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ARTICLE

Benefits, Harms, and Costs for Breast Cancer Screening After US Implementation of Digital Mammography

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Background Compared with film, digital mammography has superior sensitivity but lower specificity for women aged 40 to 49 years and women with dense breasts. Digital has replaced film in virtually all US facilities, but overall population health and cost from use of this technology are unclear.

Methods Using five independent models, we compared digital screening strategies starting at age 40 or 50 years applied annually, biennially, or based on density with biennial film screening from ages 50 to 74 years and with no screening. Common data elements included cancer incidence and test performance, both modified by breast density. Lifetime outcomes included mortality, quality-adjusted life-years, and screening and treatment costs.

Results For every 1000 women screened biennially from age 50 to 74 years, switching to digital from film yielded a median within-model improvement of 2 life-years, 0.27 additional deaths averted, 220 additional false-positive results, and $0.35 million more in costs. For an individual woman, this translates to a health gain of 0.73 days. Extending biennial digital screening to women ages 40 to 49 years was cost-effective, although results were sensitive to quality-of-life decrements related to screening and false positives. Targeting annual screening by density yielded similar outcomes to targeting by age. Annual screening approaches could increase costs to $5.26 million per 1000 women, in part because of higher numbers of screens and false positives, and were not efficient or cost-effective.

Conclusions The transition to digital breast cancer screening in the United States increased total costs for small added health benefits. The value of digital mammography screening among women aged 40 to 49 years depends on women's preferences regarding false positives.

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Over the past decade, digital mammography has rapidly replaced plain film mammography for breast cancer screening in the United States, accounting for 90% of the current market (1). This conversion was fueled in part by the 2005 Digital Mammographic Imaging Screening Trial (DMIST) report of superior digital mammography sensitivity compared with film for women aged younger than 50 years and for women with dense breasts (2). Multiple studies and recent reports from community practice show similar results as DMIST, although specificity has been modestly lower for digital mammography than film (3,4).

The overall effect of this performance trade-off on population health and economic burden is unclear for several reasons. Dense breast tissue can both mask tumors and increase the risk of breast cancer (5–8). Therefore, higher tumor detection among women with dense breasts by digital mammography could improve screening benefits. However, because breast cancer prevalence is low at any single examination, even small decrements in specificity may be associated with large increases in the number of false positives and any associated harms and costs. In the Medicare population, digital mammography has been associated with a higher rate of early-stage cancers but no change in rates of advanced disease and with higher screening and diagnostic costs compared with film (9,10). An effect on mortality has not been shown. A prior cost-effectiveness analysis of substituting digital for film mammography based on the DMIST trial assumed equivalent specificity and found that, compared with using digital mammography for all women, greater health gains could be achieved at a lower cost by reserving digital for the subgroups for whom higher sensitivity had been found, with film used in other groups (11). However, a strategy involving a mix of film and digital mammography is no longer practical in the United States given the transition to virtually fully digital facilities.

To understand the trade-offs involved in this rapid US adoption of new screening technology, we used five established

independent models developed within the Cancer Intervention and Surveillance Modeling Network (http://www.cisnet.cancer.gov) in partnership with the Breast Cancer Surveillance Consortium (BCSC; http://www.breastscreening.cancer.gov). We extended our prior collaborative modeling research (12–14) to consider the impact of breast density on both incidence and test performance in evaluating outcomes from digital vs film screening. The results are intended to contribute to policy discussions about resource allocation and how to best integrate new technology into health care.

Methods

We considered eight screening scenarios. First, the comparative effectiveness of the transition to all-digital screening in the United States was evaluated by comparing biennial digital vs film mammography from ages 50 to 74 years (eg, the 2009 U.S. Preventive Services Task Force guidelines) (15). We also examined five alternative digital screening scenarios: 1) biennial screening from ages 40 to 74 years; 2) annual screening from ages 50 to 74 years; 3) annual screening from ages 40 to 74 years; 4) annual screening from ages 40 to 49 years followed by biennial screening from ages 50 to 74 years; and 5) annual screening from ages 40 to 74 years for those with dense breast tissue (Breast Imaging Reporting and Data System [BI-RADS] 3 or 4) and biennial screening otherwise (BI-RADS 1 or 2). The last scenario was included to help guide decision-making about new state and federal legislative efforts about breast density notification (16). All scenarios were also compared with a no screening scenario.

