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Benefits and Costs of Interventions to Improve Breast Cancer Outcomes in African American Women

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A B S T R A C T

Purpose
Historically, African American women have experienced higher breast cancer mortality than white women, despite lower incidence. Our objective was to evaluate whether costs of increasing rates of screening or application of intensive treatment will be off-set by survival benefits for African American women.

Methods
We use a stochastic simulation model of the natural history of breast cancer to evaluate the incremental societal costs and benefits of status quo versus targeted biennial screening or treatment improvements among African Americans 40 years of age and older. Main outcome measures were number of mammograms, stage, all-cause mortality, and discounted costs per life year saved (LYS).

Results
At the current screening rate of 76%, there is little incremental benefit associated with further increasing screening, and the costs are high: $124,053 and $124,217 per LYS for lay health worker and patient reminder interventions, respectively, compared with the status quo. Using reminders would cost $51,537 per LYS if targeted to virtually unscreened women or $78,130 per LYS if targeted to women with a two-fold increase in baseline risk. If all patients received the most intensive treatment recommended, costs increase but deaths decrease, for a cost of $52,678 per LYS. Investments of up to $6,000 per breast cancer patient could be used to enhance treatment and still yield cost-effectiveness ratios of less than $75,000 per LYS.

Conclusion
Except in pockets of unscreened or high-risk women, further investments in interventions to increase screening are unlikely to be an efficient use of resources. Ensuring that African American women receive intensive treatment seems to be the most cost-effective approach to decreasing the disproportionate mortality experienced by this population.

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INTRODUCTION

Breast cancer is second only to lung cancer as the leading cause of potentially avoidable cancer mortality among women.[1,2] In the last two decades, the mortality rate from breast cancer has decreased by approximately 7% in younger white women.[1] However, African American women have yet to realize similar mortality reductions, and older African American women have experienced an increase in mortality, despite a lower incidence of disease than their white counterparts.[1,3] A portion of the excess mortality seen in African American women could be caused by low rates of screening, failure to receive timely and complete diagnostic follow-up, or receiving suboptimal treatment. For instance, historically, African American women had significantly lower rates of mammography screening[4-6] and later-stage diagnosis[7-12] than did white women. Although disparities in screening rates have significantly diminished in recent years,[13] some, such as poor, minority, and older women, still remain at risk for having their cancers detected at later stages.[7] Once African American women are screened, if

they have cancer, treatment is often suboptimal.[3,14-16] Thus, there are important points in the process of breast cancer control where interventions could potentially reduce the disproportionate morbidity and mortality observed in African American women.

Prior cost-effectiveness analyses of breast cancer screening have demonstrated that reductions in mortality can be achieved at a reasonable cost per life year saved in general[17-21] as well as in selected groups of older[22-25] and/or older African American women.[25] However, there are no data regarding whether additional expenditures to enhance the cancer control process for African American women would result in improved overall survival at reasonable societal expenditures.

In this study, we use a model simulating the natural history of breast cancer to test the hypothesis that the added costs of targeted programs to increase screening or enhance receipt of intensive systemic treatment will be off-set by the downstream benefits of increased survival among African American women who develop breast cancer.

METHODS

We used an event-driven, continuous-time Monte Carlo simulation model to evaluate the costs, harms, and benefits of adding new cancer control interventions to current United States patterns of care for African American women. We compared targeted clinical screening interventions (patient reminders or lay health worker) versus status quo biennial screening or receiving optimal treatment (consistent with current recommendations) versus current patterns of care. We calculated incremental cost-effectiveness ratios, where the additional costs of a strategy, divided by the added savings in life years, are compared with the next least expensive effective strategy.[26] We also calculated intermediate outcomes, including number of abnormal mammograms, number of false-positives, number of cancers diagnosed, and stage distribution associated with each strategy. All costs and effects are discounted at 3%.[26] All scenarios were examined by generating 1.25 million simulated patients, a sample size chosen to ensure that the SE of the estimated population life expectancy would be less than 2 days. We used a matched simulation approach to maximize computer resource efficiency and maximize the precision of our effect estimates.[27] Briefly, in the analyses of screening interventions as an example, each simulated woman is simulated twice: once with screening and the other time without. The random numbers used for all variables simulated for the woman are identical in the two simulations (matched), except for the fact of screening and the events after screening. The comparison between intervention scenarios was then made by varying the proportion of simulated women who are screened versus unscreened in the given scenario.

Disease Natural History Model

We developed Monte Carlo simulations[28] to portray the dynamic processes of breast cancer incidence, detection, progression, and treatment (Fig 1). The model begins with a hypothetical cohort of 40-year-old African American women and randomly assigns dates of death, symptomatic breast cancer incidence, and date of first and subsequent biennial screening mammograms. For instance, women who are destined to get breast cancer are assigned

a date at which symptomatic illness will present. The stage of symptomatic presentation is selected randomly from age-specific distributions in unscreened women. If women are screened and the tumor is detected before this time (a true-positive screen), a new stage is calculated using Bayes' theorem with a prior distribution taken from screened breast cancer incidence rates and a conditional distribution calculated from the rates of transition through the stages (ductal carcinoma-in-situ [DCIS], local, regional, and distant) and the simulated lead time. Women who are screened but do not have their tumor detected (false-negative) return to routine screening; their tumor may be detected on subsequent screening rounds or they may present with symptomatic disease. When women develop breast cancer, they are also randomly assigned an estrogen receptor (ER) status based on their age and race (African American or not). Treatment is randomly selected based on current patterns of care, given age, African American race, stage at presentation, and ER status. Recurrence and survival probabilities are assigned based on this selection.

