57 under the base-case).

Breast Density

Breast density in DMIST was defined as mammographic density recorded by the radiologist interpreting the film mammogram using the BI-RADS classification (17) (1 = fatty, 2 = scattered density, 3 = heterogeneously dense, and 4 = extremely dense). Women with dense breasts were considered those rated as having either heterogeneously or extremely dense breasts. To model strategies that targeted screening modality based on mammographic breast density, the population was split into two subgroups, those who have dense breasts and those who do not. We assumed 40% of all women have dense breasts throughout their lifetime (matching the observed proportion among women aged ≥ 50 years in DMIST) and have increased risk of breast cancer (relative risk=1.5) (22). We simulated the remaining 60% to have decreased risk of breast cancer onset such that the overall population risk was equal to the age- , year-, and cohort-specific population risk originally used in the simulation (10).

Screening Patterns

All strategies used screening patterns similar to the observed dissemination of mammography in the U.S. These patterns were informed and validated using data from the National Health Interview Survey and the Breast Cancer Surveillance Consortium (9). Age of screening initiation was assigned based on birth year, and screening frequency (annual, biennial or irregular) varied by age. The proportion of women participating increased by calendar year following observed dissemination (23). By 2000, over 50% of women were participating in screening routinely every 1 to 2 years while approximately 20% never participated in screening (15).

Costs

Resource utilization by service type and counts of distinct visits for screening and further diagnostic work-up was recorded for each DMIST participant for 12 months following the DMIST exams or before the next routine screen, whichever time was shorter. Unit costs were assigned using 2005 U.S. average Medicare reimbursements (Table 2A), and total costs for each participant were computed. Since participants had both digital and film screening mammograms, but only one diagnostic workup, for purposes of estimating work-up costs the DMIST exam was considered positive if either film or digital was positive (defined above) and negative otherwise. Average costs were computed across women who had true positive, false positive, and true negative DMIST screening mammograms and utilized in the cost-effectiveness analysis. False negatives were assumed to incur costs later as a true positive screen or interval case. Interval cancers were assigned the cost of a true positive plus an added office visit. Cost estimates for subsequent work-up, which involved diagnostic mammograms, were based on the type of screening initially used. Breast cancer treatment costs were based on published studies (25) (Table 2B).

Personal time costs associated with distinct visits for diagnostic work-up were estimated from the DMIST quality-of-life sub-study, described elsewhere (16). In brief, a random sample of participants with a positive mammogram were asked to estimate retrospectively for each visit type (imaging or biopsy) how much time away from usual activities was required. Response categories were: less than 2 hrs, 2-4, 4-6, 6-8 and more than 8 hours. Average times were computed for each visit type using category midpoints and valued based on average wages plus non-health benefits for women age 35 and older (26-28), which we estimated at $16.29 per hour.

Quality of Life

To estimate quality-adjusted life expectancy, age-specific U.S. female average health state values were derived from Medical Expenditure Panel Survey data applying the EuroQoL EQ-5D using U.S. scoring (29), which were adjusted to represent breast cancer health states (Table 2C).

Role of the Funding Source

The funding sources had no role in the design, conduct, or reporting of this study or in the decision to submit the manuscript for publication.

RESULTS

Additional Imaging Costs

The mean additional work-up costs beyond those associated with the screening exam ranged from under $15 for those with true negative screening mammograms to approximately $1,600 for those with true positive outcomes (Table 3). Personal visit time cost accounted for $3, $53, $40 and $106 for women with true negative, false positive, false negative and true positive screening mammograms, respectively.

Cost-Effectiveness Analysis

Selective use of digital mammography for women age 40 and older had costs per QALY gained ranging from $26,500 (95%CI: $21,000, 33,000) for Age-targeted to $84,500 (95% CI: $75,000, $93,000) for Age-density-targeted digital screening (Table 4). In contrast, using All-digital screening cost more and was slightly less effective than Age-density-targeted digital screening. All-digital screening was also more costly and no more effective than Age-targeted digital screening. The cost per QALY gained for All-digital relative to All-film was $331,000 (95%CI: $268,000, $403,000).