Model Overview

The models include model D (Dana-Farber Cancer Institute), model E (Erasmus University Medical Center), model G-E (Georgetown University Medical Center and Albert Einstein College of Medicine), model M (MD Anderson Cancer Center), and model W (University of Wisconsin and Harvard Medical School) and have been described elsewhere (17–21). Briefly, they begin with estimates of incidence without screening and treatment and then overlay screening use and improvements in survival associated with adjuvant treatment. Some model continuous-time tumor growth, whereas others consider progression through discrete preclinical and clinical disease states, and one makes no natural history assumptions (Supplementary Table 1, available online). On the basis of mammography sensitivity (or thresholds of detection), screening can identify disease in the preclinical period possibly at an earlier stage or smaller size than might occur by clinical detection, resulting in a reduction in breast cancer mortality. Age, estrogen receptor status, and tumor size/stage–specific treatment have independent effects on mortality. Women can die of breast cancer or other causes. The models replicate US population breast cancer trends (12,13,17–21).

For this analysis, we used the cohort of women born in 1960. Outcomes were counted for their lifetimes, beginning at age 40, assuming they adhered to screening schedules and received recommended treatment based on age and tumor characteristics (13). All models used common inputs and assumptions (Table 1).

Model Parameters

Breast Density. Women were assigned a density based on the distribution of BI-RADS breast density categories (22) among ages 40 to 49 years observed in the BCSC (Table 1). Based on BCSC data, density was assumed to decrease by one BI-RADS category at age 50 years and remain at that level thereafter for 41% of women across all categories, reflecting perimenopausal reductions in breast density; the remainder maintained the same density after age 50 years. Breast cancer incidence (23) was conditional on relative risks by BI-RADS categories at ages 40 to 49 years (7,24).

Mammography Performance. Mammography sensitivity, specificity, and cancer detection rates were estimated for film and digital mammography by breast density, age group (ages 40–49 or 50–74 years), and screening interval (first, annual, biennial) by fitting logistic regression models to data on nearly two million examinations performed between 2001 and 2008 in women aged 40 to 74 years with BI-RADS information in the BCSC (Table 2; Supplementary Tables 2 and 3, available online). In the models, mammography performance changed according to age and breast density.

Health Effects. We estimated breast cancer mortality, mortality reductions, and life-years. Age- and sex-specific health utilities, adjusted for diagnosis and treatment, were used to estimate quality-adjusted life-years (QALYs) (Table 1) (25,26). In our base case, we assumed no utility decrements associated with screening participation or experiencing false positives. In supplemental analysis, we included small reductions in utility from screening participation (0.006 for 1 week) and a positive screen (0.105 for 5 weeks) (27).

Costs. Medicare reimbursement rates were used for costs of digital and film screens. Diagnostic costs were based on use patterns in the Group Health BCSC registry and average Medicare reimbursement rates within age and screening result strata (true positive or false positive) (Table 1; Supplementary Table 4, available online). Treatment costs were based on published estimates (28). All costs were converted to 2012 US dollars (29).

Analysis

Costs and health effects were discounted at 3% as recommended (30). The analysis was conducted using a federal payer perspective. Within models, all strategies were first compared with no screening and then ranked by total costs and compared with each other. If a strategy was more expensive and yielded fewer QALYs, it was considered "dominated." Incremental cost-effectiveness ratios between each strategy and the next most costly nondominated strategy were calculated as the difference in costs divided by the difference in QALYs. If the incremental ratio for one strategy was higher than the incremental ratio for the next more costly and effective strategy, it was considered "weakly dominated" and excluded. Final rankings were compared across models, and results per strategy and differences between strategies are presented as medians across models.