For women who do not develop cancer, the probability of a false-positive mammogram is based on the general age-specific specificity of mammogram and the number of mammograms received between age 40 years and the date of death. Finally, interventions designed to improve screening use and rates of receipt of intensive treatment modify events in the model (eg, increase probability of screen detection, increase survival through use of chemotherapy to treat ER-negative disease). We chose a biennial screening interval because this is the standard tested in randomized trials and the interval used in most prior cost-effectiveness analyses of breast screening.

Model Assumptions

There are several underlying assumptions in our model (Table 1). The key assumption is that the differences in distribution of ER status by race represent a proxy for general race-specific differences in tumor markers. Although biologic factors seem to only account for a small proportion of the variance in survival between African American and white women,[29,30] African American women are significantly more likely to have ER-negative tumors than white women,[31] and stage for stage, women with ER-negative tumors have shorter disease-free and overall survival than women with ER-positive tumors.[30,32-34] Although other markers of biologic variability, such as tumor differentiation,[35] S-phase fractions,[30] and new genetic biomarkers (eg, erb-b-2),[35,36] also affect survival and may vary by race, there are presently insufficient race-specific treatment and survival data by these markers to include in our model.

Second, at this time there are insufficient good-quality ER-stratified survival data for DCIS, so we assume that all women diagnosed with carcinoma-in-situ will have overall age-specific DCIS survival. We also make the simplifying assumption that lobular carcinoma-in-situ and DCIS have the same natural history and survival.

Next, although there are good-quality data for the short-term effects of the screening interventions we evaluate, there are little data available to describe their long-term effects. Although there is some evidence that effectiveness declines over time to baseline,[37] we model the interventions as having an enduring effect on the relative risk of remaining unscreened (favors enhanced screening). Fourth, because the age-, ER-, and treatment-stratified survival we used were based on up to 15 years of observation, we made several simplifying assumptions about average survival beyond this period. We assumed that women either diagnosed with DCIS
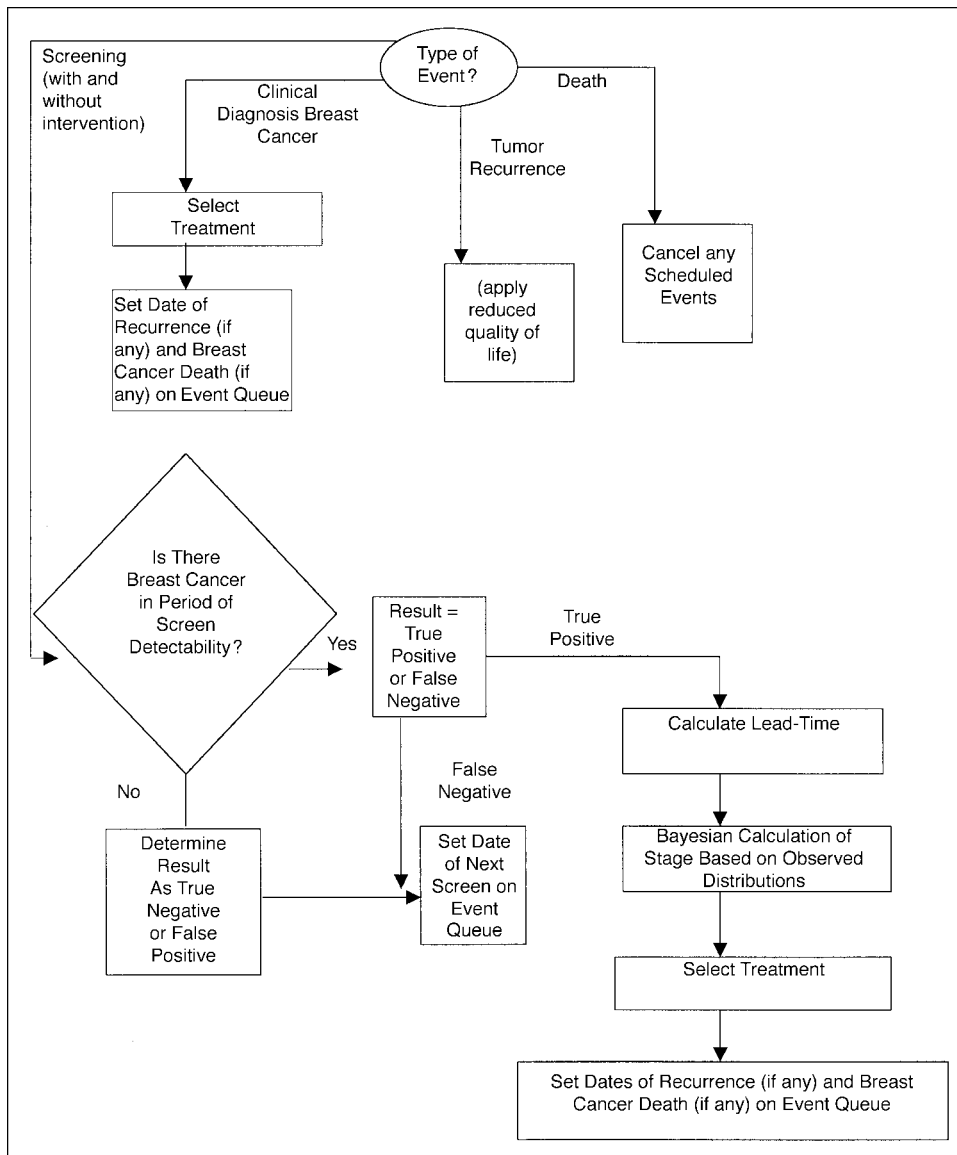
Fig 1. Model structure for evaluating the benefits and costs of breast cancer–control intervention to improve outcomes in African Americans. Flow of events processed in the simulation of the natural history of breast cancer is shown. Some events incur costs or quality-of-life reductions. At the end of the simulation, events are tallied, and costs and quality adjustments are applied.