Among women age 65 and older, Density-targeted digital screening cost $97,000 per QALY gained (95%CI: $77,000, $131,000). Relative to the Density-targeted strategy, All-digital screening was more costly and resulted in slightly lower QALYs per woman. Under the alternative case analysis for older women, Density-targeted digital screening became much more costly at $257,000 per QALY gained (95%CI: $91,000, $536,000). All-digital screening remained more costly and less effective (i.e., more cancer deaths and fewer QALYs per woman) than All-film screening.

When the relative risk of developing breast cancer among women with dense breasts was varied from 1.0 to 3.0 (base-case 1.5), the cost-effectiveness of Age-density-targeted strategies changed by less than $5,000. In contrast, varying the prevalence of women with dense breasts from 25% to 50% (base-case 40%) had a marked impact on the cost-effectiveness of Density-targeted strategies. When prevalence was 25%, the cost per QALY gained for density-targeted screening dropped from $84,200 to $53,800. When prevalence of dense breasts was 50%, the cost per QALY gained increased to $106,000. This finding was consistent across relative risks (data not shown).

As the cost of digital mammography was lowered from its 2005 Medicare reimbursement amount ($50 more than film), the economic value of targeted digital strategies improved (Figure 2); however costs per QALY gained remained high under the sensitivity analysis for those 65 and older until digital mammography cost approached that of film. All-digital screening was less effective than targeted digital screening, therefore its value did not improve with decreased digital costs.

DISCUSSION

To address the economic value of breast cancer screening with digital rather than conventional film mammography, we incorporated DMIST estimates of sensitivity and specificity using clinically-based definitions of mammogram positivity and DMIST resource utilization data in a model-based cost-effectiveness analysis. This analysis has policy relevance for insurers who must decide whether the higher costs of digital mammography screening are justified by improved health outcomes. Based on DMIST finding, our analysis indicates that digital mammography screening does not result in sufficient health gains to warrant its increased cost unless its use is limited to younger women. Under current mammography reimbursements, All-digital mammography screening is not cost-effective, because it is more costly and it does not improve health outcomes relative to selective use of digital screening (i.e., Age- , Age-density-, or Density-targeted screening strategies). While Age-targeted digital mammography screening, which restricts digital mammography use on the basis of age, has favorable economic value ($26,500 per QALY gained), strategies that direct digital use on the basis of breast density are of questionable value. Relative to age-targeted digital screening, the cost-effectiveness of density-targeted screening was much less favorable ($97,000 per QALY gained in base-case) and uncertain ($257,000 per QALY gained in alternative-case with wide confidence interval).

This cost-effectiveness analysis was challenging because although DMIST found no statistical difference in overall diagnostic accuracy between modalities, it showed digital mammography to be more accurate in women under age 50 and those with dense breasts (1,18). Because our analysis had to account for all subgroups and the overall result simultaneously, this presented a dilemma—particularly in women age 65 and older where film was observed to have a higher, but not statistically higher, sensitivity. To examine the impact of changing the sensitivity of the modalities among older women, the alternative-case analysis was undertaken. The results of this analysis highlighted the striking negative impact that just slightly higher sensitivity for film in older women may have on the economic value of Density-targeted screening. While we speculate that digital mammography as performed in DMIST may have been optimized for screening dense rather than non-dense breasts, it is important to note that medical technologies are always evolving. Indeed, it is likely that improvements to both film and digital mammography have been implemented since completion of DMIST. In addition, although mammography sensitivity appeared to vary markedly in older women according to breast density, very few cancers in DMIST occurred among Medicare-aged women with dense breasts. This makes sensitivity estimates for both modalities uncertain in this population subgroup and highlights challenges inherent in subgroup analyses even in very large prospective screening studies such as DMIST, which enrolled over 45,000 women.