Sensitivity Analyses

Comparative modeling is one way to test the impact of model structure and parameter uncertainty on results. One-way sensitivity analyses

Table 1. CISNET breast cancer model inputs for analysis of transition from film to digital mammography*

Breast density†		Prevalence by age, %		Relative risk of breast cancer	
BI-RADS category		40–49 y	≥50 y	Base-case (5)	Sensitivity analysis (6)
1	Almost entirely fat	4.4	11.4	1	1
2	Scattered fibroglandular densities	34	51.4	2.49	2
3	Heterogeneously dense	48.2	33.2	3.64	3.34
4	Extremely dense	13.4	3.9	4.35	3.93

Screening mammography: cost by modality and associated quality of life effects‡		
	Cost, $	Quality-of-life adjustments (27)
Plain film	81.35	0.006 for 1 week
Digital	139.89	0.006 for 1 week

Diagnostic work-up: cost by age and screening mammography result and quality of life effects§				
		False positive, $		
Age group, y	True positive, $	Additional imaging	Invasive procedures	Quality-of-life adjustments (27)
40–49	2187.89	134.80	890.20	0.105 for 5 weeks
50–64	2053.74	134.80	1290.68	0.105 for 5 weeks
65–74	2065.13	134.80	1297.67	0.105 for 5 weeks
≥75	1741.30	134.80	1374.69	0.105 for 5 weeks

Treatment: cost by stage at diagnosis and phase of case and quality of life effects‖			
	Phase of care (28)		
Stage at diagnosis	Initial, $	Terminal, $	Quality-of-life adjustments (26)
In situ and localized	13 055	35 335	0.9 for 2 years
Regional	24 682	41 825	0.75 for 2 years
Distant	38 119	58 665	0.6 until death

* CISNET = Cancer Intervention and Surveillance Modeling Network; BI-RADS = Breast Imaging Reporting and Data System. Numbers in parentheses are references.

† Data from the Breast Cancer Surveillance Consortium (BCSC).

‡ National reimbursement rates for screening mammography from the 2012 Centers for Medicare and Medicaid Services fee schedule. In a sensitivity analysis, relative decrements to quality of life were applied to the woman's current age-specific health state weight based on screening participation. These decrements were not included in the base-case analysis.

§ Costs for diagnostic work-up were estimated from utilization frequencies among women in the Group Health BCSC registry. All women who had a false-positive mammogram were assumed to receive additional diagnostic imaging, and 10.6% of them were assumed to also incur invasive diagnostic procedure(s). National reimbursement rates from 2004–2005 Centers for Medicare and Medicaid Services fee schedules were applied to utilization frequencies and costs inflated to 2012 US dollars. In a sensitivity analysis, relative decrements to quality of life were applied to the woman's current age-specific health state weight based on screening participation. These decrements were not included in the base-case analysis.

‖ Treatment costs were inflated to 2012 US dollars. Initial treatment costs cover the first 12 months after diagnosis. Terminal treatment costs cover the final 12 months of life for a woman who has breast cancer. Relative decrements to quality of life were applied to the woman's current age-specific health state weight based on stage and time since breast cancer diagnosis.

were also conducted in each model to explore the impact of varying key parameters, including reductions in digital prices, improvements in digital specificity, and effects of density on incidence (6).

Results

Biennial Screening of Women Aged 50 to 74 Years vs No Screening

The five models estimated that screening women aged 50 to 74 years biennially with film mammography would result in a median reduction in breast cancer mortality of 21% (range across models = 16%–34%) compared with no screening. This translated into 32 (discounted) life-years gained per 1000 women (range = 21–48) (Table 3; Supplementary Table 5, available online). The median lifetime cost of screening and treatment was estimated to be $2.71 million per 1000 women (range = $2.12–$2.77 million), a median within-model increase of $0.49 million in costs compared with no screening.