destined to progress to local stage-invasive disease or those diagnosed with local stage who survived for 15 years without recurrence would have similar survival after that time as their age- and race-matched non–breast cancer cohort (eg, are cured). Survival for women with DCIS and local disease who have recurrent disease at 15 years, or for women with regional disease surviving 15 years, was estimated using stage-specific declining exponential approximation of life expectancy.[38] We also assume that survival is the same for women with screen-detected and clinically detected cancers. This assumption is likely to underestimate the effectiveness of mammography.

Finally, in our model, the effectiveness of mammography is represented purely by the resulting stage shift. We use the stage distributions of tumors observed in a period before mammography (1975 to 1979) and in the current period (1995 to 2001) when use was high to represent the stage distributions of clinically detected and screen-detected lesions, respectively.

Model Parameters

To estimate the probability of all costs and events in the model, we reviewed the literature for population-based studies applicable to African Americans. If race-specific data were not available, we used data from the general population. Parameters are listed in Tables 2 and 3.

Disease Natural History

Breast cancer incidence rates for African American women were estimated from Surveillance, Epidemiology, and End Results (SEER) data.[1] Stage distributions for screened and unscreened women were taken from two different sources. Data from SEER from 1975 to 1979 were used to approximate the distribution of events in the absence of screening.[1] Data from the Breast Cancer Surveillance Consortium[39] from 1995 to 2001 were used to represent the stage distribution for screen-detected African American women (Breast Cancer Surveillance Consortium, W. Barlow, per-

Table 1. Model Assumptions

Disease biology

  ER status is a proxy for race differences in biology of invasive cancer

  Lobular and ductal in-situ cancers have the same survival

  Survival after 15 years

    DCIS and local = general population

    Regional or recurrent disease = DEALE

  Screen-detected and clinically detected cancers have the same survival

Screening

  Intervention effects persist over the long term

Abbreviations: ER, estrogen receptor; DCIS, ductal carcinoma-in-situ; DEALE, declining exponential approximation of life expectancy.

sonal communication, June 2002). Screen-detected cancer was defined as a cancer diagnosed within 3 months of a positive screening mammogram performed in the absence of symptoms; screening intervals reflected average population use. Because women who were reported as having stage unknown in SEER[1] in both periods had survival rates between those of women with regional and distant disease. Therefore, among the 10% of women with missing stage for each period, we reassigned 50% as regional and 50% as distant.

Time to stage progression (eg, from DCIS to invasive cancer, from local to regional disease, or from no active disease to recurrence) was estimated based on data from randomized clinical trials of breast cancer screening and simulating stage distributions in the screened and unscreened settings.[40-44] Average dwell times were assumed to have an exponential distribution.[43,44]

Test Characteristics

We used age-specific test characteristics[45] for all races of women, because the health-insurance plan trial demonstrated similar effects of mammography on mortality for African American and white women.[40] We use different values for the sensitivity and specificity of the first versus subsequent mammogram, because the first screen detects more prevalent than incident disease. Prevalent tumors are, on average, larger than incident tumors, and potentially easier to detect than new tumors.[45]

Rates of Mammography Use

Current rates of recent mammography use are, on average, quite high (76%).[4] Because average rates may mask pockets of underscreening, we tested the cost-effectiveness of enhanced screening interventions across a range of baseline screening rates in sensitivity analyses.

Interventions to Improve Mammography Use

We evaluated the effects (and costs, discussed further herein) of patient reminder letters[46-48] and outreach by lay health workers[49-53] to increase use of initial and subsequent screening. We also considered but did not include other interventions, including church-based workers, theory-based educational counseling telephone calls, scheduling of mammography the same day as the medical referral visit, and physician reminders or audit with feedback to prompt physicians to order screening.[79,80] These latter interventions were not included because they were of similar or lesser effectiveness and/or were more costly than patient reminders and lay workers.