The economic value of breast cancer screening reported in our study is similar to previous reports (2-6). For example, an evaluation of film screening programs by Stout et al. (6), which applied the Wisconsin simulation model (7), reported costs per QALY gained ranging from $27,000 to 58,000 in 2000 US dollars for film-based strategies differentiated on screening interval, and age of initiation/ termination. Gains of 1.7 million QALYs among 95 million women were reported, which translate into an average gain of 0.018 QALYs per women relative to no screening. QALY gains in our analysis were much more modest because we did not complete our analysis relative to "no screening." Instead, we focused on screening strategies with digital mammography relative to status quo film screening where even smaller incremental benefits per woman screened would be expected. When measured as average individual gains in life expectancy in the population the benefits of screening are modest, yet the lifetime discounted costs are notable. This is true of most screening programs and the reason their economic value is assessed as a ratio of cost per unit of health gained.

Our analysis has limitations. First, we utilized Medicare standardized payment amounts as a surrogate for mammography cost. Medicare reimbursement for digital mammography has unknown relation to its actual cost. There is need for detailed cost studies of the modalities in a changing radiology environment. Costs to providers undoubtedly vary by the amount of digital technology they have adopted in other areas of their practices. While digital mammography equipment is priced higher than film, it is possible that the infrastructure costs for supporting digital are less than they are for film mammography in otherwise all-digital departments. That said, for the age 65 and older population it appears unlikely that there is a measurable health benefit to digital mammography screening.

Second, we did not account for any added cost for establishing breast density prior to screening initiation. By ignoring these costs we provided optimistic estimates of the value of Age-density and Density-targeted screening strategies. However, because costs per QALY gained for these screening strategies already exceeded $50,000 by substantial margins, these strategies would not be viewed as having highly favorable economic value (30).

Third, DMIST showed digital mammography screening to be more sensitive than conventional film mammography for pre- and perimenopausal women and for women with dense breasts. We have recast the DMIST data by age groups, breaking at ages 50 and 65 due to structural limitations in our simulation model. The age 50 cut-point in the analysis approximates the mean age at which U.S. women experience menopause (52 years) and is therefore a close surrogate for analysis by menopausal status. Selective use of digital mammography based on age-targets has appeal because of the ease with which it can be implemented. In contrast, targeting based on density carries with it the inherent problem of appropriately classifying women by breast density, which may change over time (31). Nonetheless, recently reported findings suggest that mammographic density is a risk factor that should be considered in clinical counseling (32,33).

Fourth, our analysis considered the economic value of alternative breast cancer screening strategies from a societal perspective, and not from a practice-based perspective. While targeting digital mammography use on the basis of age is likely to be an appealing way to direct scarce digital mammography availability in large centers running multiple machines in the near-term, it may not be economically viable in the long-run. A practice-based perspective will be of interest to many mammography centers as they weigh the cost of investing in and maintaining a digital mammography unit against the cost of maintaining film units with the associated film storage and retrieval costs.

Finally, our analysis did not evaluate the cost-effectiveness of screening strategies that utilize <u>both</u> film and digital mammograms to screen a woman (34). However, it is not likely that such a screening strategy could produce enough additional life years or QALYs to warrant a near doubling in screening costs. In addition, we did not evaluate strategies involving breast MRI, which has previously been evaluated for high-risk populations (35). Although breast MRI is recommended for screening high-risk populations (36), to date no groups have advocated it as a modality for use in routine general screening.

Based on potential impact on the economic value of digital mammography screening, our analysis identified several areas that warrant further investigation. Most prominent among these is the accuracy with which each modality detects breast cancer among older women with non-dense breasts. If digital mammography proves inferior to film in this subgroup, it would have important policy implications as highlighted in the alternative case sensitivity analysis. As more is learned about the measurement of breast density and the its role as a breast cancer risk factor (e.g., impact of longitudinal breast density changes), the cost-effectiveness of additional breast cancer screening strategies will need to be reassessed. In addition, recently observed trends in both breast cancer incidence and screening behavior warrant consideration (37-40) . Although trend changes have been modest among younger women where our analysis suggests that digital mammography screening has most value, declines in breast cancer incidence and screening among older women are unlikely to improve the cost-effectiveness of digital mammography screening.