Substituting digital mammography for film given biennial screening from ages 50 to 74 years yielded similar outcomes: a median 22% mortality reduction (range = 19%–35%) and 38 life-years gained per 1000 women relative to no screening (range = 23–49). The median within-model improvement in life years with biennial digital relative to film was approximately 2 life-years per 1000 women (0.73 days per woman) with 0.27 additional deaths per 1000 women averted. However, compared with using film, digital generated an additional 220 false positives per 1000 women and increased total costs by $0.35 million per 1000 women.

Alternative Strategies for Use of Digital Mammography

The models generated consistent rank orderings of the other digital strategies relative to biennial digital screening for women aged 50 to 74 years (Supplementary Table 5, available online). As the age range and screening frequency increased, so did the benefits, costs, and false positives. Targeting annual screening to women with high breast density was slightly more effective than targeting annual screening to women in their 40s (57 vs 56 life-years gained per 1000 women) but was also slightly more costly ($4.48 million vs $4.41 million per 1000 women) and led to more

Table 2. Mammography sensitivity and specificity by modality, screening interval, age group and breast density from BCSC, 2001–2008*

BI-RADS breast density	Age, y	Interval	Sensitivity		Specificity	
			Film	Digital	Film	Digital
1 Almost entirely fat	40–49	First	0.90	0.84	0.92	0.90
		Annual†	0.80	0.69	0.96	0.95
		Biennial‡	0.85	0.76	0.95	0.94
	50–74	First	0.93	0.88	0.93	0.92
		Annual	0.85	0.76	0.96	0.95
		Biennial	0.89	0.82	0.96	0.95
2 Scattered fibroglandular density	40–49	First	0.89	0.91	0.86	0.83
		Annual	0.78	0.82	0.92	0.90
		Biennial	0.84	0.87	0.91	0.89
	50–74	First	0.92	0.94	0.88	0.85
		Annual	0.84	0.87	0.93	0.92
		Biennial	0.88	0.90	0.92	0.90
3 Heterogeneously dense	40–49	First	0.86	0.86	0.82	0.78
		Annual	0.73	0.74	0.90	0.87
		Biennial	0.79	0.80	0.88	0.85
	50–74	First	0.90	0.90	0.85	0.81
		Annual	0.79	0.80	0.91	0.89
		Biennial	0.84	0.85	0.90	0.88
4 Extremely dense	40–49	First	0.75	0.87	0.84	0.82
		Annual	0.57	0.74	0.91	0.90
		Biennial	0.65	0.80	0.89	0.88
	50–74	First	0.81	0.90	0.87	0.85
		Annual	0.65	0.80	0.92	0.92
		Biennial	0.73	0.85	0.91	0.90

* Sensitivity and specificity were based on a 12-month follow-up period for defining interval cancers (models E and W). Sensitivity and specificity using a variable interval follow-up (models D and G-E) and cancer detection rates (model M) are available in Supplementary Tables 2 and 3 (available online). Multivariable logistic regressions were used to estimate these parameters. Covariables included age, mammography modality (film, digital), screening frequency, breast density, and an interaction between density and modality. BCSC = Breast Cancer Surveillance Consortium; BI-RADS = Breast Imaging Reporting and Data System.

† Screening exams with a prior screen between 9 and 18 months before are included in the calculation.

‡ Screening exams with a prior screen between 19 and 30 months before are included in the calculation.

Table 3. Median and range of the expected mortality reduction, breast cancer deaths averted, life-years, and quality-adjusted life-years gained relative to no screening, false positives, and total costs across five simulation models per screening scenario reported per 1000 women*