To estimate the effect of patient reminders and lay health workers, we combined data from studies in random-effects meta-analysis models to calculate the relative risk of remaining unscreened after the one-time application of the intervention.

Diagnostic Evaluation

We assumed that women with an abnormal mammogram undergo diagnostic evaluation; women who have breast cancer also have a staging evaluation.

Treatment

Current patterns of age-, race-, and stage-specific local surgical therapy were estimated from SEER public use files.[1] We assumed that initial decisions about use of mastectomy, breast conservation, and radiation are independent of ER status. Age- and race-specific patterns of adjuvant treatment were estimated from published data.[54] These latter data are not available by ER status.

Improving Treatment Patterns

Rates of use of adjuvant therapies are below those advocated by professional groups.[55,56] We assessed the effectiveness of providing all women with the most intensive indicated adjuvant therapy, defined as all women with ER-negative invasive tumors receiving multiagent chemotherapy and all women with ER-positive invasive tumors receiving both multiagent chemotherapy and tamoxifen. Because we are not aware of any interventions to increase use of chemotherapy, we calculated a cost threshold.

Life Expectancy

The probability of dying within each 1-year age interval beginning at age 40 years was abstracted from life tables for African American women compiled by the National Center for Health Statistics.[81] For women with breast cancer, we used pooled data from thirteen National Surgical Adjuvant Breast and Bowel Project treatment trials evaluating surgery, radiotherapy, hormonal therapy, and chemotherapy treatments among approximately 20,000 women to estimate relapse-free and overall survival up to 15 years by stage, treatment, age ($<$ 40 years; 40 to 49 years; 50 to 59 years; 60+ years), and ER status.[57-69]

Costs

We included medical care (consumable supplies, personnel, laboratory, and procedure costs) and nonmedical care (patient time costs) direct costs (Table 3). All costs are converted to year 2000 United States dollars using the medical care component of the consumer price index for the year of data collection.[82] The cost of routine screening mammography was based on an extended office visit to discuss mammography plus the costs of a mammogram.[70,71] Costs of an evaluation of a false-positive abnormal mammogram were estimated to be $93.35.[72] The costs of cancer diagnosis, treatment, continuing, and terminal care were estimated from linked SEER-Medicare reimbursement data from 1990 to 1999 using the method described by Warren et al[73] and Brown et al.[83] These phase-specific data do not specify the costs for specific therapies; rather, they provide an average of the costs of all regimens actually consumed by women in the period of observation. We assume that Medicare reimbursements, which are based on the Medicare Resource-Based Relative Value Scale, closely approximate societal costs.[84] Because Medicare does not cover the costs of tamoxifen, we added the wholesale costs of tamoxifen for women receiving this treatment.[77] The costs of optimal treatment were based on Medicare costs plus the added costs of tamoxifen and chemotherapy; chemotherapy costs were based on wholesale costs.[77] Because some chemotherapy

Table 2. Natural History of Disease Parameters in African American Women

Parameter	Estimate (%)				Reference No.
	In-Situ	Local	Regional	Distant	
Stage distribution for screen-detected breast cancers 1995-2001 for African American women* by age, years					
40-44	16.0	32.0	41.5	9.5	Breast Cancer Surveillance
45-49	25.0	38.0	31.5	6.5	Consortium, personal
50-54	18.0	48.0	22.5	12.5	communication, June
55-59	7.0	66.0	17.5	9.5	2002; 39
60-64	12.0	51.0	26.0	11.0	
65-69	17.0	46.0	24.5	12.5	
70-74	17.0	40.0	25.0	18.0	
75-79	19.0	44.0	23.5	12.5	
80-84	14.0	64.0	13.5	9.5	
85+	25.0	75.0	0	0	
Stage distribution for non–screened-detected breast cancer cases 1975-1979 for African American women* by age, years					1
40-44	3.8	38.0	48.4	9.8	
45-49	6.5	39.3	43.7	10.5	
50-54	3.4	37.5	47.7	11.4	
55-59	3.5	39.9	45.0	11.6	
60-64	3.3	38.3	44.2	14.2	
65-69	3.9	36.6	46.2	13.3	
70-74	5.8	36.4	38.4	19.4	
75-79	5.2	39.9	39.3	15.6	
80-84	0	28.6	45.9	25.5	
85+	2.5	33.3	45.1	19.1	
	Mean	95% CI	RR†	SD	Reference No.
Estrogen receptor positivity for African American women by age in years, %					31
35-49	48	42.8 to 53.2			
50-64	66	61.1 to 70.9			
65-79	76	71.5 to 81.5			
Transition probabilities for all women, *P*					40-42
DCIS-DCIS	.714			.452	
DCIS-Loc	.286			.452	
Loc-Loc	.828			.377	
Loc-Reg	.172			.377	
Reg-Reg	.916			.201	
Reg-Dist	.084			.201	
Dist-Dist	.99			0	
Dwell time for all women (time in one stage until progression to the next stage), years					43,44
≤ 59	2.1				
60-69	3				
70+	4.7				
Mammography sensitivity for all women, %					45
First screen, years					
50-59	93.6				
60-69	94.1				
70+	91.2				
Subsequent screens, years					
< 50	76.5				
50+	73.8				
Mammography specificity for all women, %					45
First screen, years					
50-59	92.9				
60-69	92.6				
70+	93.4				
Subsequent screens, years					
< 50	98.1				
50+	98.2				
Mammography use, African American women having reported mammogram in past 2 years, %					13
Median	76.1				
Range	44.3-85.5				
Mammography use, relative risk of being unscreened after patient reminder interventions		0.58 to 0.92	0.73		46-48
Relative risk of remaining unscreened after exposure to lay health worker intervention		0.75 to 0.89	0.82		49-53