In summary, our analysis addresses the likely population impact that screening with digital mammography would have on the health of the population. When digital mammography is used in a targeted fashion, it is projected to increase the number of screen-detected cancers and to lead to fewer cancer deaths when compared with film screening. Do these changes result in sufficient long-term health gains to warrant the increased costs associated with digital mammography screening? Our findings suggest that while Age-targeted digital mammography screening is cost-effective, other approaches to digital mammography screening are not. Some may question the relevance of our analysis: Why compare digital mammography to film when film is quickly becoming obsolete? An important reason to do so is to gain insight into how various population subgroups are affected by technological innovation. DMIST results suggest no clear benefit for digital mammography screening in the elderly and also provide a hint that some elderly subgroups (e.g., those with non-dense breasts) may have better breast cancer detection with film rather than digital mammography (18). The DMIST cost-effectiveness analysis has shown how a shift to All-digital mammography screening has the potential to result in health gains for younger women (especially those with dense breasts) possibly at the expense of older women (especially those with non-dense breasts). We conclude that age-targeted digital mammography screening is at present the most efficient approach to provision of digital mammography screening in the US population.

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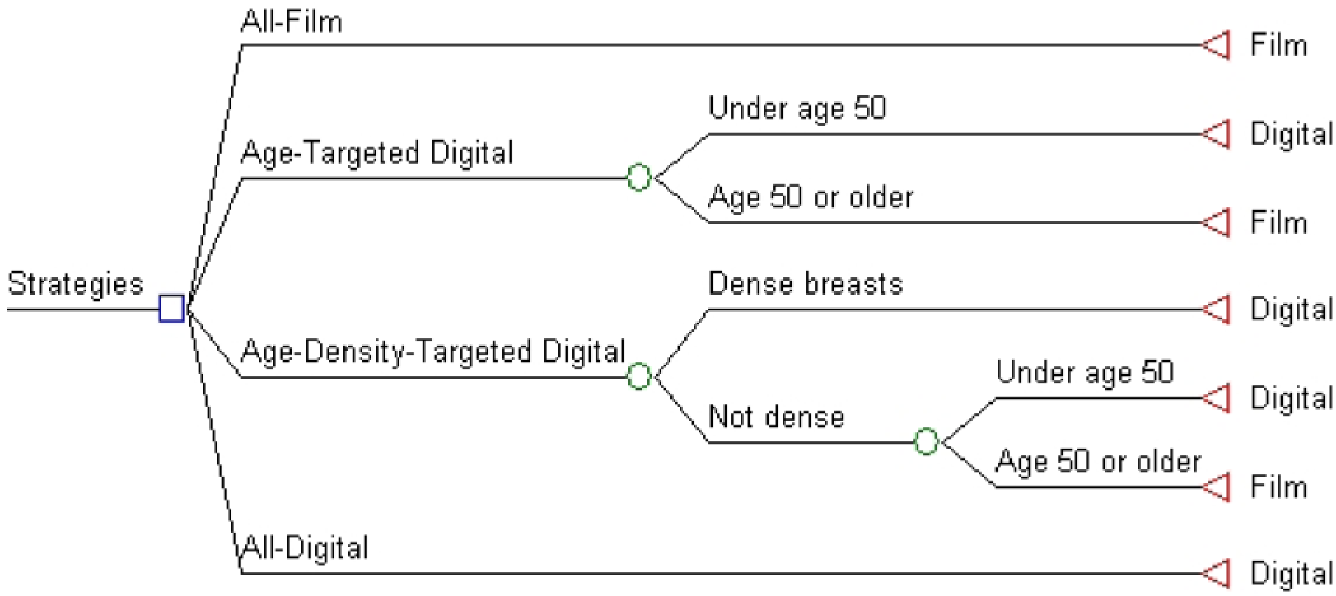

Figure 1.
Diagram of screening strategies evaluated. Each year women enter either a “Film” or “Digital” simulation on the basis of their breast density and current age.