Screening scenario			Mortality reduction, %	Breast cancer deaths averted	Life-years gained	QALYs gained	False positives	Total costs, million $
No screening							0	2.03 (1.4-2.32)
Current USPSTF screening	Film	Biennial 50–74 y	21 (16–34)	5.8 (5.4–7.4)	32 (21–48)	28 (14–39)	891 (753–932)	2.71 (2.12–2.77)
	Digital	Biennial 50–74 y	22 (19–35)	6.8 (5.7–7.6)	38 (23–49)	30 (15–40)	1111 (942–1163)	3.06 (2.48–3.12)
Extending digital	Digital	Biennial 40–74 y	27 (20–42)	7.6 (7.1–9.2)	52 (33–70)	42 (23–58)	1741 (1539–1803)	3.75 (3.21–3.82)
	Digital	Annual 50–74 y	27 (21–45)	7.8 (6.9–10)	44 (25–65)	38 (16–54)	1894 (1645–1939)	3.90 (3.4–3.98)
	Digital	Annual 40–49 y, Biennial 50–74 y	28 (21–45)	8.4 (7.4–9.9)	56 (36–79)	44 (25–66)	2225 (1994–2279)	4.41 (3.89–4.47)
	Digital	Annual 40–74 y BI-RADS 3 and 4 and Biennial 40-74y BI-RADS 1 and 2	29 (22–49)	9 (7.7–10.7)	57 (38–83)	46 (26–69)	2379 (2151–2461)	4.48 (3.98–4.52)
	Digital	Annual 40–74 y	31 (23–56)	9.8 (8.2–12.2)	61 (41–95)	49 (28–79)	3014 (2698–3052)	5.26 (4.8–5.27)

* Life-years, quality-adjusted life-years, and total costs were discounted at 3% per year. BI-RADS = Breast Imaging Reporting and Data System; QALY = quality-adjusted life-year; USPSTF = U.S. Preventive Services Task Force.

false-positive mammograms (2379 vs 2225 per 1000 women) (Table 3).

Screening annually from ages 40 to 74 years resulted in the maximum life-years gained across all models (median = 61 per 1000 women) but also markedly higher costs and false positives (median = $5.26 million and 3014, respectively, per 1000 women) (Table 3).

Incremental Cost-Effectiveness Analysis

Three digital strategies were deemed efficient by all models (Table 4; Figure 1A). For instance, compared with biennial screening from ages 50 to 74 years, starting at age 40 was associated with incremental cost-effectiveness ratios ranging from $33 200 to $113 300 per QALY gained across the five models. Annual

Table 4. Incremental cost per quality-adjusted life-year gained for base-case analysis and analysis assuming small negative health-related quality of life effects from screening participation across five models*

Screening scenario		Incremental cost-effectiveness ratios by model, $/QALY									
		D		E		G-E		M		W	
		Base case	With QoL effects from screening	Base case	With QoL effects from screening	Base case	With QoL effects from screening	Base case	With QoL effects from screening	Base case	With QoL effects from screening
Digital	Biennial 50–74 y	—	—	—	—	—	—	—	—	—	—
Digital	Biennial 40–74 y	113 300	704 800	33 200	44 000	55 100	96 200	90 000	277 600	40 400	47 700
Digital	Annual 50–74 y	DOM	DOM	DOM	DOM	DOM	DOM	DOM	DOM	DOM	DOM
Digital	Annual 40–49 y, Biennial 50–74y	DOM	DOM	DOM	DOM	DOM	DOM	DOM	DOM	DOM	DOM
Digital	Annual 40–74 y BI-RADS 3 and 4 and biennial 40–74 y BI-RADS 1 and 2	168 000	DOM	73 000	122 900	181 700	DOM	264 700	DOM	59 300	72,200
Digital	Annual 40–74 y	582 000	DOM	99 500	169 400	251 600	DOM	485 100	DOM	74 400	89 600

* Strategies ranked according to increasing costs. Strategies may be either strongly dominated (greater costs and fewer quality-adjusted life-years) or weakly dominated (incremental ratio greater than next more costly strategy). Base case included only quality-of-life adjustments for age and treatment for breast cancer. Analysis that included quality-of-life effects from screening included small decrements in health-related quality of life for participating in screening and for receiving a false-positive mammogram. BI-RADS = Breast Imaging Reporting and Data System; DOM = dominated strategy; D = Dana-Farber Cancer Institute; E = Erasmus Medical Center; G-E = Georgetown University/Einstein; M = MD Anderson Cancer Center; QALY = quality-adjusted life-year; QoL = quality of life; W = University of Wisconsin/Harvard.

screening for women aged 50 to 74 years and annual screening for women in their 40s with biennial screening from ages 50 to 74 years were dominated across all models.