(continued on following page)

Table 2. Natural History of Disease Parameters in African American Women (continued)				
	%			
	Breast Conservation	Breast Conservation + Radiation	Mastectomy	Reference No.
Distribution of local treatment for African American women diagnosed with breast cancer between 1993-1997				1
DCIS, years				
40-44	42.2	35.8	22.0	
45-49	45.2	31.9	22.9	
50-54	45.4	29.8	24.8	
55-59	35.8	35.0	29.2	
60-64	35.9	29.7	34.4	
65-69	41.9	30.2	27.9	
70-74	35.7	32.2	32.2	
75-79	42.7	18.3	39.0	
80-84	47.8	21.7	30.4	
85+	81.0	4.8	14.3	
Local, years				
40-44	24.4	45.5	30.1	
45-49	18.4	46.5	35.1	
50-54	18.4	46.8	34.8	
55-59	13.2	46.8	40.0	
60-64	15.6	40.8	43.6	
65-69	10.5	39.9	49.6	
70-74	18.2	39.4	42.4	
75-79	22.1	31.3	46.6	
80-84	36.7	20.3	43.0	
85+	48.6	15.9	35.5	
Regional, years				
40-44	8.1	31.9	60.0	
45-49	13.9	29.5	56.6	
50-54	15.5	25.9	58.6	
55-59	10.3	20.7	69.0	
60-64	10.6	24.6	64.8	
65-69	12.9	19.9	67.2	
70-74	12.2	19.6	68.2	
75-79	7.0	14.8	78.1	
80-84	18.2	15.2	66.7	
85+	17.5	5.0	77.5	
Distant				
40-49	25.8	21.0	53.2	
50-59	20.4	20.4	59.3	
60-69	19.6	15.7	64.7	
70+	32.1	13.2	54.7	

	ER+, ER− (%)				
	Chemotherapy	Tamoxifen	Both	Neither	
Systemic treatment distribution by stage for African American women, 1995					54
DCIS, years					
Age < 50	0.0	16.0	0.0	84.0	
Age 50-64	0.0	40.1	0.0	59.1	
Age ≥ 65	0.0	48.7	0.0	52.3	
Local, years					
Age < 50	34.1	16.6	11.0	38.4	
Age 50-64	13.6	40.1	10.9	35.3	
Age ≥ 65	2.0	48.7	0.3	49.0	
Regional/distant, years					
Age < 50	53.8	2.9	32.4	11.0	
Age 50-64	26.6	18.8	42.3	12.3	
Age ≥ 65	11.4	45.0	23.4	20.2	

	ER+	ER−	Reference No.
Most aggressive treatment for all women			55,56
DCIS	Tamoxifen	—	
Local	Chemotherapy + tamoxifen	Chemotherapy	
Regional	Chemotherapy + tamoxifen	Chemotherapy	
Distant	Chemotherapy + tamoxifen	Chemotherapy	
5-year recurrence-free survival probability for all women	See text		57-69
5-year survival probability for all women	See text		57-69

Abbreviations: RR, relative risk; SD, standard deviation; DCIS, ductal carcinoma-in-situ; Loc, local; Reg, regional; Dist, distant; ER, estrogen receptor.
*The 10% of unstaged women were distributed as follows: 50% regional and 50% distant based on survival.
†Random effects model estimate RR (unscreened).

		Treatment ($)						
		Breast-Conserving Surgery		Breast Conservation + Radiation		Mastectomy		
Cost Parameter	Estimate ($)	Mean	SD	Mean	SD	Mean	SD	Chemotherapy	Reference No.
Mammography interpretation for all women	52.51								70,71
Mammography visit	30.00								70,71
Total cost of evaluating abnormal mammogram for all women	95.35								71,72
Average monthly treatment costs for African American women by phase and stage									72,73
Initial phase†									
DCIS		448	89	2,073	186	1,646	177		
Local		1,355	107	2,261	166	1,874	201		
Regional		2,217	390	2,597	179	2,435	112		
Distant		2,434	616	2,852	454	2,623	296		
Continuing phase‡									
DCIS		148	49	198	58	152	39		
Local		241	43	156	29	210	22		
Regional		289	116	166	47	212	28		
Distant		394	201	573	208	196	117		
Terminal phase§									
DCIS		2,168	455	1,266	890	2,505	663		
Local		3,283	400	2,583	365	3,318	833		
Regional		2,469	472	3,204	338	2,731	271		
Distant		3,146	693	3,173	425	2,785	519		
Monthly patient time costs (travel, treatment)									74-76
Initial phase									
All stages		26		91		61		39	
Continuing phase									
DCIS/local		5.08/year		5.08/year		5.08/year		5.08/year	
Regional/distant		6.33/year		6.33/year		6.33/year		6.33/year	
Terminal phase									
All stages		10		10		10		10	
Cost of tamoxifen over 5-year period	6,352								77
Cost of adjuvant chemotherapy for initial treatment	4,725								77
Interventions to enhance screening for all women‖	(per patient)								74,75,78
Reminder letter	56								
Lay health worker	63								