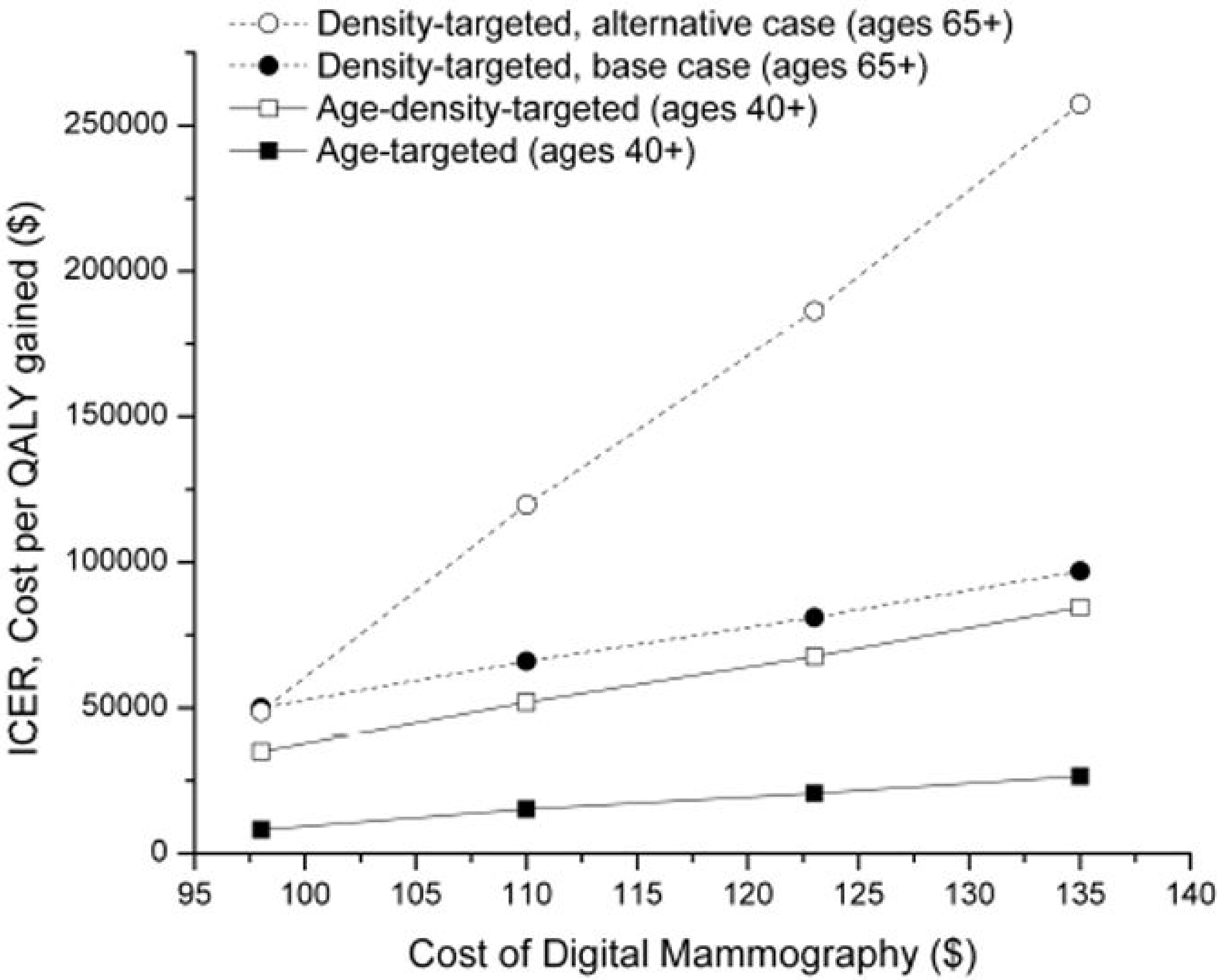

Figure 2.
Impact of digital mammography cost on the incremental cost-effectiveness ratio (ICER) reported as cost per QALY gained in 2005 US Dollars for various screening strategies, age groups, and assumptions. Digital mammography cost may be interpreted as a premium over film where $98 represents a $12 premium and $135 represents a $50 premium over film. The ICER for Age-density-targeted screening is computed relative to Age-targeted screening. ICERs for all other strategies are computed relative to film screening.

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Table 1

Screening strategies and performance characteristics associated with mammography use for relevant population subgroup in: A) Women age 40 and older (general population) and B) Women age 65 and older (Medicare population). Sample sizes shown in the table reflect the number of women with breast cancer in DMIST used to estimate sensitivity within each strategy.