For the remaining two strategies on the frontier, there was variability across models in the ratios because of the relatively small incremental benefits achievable from screening. Extending annual screening to women with BI-RADS 3 or 4 breast density relative to screening all women aged 40 to 74 years biennially resulted in incremental ratios between $59 300 and $264 700 per QALY gained. Screening all women aged 40 to 74 years annually generates the most benefits, but the incremental ratios ranged from $74 400 to $582 000 per additional QALY compared with the next most costly and beneficial strategy, which reserved annual screening for those women who have the highest breast density (ie, BI-RADS 3 or 4).

When short-term negative quality of life effects from screening participation and positive test results were included, the incremental benefits between strategies were attenuated. The median cost-effectiveness ratio for extending biennial screening to women in their 40s increased from $55 100 per QALY gained to $96 200 per QALY compared with screening biennially from ages 50 to 74 years. Strategies that included more frequent intervals were dominated in three of the five models compared with biennial screening from ages 40 to 74 years (Table 4; Figure 1B; Supplementary Table 6, available online).

Sensitivity Analysis

If digital cost is reduced from $140 to that of film ($81), extending screening to women aged 40 to 49 years becomes more cost-effective (Figure 1B; Supplementary Table 7, available online). Changing digital specificity or the relative risk for breast cancer based on breast density had little effect on results (Supplementary Tables 8–10, available online).

Discussion

Five independent breast cancer simulation models evaluated the US population impact of the transition from film to digital mammography. Compared with film, all five modeling groups showed that biennial digital screening of women aged 50 to 74 years resulted in net health gains, albeit at the expense of increased false positives and overall spending. Annual digital screening from ages 40 to 74 years maximizes health benefits but markedly increases costs given the nearly twofold higher number of screens and false positives compared with biennial screening. Annual screening strategies and those starting screening at age 40 years are less effective when potential decrements in quality of life associated with being screened or having a false-positive test are considered.

Prior cost-effectiveness analyses of screening mammography (11,26,31–33) have not assessed the impact of replacing plain film with digital mammography in US community practice. Although there is good trial evidence that replacing film with digital mammography will benefit younger women and women with dense breasts (2,4) and that use of digital mammography is cost-effective in these groups (11), it is difficult to restrict new technology to specific population segments (1).

Our results indicate that the digital transition across the entire population likely increased costs with only small health benefits.