Table 3. Costs of Breast Cancer Care (year 2000 costs)

Abbreviation: DCIS, ductal carcinoma-in-situ.
*Year 2000 dollars.
†The initial phase of care includes all costs incurred by breast cancer patients for the 12-month period after the date of diagnosis (eg, initial evaluation, hospitalizations, and surgery, and any adjuvant chemotherapy, medical visits, laboratory procedures).[73]
‡The continuing care phase includes all costs after the initial phase up to the 12 months period to death (eg, medical visits, hospitalizations, mammograms, laboratory procedures, etc).[73]
§Terminal care costs refer to all costs in the last 12 months of life (eg, hospitalizations, chemotherapy, laboratory procedures, and medical visits).[73]
‖Interventions were micro costed.

costs are already included in the Medicare costs, we overestimated costs, which biases against interventions to enhance therapy.

Costs associated with the screening interventions were calculated using micro-costing methods. Nonmedical costs included patient time spent receiving screening, diagnostic evaluation, and treatment, and travel and waiting time for receiving care. Average travel and waiting times and time spent receiving services were estimated from prior research and clinical estimates.[74-76] Costs were obtained by multiplying these times by median United States wage rates for African American women.[82] The costs of lost pro-

ductivity as a result of breast cancer morbidity and mortality would be accounted for by decrements in utilities used to quality-adjust years of life saved (see next section).

Sensitivity Analyses

We varied individual parameters and combinations of parameters over different ranges to examine the robustness of the model results under a variety of conditions. We used life years saved as our base model because utilities did not affect conclusions. Quality-adjusted life years are examined in sensi-

tivity analyses (1.0, healthy, no cancer; 0.85, local; 0.7, regional; 0.5, distant).

Model Validation and Statistical Testing

Programming accuracy was verified using input designed to test the model under hypothetical conditions in which the results should be obvious. Our scientific advisors reviewed model face and clinical validity.

Role of Funding Source

The funding agencies had no role in data analysis, interpretation of results, or decisions to publish the results.

RESULTS

Screening

African American women have a 7.2% cumulative risk of developing breast cancer from age 40 years to death in our simulation. At status quo baseline screening rates of 76%, with a program of biennial screening beginning at age 40 years, each woman will undergo an average of 10 mammograms in her lifetime and has a 54% cumulative risk of having a false-positive screening result in this period (Table 4). Compared with no screening, screening saves 11 days of life per capita (undiscounted).

Using patient reminders or lay workers increases the average number of mammograms from the status quo by less than one over a lifetime and increases the risk of a false-positive screen by 6.5%. At current screening levels, enhanced screening efforts are associated with only a slight increase in population life expectancy after age 40 years (< 1 day per woman, undiscounted); there is only a marginal difference between the two approaches. Among women destined to develop breast cancer, increasing screening saves an additional 11 days of life compared with the current status quo.

The incremental cost-effectiveness ratios associated with increased screening resulting from patient reminders and lay navigation are shown in Table 4. Comparing each approach to the status quo, both result in cost-effectiveness ratios of greater than $100,000 per life year saved. These high costs reflect increased use of mammography and earlier expenditures on treatment without appreciable benefits in life extension.

Treatment

Compared with current patterns of care, if all women were to receive the most intensive systemic therapy, an average of 0.053 years or 19.3 additional days would be saved, spread out over the entire population (undiscounted). These savings are attributable to the additional savings of 266 days of life among the breast cancer patients. If all women received the most intensive treatment recommended in consensus guidelines compared with status quo patterns, it would cost $52,678 per life year saved (Table 4). Investments in interventions to enhance treatment adherence to this level of up to $6,000 per breast cancer patient would still yield cost-effectiveness ratios of less than $75,000 per year of life saved.

Sensitivity Analysis

If we assume maximal screening intervention effectiveness of patient reminders and apply the intervention in populations of women with the lower bound of current screening rates (44%), the cost per life year saved remains high: $98,447 compared with the status quo. However, investments in enhanced screening (eg, reminders) become cost-effective in areas with pockets of unscreened or very underscreened women (eg, $51,537 compared with no screening). If screening is targeted to women with a two-fold baseline increase in risk of developing breast cancer (eg, a first-degree relative with breast cancer), then enhanced screening using patient reminders has greater benefits than in the general population, and results in a cost-effectiveness ratio of $78,129 per life year saved compared with the status quo situation.