	DMIST Performance				Base-Case Modeled Peformance*	
Screening Strategies	**Sensitivity†**	**(95% CI)**	**Specificity**	**(95% CI)**	**Sensitivity**	**Specificity**
A) Women age 40 and older						
All-Film (n=334)	0.52	(0.47, 0.57)	0.92	(0.92, 0.92)	0.52	0.93
Age-targeted:						
Digital if age <50 yr (n=72)	0.68	(0.56, 0.77)	0.90	(0.90, 0.91)	0.68	0.90
Film if age 50+ yr (n=262)	0.54	(0.48, 0.60)	0.93	(0.92, 0.93)	0.53	0.93
Age-density targeted:						
Digital if age <50 (n=72)	0.68	(0.56, 0.77)	0.90	(0.90, 0.91)	0.68	0.90
Digital if age 50+ & dense breasts (n=113)	0.56	(0.47, 0.65)	0.91	(0.91, 0.92)	0.55	0.91
Film if age 50+ & not dense (n=148)	0.59	(0.51, 0.66)	0.94	(0.93, 0.94)	0.55	0.94
All-Digital (n=332)	0.56	(0.50, 0.61)	0.92	(0.92, 0.92)	0.55	0.93
B) Women Age 65 and older						
All-Film (n=96)	0.62	(0.53,0.72)	0.93	(0.93, 0.94)	0.54	0.93
Density- targeted:						
Digital if dense (n=33)	0.55	(0.38, 0.70)	0.91	(0.90, 0.92)	0.55	0.91
Film if not dense (n=62)	0.69	(0.57, 0.79)	0.95	(0.94, 0.95)	0.59	0.95
All-Digital (n=94)	0.53	(0.43, 0.64)	0.93	(0.92, 0.94)	0.54	0.93

*Sensitivity observed in simulation model after calibration to DMIST performance characteristics.

†A 455 day window was used to assess cancer status in these analyses.

Table 2

Costs (2005 U.S. dollars) and health state values used in the cost-effectiveness analysis: A) Unit costs used to estimate work-up costs, B) Breast cancer treatment costs by time since diagnosis and stage at diagnosis, and C) Health state values by age and breast cancer status.

A) Unit Costs

Screening Mammogram	**CPT Code(s)**	**Cost**
Screen-Film	76092	$85.65
Digital	HCPCS* G0202	$135.29
Additional Imaging (Diagnostic)		
Diagnostic Mammogram		
Digital (unilateral)	G0206	$115.21
Screen-Film (unilateral)	76090	$78.45
Digital (bilateral)	G0204	$142.50
Screen-Film (bilateral)	76091	$97.40
Ultrasound (unilateral or bilateral)†	76645	$70.11
MRI		
unilateral	76093	$787.13
bilateral	76094	$1,037.63
Procedures		
FNA (cyst aspiration)	10022, 76942, 88172, 88173	$456.52
Core Needle Biopsy		
Ultrasound-guided	76942, 19102/19103*, 88305	$723.05
Stereotactic	76905, 19102/19103, 19295, 88305	$1,130.76
Mammography	76096, 19102/19103, 19295, 88305	$946.51
MRI-guided	76392, 19102/19103, 88305	$1,044.54
Palpation-guided	19100, 88305	$351.26
Guidance not specified	‡	$933.44
Open Biopsy		
Needle Localization	76096, 99242, 19125, 19290, 76098, 88307, 00400	$2,061.01
Palpation Guided	76098, 99242, 19101, 88307, 00400	$1,699.06
Type not specified	§	$2,061.01
2 on same day (diff breasts)		$3,053.30
Visit Costs		
Office visit with physician		$45.02
Radiology (imaging) visit personal time		$38.46
Procedure (biopsy) visit personal time		$54.11

B) Treatment Costs‖	**In Situ**	**Localized**	**Regional**	**Distant**
Initial Treatment – 1st 6 mos.	$14,510	$18,470	$20,920	$0
Ongoing Treatment	$ 1,510	$ 1,630	$ 2,430	$4,980

B) Treatment Costs[//]	In Situ	Localized	Regional	Distant
Terminal Treatment- last 6 mos.	$15,400	$20,530	$27,880	$25,560