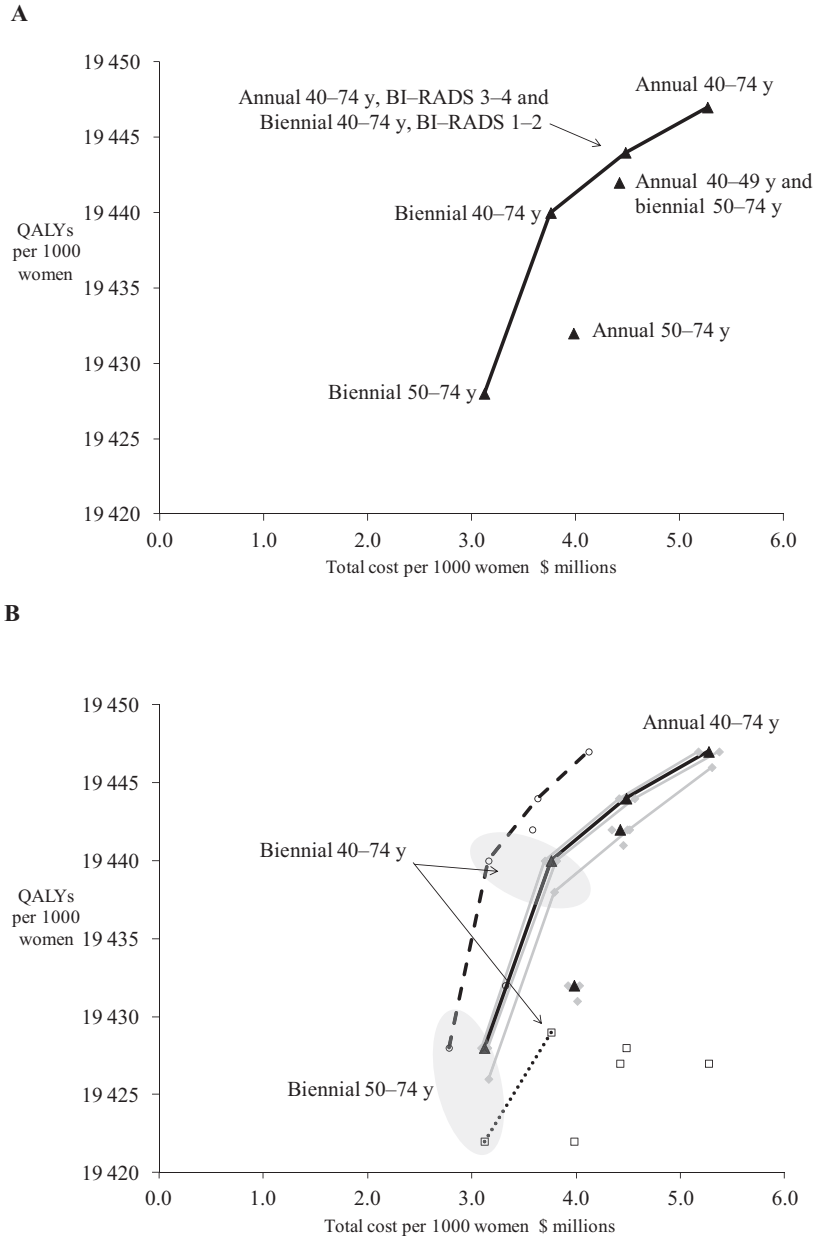

Figure 1. Discounted costs and discounted quality-adjusted life-years (QALYs) per 1000 women. **A**) Six digital screening scenarios (triangles) under the base-case assumptions for an exemplar model. Those strategies considered efficient form the efficiency frontier (**solid line**). The base case did not include quality-of-life decrements for participating in screening or for receiving a false-positive mammogram. **B**) Sensitivity analysis for an exemplar model. Changing the specificity of digital or relative risk of breast cancer by breast density (**solid gray lines, diamonds**) did not appreciably change results from the base case (**solid black lines, triangles**) in the middle. Reducing the cost of a digital mammogram improved the efficiency of screening (**dashed line, circles**), whereas including quality-of-life decrements from screening reduced efficiency (**dotted line, squares**).

Such a result was noted in an analysis of the Medicare program, where investment in the higher costs of digital screening did not reduce advanced cancer rates or treatment costs (9). Nonetheless, US screening facilities have already converted to digital technology. It is notable that the models consistently found that relative to initiation at age 50 years, extending biennial screening to women aged 40 to 49 years would lead to a median within-model gain of 5 days in life expectancy (range = 2.6–8.8), avert 1.1 additional deaths per 1000 women (range = 0.5 to 2.0), and increase costs by $0.69 million (range = $0.64–$0.73). This translates to a median incremental cost of $55 100 per QALY gained, which is generally considered of reasonable value in the United States. Annual screening, however, was either dominated or associated with incremental costs of greater than $150 000 per QALY gained in the majority of the models.