			Table 4. Incremental Costs and Benefits of Enhanced Screening and Treatment				
Strategy	No. of Mammograms	No. of False Positives	Costs (3% discounted, $)	Incremental Costs ($)	Life Expectancy (3% discounted, years)	Incremental Life Expectancy (years)	Incremental Cost Effectiveness ($)
No screening	—	—	3,511.93	N/A	21.299179	N/A	N/A
Status quo screening and treatment*	9.97	0.66	4,138.93	627.00	21.30649	0.007312	85,755/LY
Lay health worker v status quo	10.53	0.70	4,238.18	99.24	21.307290	0.000800	124,053/LY
Patient reminder v status quo	10.82	0.71	4,247.00	108.07	21.30736	0.000870	124,217/LY
Enhanced treatment v status quo†	9.97	0.66	5,143.50	1004.57	21.32556	0.019070	52,678/LY

Abbreviations: N/A, not applicable; LY, life years.
*Status quo is compared with no screening. Status quo treatment refers to patterns of care reported to Surveillance, Epidemiology and End Results.[1,54]
†All women receive intensive therapy following consensus guidelines (surgery [and radiation after lumpectomy] plus adjuvant therapy, where all women with local and regional disease who are estrogen receptor-negative receive chemotherapy; women who are estrogen receptor-positive receive tamoxifen and chemotherapy).[55,56]

Adjustment for a range of utility values does not change the conclusion that enhanced screening is not cost-effective at current screening levels (eg, using patient reminders *v* status quo screening is also very expensive when utilities are considered, costing $200,000 per quality-adjusted life years). Delays in the timing of diagnostic evaluation of an abnormal screening test decrease the cost-effectiveness ratios for screening minimally, because delay would have to lead to stage progression from one stage to the next to have a significant impact on life expectancy (data not shown).

DISCUSSION

This is the first analysis that we are aware of that examines the cost effectiveness of breast cancer screening in African American women and examines the costs and benefits of enhancing screening or treatment. Overall, our results suggest that maximal improvements in breast cancer outcomes could be achieved by concentrating resources on delivery of the most intensive treatment regimens to all African American patients with breast cancer. Additional investments in screening should be reserved for situations in which there are pockets of unscreened women or for ensuring that all high-risk women are screened.

Meta-analyses of breast cancer polydrug chemotherapy and tamoxifen clinical trials have demonstrated statistically significant reductions in overall mortality in general populations around the world.[85,86] On the basis of these results, current standards of care for local and regional breast cancer include recommendations for systemic treatment.[55,56] Currently, there is no evidence to suggest that chemotherapy pharmacokinetics, which may differ by race, influence treatment effectiveness.[87] For instance, Dignam et al[88,89] demonstrated equal efficacy of adjuvant tamoxifen and chemotherapy in African American and white breast cancer patients treated in cooperative group trials. Current patterns of treatment remain suboptimal, and nationally only one half of African American women with breast cancer who are eligible for systemic adjuvant chemotherapy are, in fact, receiving some form of systemic treatment.[54]

At present, we do not know the reasons for the divergence of the patterns of care and guidelines for African American women. It is possible that physicians are emphasizing treatment toxicity and quality of life, and not survival, or that patients are poorly informed about chemotherapy risks and benefits. Significant comorbidity or strong patient preferences may be very legitimate reasons for the omission of systemic adjuvant treatment, whereas lack of insurance, race, socioeconomic status, or incomplete understanding should not preclude this treatment. Unfortunately, there are pervasive differences in access to cancer treatment services, including chemotherapy and referral to a medical oncologist[3] by race, income, education, or insurance and setting of care.[90-98] Although National Cancer Institute cooperative group trials have enrolled numbers of African Americans proportional to the population cancer burden,[99] African Americans are still less likely to be offered trial participation than white patients.[100]

Patient beliefs may also affect patterns of care. Cancer is a disease with strong stigma.[101-103] Cancer treatments are often perceived as "worse than the disease" and can "make you sicker instead of better."[104] Decision making and prognosis are often deferred to God: "If it's my time, God will decide" and "God directed me...to the treatments I had."[104] After the Tuskegee Study, such ideas are compounded by mistrust of the medical care system by African American patients.[105,106]

Our results suggest that substantial investments could be made in educational or other interventions to overcome barriers to care and improve referral for and uptake of systemic adjuvant therapy for breast cancer among African American women. Such investments results in costs per live years saved that are well within acceptable ranges.[84] Examples of interventions that might be used to increase the proportion of African American women receiving recommended treatment include peer treatment workers (addressing trust and shared cultural perspectives), tailored decision aides (using cultural and patient-specific tailoring to overcome barriers), physician education (enhancing sensitivity and elicitation of patient preferences), and physician chart audit with feedback. We estimate that any of these approaches would cost less than our threshold of approximately $6,000 per patient. However, given the complexity of treatment delivery and decisions and patient adherence, the optimal benefits projected in our model may not be fully realized, even with the best interventions. Nonetheless, given current patterns of care, any improvement in dissemination of recommended treatment should be cost effective.