C) Health State Values[**]

Age	Healthy	In Situ or Localized	Regional	Distant
40-49	0.86	0.78	0.65	0.52
50-59	0.84	0.75	0.63	0.50
60-69	0.81	0.73	0.61	0.49
70-79	0.77	0.69	0.58	0.46
80+	0.72	0.65	0.54	0.43

[*]Health Care Common Procedure Coding System

[†]A 10%/90% split in 19102/19103 was used for costing

[‡]Average of ultrasound-, stereotactic-, and mammography-guided

[§]Assumes needle localization

[//]Updated to 2005 U.S. dollars using the medical care component of the consumer price index (24)

[**]EuroQoL EQ-5D U.S. Population weights computed from year 2000 Medical Expenditure Panel Survey data (6). Reductions in weights of 10%, 25% and 40% were assumed for local, regional and distant breast cancer health state, respectively.

Table 3

Mean work-up costs observed within 12 months of initial screen and 95% confidence intervals (CI) among 42,760 DMIST participants by screening mammogram result and true cancer status at one year.

	No Breast Cancer				Breast Cancer			
	True Negative (n=36,670)		**False Positive (n=5,755)**		**False Negative (n=98)**		**True Positive (n=237)**	
Work-Up Costs	**Mean**	**95% CI**	**Mean**	**95% CI**	**Mean**	**95% CI**	**Mean**	**95% CI**
Additional Imaging with Film	$8	($7.92, $8.55)	$160	($158, $163)	$66	($48, $83)	$207	($185, $229)
Additional Imaging with Digital	$11	($10.41,$11.23)	$201	($198, $204)	$86	($64, $109)	$252	($228, $275)
Biopsy	$3	($1.89, $3.47)	$170	($156, $184)	$375	($239, $510)	$1,336	($1,230, $1,441)
Total Cost with Film	$11	($10.03, $11.80)	$330	($315, $344)	$441	($298, $583)	$1,542	($1,435, $1,649)
Total Digital with Digital	$13	($12.56, $14.43)	$371	($356, $385)	$461	($317, $606)	$1,587	($1,479, $1,696)

Table 4

Screening simulation results by strategy and population group and case.

Screening Strategy	Screen Detected Cancers*	Clinically Detected Cancers*	Cancer Deaths*	Cost per Woman	QALYs Per Woman	Incremental Cost per QALY Gained (95%CI)
Women Age 40 and Older: Base Case						
All Film	4,744,200	3,942,300	1,435,700	$2,749	13.280	--
Age-targeted Digital	4,785,800	3,919,500	1,430,000	$2,773	13.281	$26,500 ($21K, 33K)
Age-density-targeted Digital	5,155,600	3,780,600	1,395,900	$2,915	13.282	$84,500 ($75K, 93K)
All Digital	4,785,800	3,919,500	1,430,000	$3,056	13.281	Dominated†
Women Age 65 and Older: Base Case						
All Film	964,100	731,900	315,600	$2,058	7.325	--
Density-targeted Digital	1,062,800	698,100	308,400	$2,163	7.326	$97,000($77K, 131K)
All Digital	964,100	731,900	315,600	$2,234	7.325	Dominated‡
Women Age 65 and Older: Alternative Case§						
All Film	1,187,200	627,000	286,100	$2,086	7.330	--
Density-targeted Digital	1,187,500	625,100	284,600	$2,148	7.331	$272,000 ($103K,536K)
All Digital	1,011,700	698,700	303,000	$2,218	7.328	Dominated‡

*Approximate 95% confidence limits are ±30,500, ±30,000, and ±18,000 for screen-detected cancers, clinical-detected cancers and cancer deaths in those age 40 and over, respectively. Respective limits are ±14,000, ±13,000 and ±10,000 for women age 65 and older.

†Cost per QALY gained for All Digital vs All Film is $331,000 (see text).

‡This screening strategy is more costly and equally effective (base case) or more costly and less effective (alternative case) than all film screening.

§QALYs per woman are higher under the Alternative Case because population health when screening strategies are implemented in 2000 is affected by the accuracy of film screening in the pre-2000 period, which is higher under the Alternative Case.