"Personalizing" screening based on age or high breast density fell short of its anticipated promise. Our prior work showed that women in their 40s who are at twofold to fourfold or greater than average risk would have similar screening benefit–harm ratios to average-risk women in their 50s (14). In this analysis, targeting digital mammography intervals at age 40 years based on breast density (annual if high density, biennial if low density) actually led to a tripling of the costs per QALY gained ($168 000 per QALY) compared with biennial screening for all women aged 40

to 74 years. This result was largely due to the small incremental benefits of annual screening in the 40s, even among women at higher-than-average risk based on breast density. This result is consistent with a prior cost-effectiveness analysis that examined screening among specific risk groups and included additional risk factors beyond breast density (31). Moreover, our results may overestimate the actual benefits achievable and underestimate costs of targeting based on density. A recent study reported that there may only be added benefit for annual screening among women aged 40 to 49 years with extremely dense breasts (BI-RADS 4) (34), whereas we modeled benefit for BI-RADs 3 and 4. We also assumed no measurement error, yet BI-RADS 2 and 3, the most prevalent categories, have low inter-rater reliability (35). Despite this, efforts to legislate supplemental screening based on breast density at the state level are increasing (16) and will need to be re-evaluated.

In the United States, the risk of having at least one false-positive film mammogram over a 10-year period of annual screening is greater than 50% (36). Given the higher false-positive rates for digital vs film, this cumulative risk will certainly be higher. Anxiety and other potential short-term quality of life effects from mammography, false positives, and invasive work-up in approximately 10% of false positives have been reported (37,38). Although small and short-lived for any individual woman, when aggregated to a population level, the impact is nontrivial. When we considered small decrements associated with these short-term outcomes, all models found that costs per additional QALY gained substantially increased for extending biennial screening to women in their 40s, and all annual screening strategies were either dominated or very costly. Overall, these results support the idea that screening in the 40s should be a personal choice rather than a universal recommendation.

Despite our consistent results, the study had some limitations. First, evidence gaps remain about the natural history of breast cancer and the effectiveness of screening and treatment. Each model accounts for these differently. Therefore there is some variability across models, which parallels our prior comparative modeling findings. For instance, models E and W tend to show the greatest benefits for more intensive screening (and therefore better cost-effectiveness), based, in part, on assumptions about treatment effectiveness (13,14,26). Some variability in results is also likely due to the small magnitude in health effects, which translate into wide ranges of cost-effectiveness ratios. Although not directly comparable because of differences in input costs and screening performance, the small incremental health benefits between strategies are consistent with prior cost-effectiveness analyses of breast cancer screening (32,39,40). Next, overdiagnosis is a key harm from screening. Overdiagnosed women do not have a change in life years and have worse QALYs because of diagnosis and treatment. These effects are reflected in comparisons of these outcomes across strategies but not explicitly as a separate outcome. Additionally, although we included differences in risk and test performance by breast density, we made the assumption that effects on risk were based on density at ages 40 to 49 years based on cumulative exposure hypothesis (7), although this may overestimate the effects of high breast density and screening benefits. Thus, our results are biased in favor of targeted screening but still do not find this cost-effective.

Our analysis was conducted from the payer perspective and did not include societal costs such as patient time costs. Inclusion of these would make the results even less favorable to more-intensive screening strategies (eg, annual screening). Additionally, we assumed 100% screening and treatment adherence to evaluate program efficacy. Actual population benefits will fall short of our projections because adherence is not perfect. Finally, digital mammography's lower specificity compared with film has partly been attributed to a learning curve, and the specificity of digital may improve over time (10,41). However, when we assumed equivalent digital specificity to film, model conclusions were unaffected, suggesting that unless specificity is dramatically improved, conclusions about the value of annual screening relative to biennial are likely to be unchanged. Thus in other countries where specificity is already much higher than the US film specificity, the cost-effectiveness of annual screening may be more favorable.

Overall, this comparative modeling research suggests that the transition from film to digital screening for breast cancer in the United States has increased costs but with small benefits in life extension, especially for women aged 40 to 49 years. However, these already small benefits are decreased substantially if women experience decrements in quality of life when being screened or experiencing (false) positive results. Such unintended consequences should be evaluated for their impact on population health and health costs ahead of the widespread adoption of new technology.

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Notes

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