The fact that screening rates are high in the United States and that rates are similar for African American and white patients[13] reflects the success of decades of screening interventions. We evaluated the ability of the most effective (and least costly) interventions[79,80] to further improve outcomes at the current point in time. Given the success of prior programs, additional efforts are quite expensive relative to the additional savings in lives, unless targeted to pockets of unscreened women or to women at twice the average risk of disease. Thus reaching hard to reach women who are unscreened or underscreened and educating women about risk factors remain important goals. It is also possible that screening results would differ with the availability of newer, more sensitive screening tests. Additionally, for women destined to develop ER-positive cancer, tamoxifen seems to be cost effective in high-risk white women.[107] It will be important to examine the balance of risks and benefits for African American women, who have fewer ER-positive tumors and a higher prevalence of car-

diovascular diseases that predispose to side effects than white women.[108]

Our model results are similar to other evaluations of screening in general populations. For instance, Elmore et al[109] estimated that the cumulative risk for 40- to 49-year-old women having a false-positive mammogram is approximately 56% after 10 screens, and our model predicts a 54% risk. Our estimate of the lifetime risk of breast cancer (7.2%) is also similar to that calculated by Eddy[21] in 1989 (approximately 6.5%).

Our analysis has several important strengths, including use of current standards for cost-effectiveness analyses,[26] evaluation of an important population subgroup, inclusion of the best quality and least biased data, a robust model, comparison of different cancer control strategies, and assessment of uncertainty.

Despite these strengths, there are several caveats that should be considered when interpreting our results, such as precision in estimating the natural history of breast cancer in African Americans, our method of evaluating mammography effectiveness and choice of screening technology, use of modeling, disutility of having a false-positive screen for cancer, ability to detect small effects, and generalizability. We have used the best data available to delineate the natural history of breast cancer in African American women. However, many aspects of the disease behavior are poorly understood, and there are insufficient data at this point in time to model other markers of disease aggressiveness. Our model is designed to incorporate such data as they become available.

Our results must be considered in the context of the current controversies about the effectiveness of mammography.[110] We rely on observed stage distributions among screened and unscreened populations to calculate screening benefits. Our results are compatible with the view that screening is associated with small improvements in life expectancy. We did not evaluate the impact of new technologies that are currently under evaluation as alternative screening approaches, such as digital mammography or breast magnetic resonance imaging. When data are available on test characteristics of these strategies, we could reassess the cost effectiveness of the new technologies relative to mammography or to treatment enhancement.

Ideally, large-scale randomized studies would be conducted to evaluate optimal cancer control approaches in African American women. However, because breast cancer is a rare event, conducting trials of all possible approaches is not feasible (or ethical). Under these circumstances, models can be useful to combine the best data available and project events over a sufficiently long time horizon to observe incidence and mortality end points.[111] To the extent that data are of poor quality, or assumptions are incorrect, model results can be inconclusive. However, there are reliable data on the natural history of breast neoplasia, and our results were robust over wide ranges of multiple parameters.

Our model does not capture the effects of distress associated with a falsely positive screen or the disutility of having cancer. We know of no data that measure breast cancer utilities among African American women. However, the transient nature of false-positives is not likely to alter conclusions of the analysis, and results were not sensitive to assumptions about utilities for cancer states.

There were very small screening benefits associated with enhanced use of mammography. It was difficult to detect larger screening intervention effects for several reasons. First, current rates of mammography use are quite high.[13] At these rates, the modest effects of a prototypical intervention are insufficient to produce an appreciable effect on life expectancy. Second, this type of intervention has, in part, become part of standard care that we used as a comparator. Third, current treatment regimens for DCIS, local, and regional disease are highly effective. Large improvements in survival resulting from screening occur primarily in women who avoid presenting with distant disease. Such women represent only a minority of women in populations where screening is in widespread use. Finally, the relatively high cost-effectiveness ratio for enhanced screening compared with improving treatment is also related to the fact that screening the entire population is very costly. However, the benefits only accrue to the small number of women who develop cancer but are averaged over the whole population, yielding a small per woman benefit. In contrast, the costs of treatment interventions are applied to a much smaller number of women, all of whom will benefit directly.

Finally, our results are only generalizable to African American women. We did not examine results for black patients from other countries or for white women. Because certain populations of white patients, such as low-income or uninsured women in the United States, are also at risk for poor cancer outcomes, this will be an important area for future extensions of our model. The survival data we used may not be representative of the general population of African American women, because clinical trials generally enroll healthy volunteers. However, these trials did include a representative sample of African American women (10% to 12%), enhancing the external validity of our results.

The results of this cost-effectiveness analysis are intended to inform clinical and policy debates about cancer services for vulnerable populations. Overall, our results suggest that except in pockets of unscreened or high-risk women, investments in further improvements in screening use are unlikely to be an efficient use of limited health care resources. The most cost-effective interventions are likely to be those ensuring that African American women receive the most intensive treatment once cancer is diagnosed.

Acknowledgment and Appendix

The acknowledgment and appendix are included in the full-text version of this article, available on-line at www.jco.org. They are not included in the PDF (via Adobe® Acrobat Reader®) version.

Authors' Disclosures of Potential Conflicts of Interest

The authors indicated no potential conflicts of interest.

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