Cost Effectiveness of Mammography Screening for Chinese Women

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BACKGROUND. Although the cost effectiveness of screening mammography in most western developed populations has been accepted, it may not apply to Chinese women, who have a much lower breast cancer incidence. The authors estimated the cost effectiveness of biennial mammography in Hong Kong Chinese women to inform evidence-based screening policies.

METHODS. For the current study, a state-transition Markov model was developed to simulate mammography screening, breast cancer diagnosis, and treatment in a hypothetical cohort of Chinese women. The benefit of mammography was modeled by assuming a stage shift, in which cancers in screened women were more likely to be diagnosed at an earlier disease stage. The authors compared costs, quality-adjusted life years (QALYs) saved, and life years saved (LYS) for 5 screening strategies.

RESULTS. Biennial screening resulted in a gain in life expectancy ranging from 4.3 days to 9.4 days compared with no screening at an incremental cost of from US$1166 to US$2425 per woman. The least costly, nondominated screening option was screening from ages 40 years to 69 years, with an incremental cost-effectiveness ratio (ICER) of US$61,600 per QALY saved or US$64,400 per LYS compared with no screening. In probabilistic sensitivity analyses, the probability of the ICER being below a threshold of US$50,000 per QALY (LYS) was 15.3% (14.6%).

CONCLUSIONS. The current results suggested that mammography for Hong Kong Chinese women currently may not be cost effective based on the arbitrary threshold of US$50,000 per QALY. However, clinicians must remain vigilant and periodically should revisit the question of population screening: Disease rates in China have been increasing because of westernization and socioeconomic development. ***Cancer*** **2007;110:885–95.** © *2007 American Cancer Society.*

KEYWORDS: mammography, screening, cost effectiveness, Chinese.

Screening mammography has become established in many western countries. Eight trials that enrolled > 500,000 women collectively demonstrated the survival benefit of regular mammography,[1] although those results recently were challenged[2] and later were defended.[3] A modeling consortium in the U.S. suggested that from 28% to 65% (median, 46%) of the total reduction in breast cancer-related mortality could be attributed to screening[4]; and a review of the English breast-screening program concluded that, annually, regular mammograms save 1400 lives.[5] Prior cost-effectiveness studies also justified screening on economic grounds.[6–9]

Although breast cancer is responsible for the majority of new malignancies among Hong Kong Chinese women[10] with a rising incidence,[11] it remains at only approximately 50% of the incidence among Caucasians.[12] Even assuming that the survival benefit of mammog-

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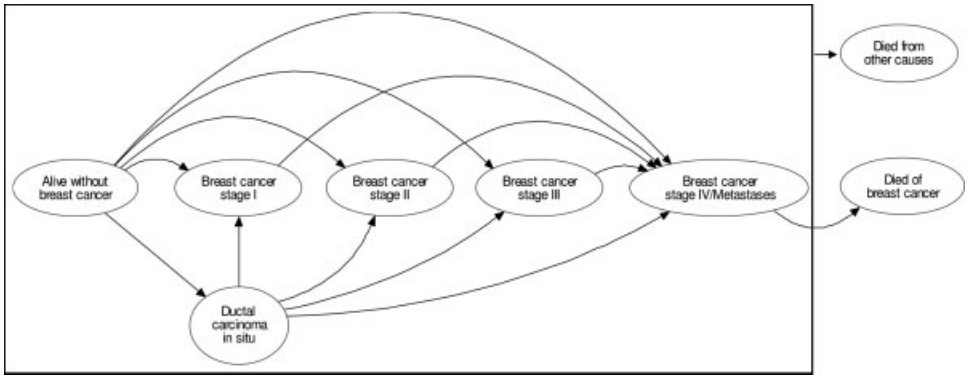

FIGURE 1. Health states and transitions (denoted by arrows).

raphy scales linearly at a lower prevalence at screening, this different epidemiologic burden immediately translates into a reduced positive predictive value,[13] thus casting doubt on the generalizability of effectiveness and efficiency estimates among non-Chinese populations. To derive evidence-based guidance in the East-Asian context, we developed a decision-analytic model to assess the incremental cost effectiveness of an organized screening program.

MATERIALS AND METHODS

Model

We developed a state-transition Markov model to simulate biennial mammography, breast cancer diagnosis, and treatment in a hypothetical, population-based cohort of Hong Kong Chinese women (Fig. 1). The model tracks a cohort of cancer-free women aged 40 years over their lifetime. Each year, they may transition to 1 of 5 breast cancer states, namely, ductal carcinoma in situ (DCIS) and 4 American Joint Committee on Cancer[14] invasive cancer stages, or they could die or remain cancer-free. Women with a history of DCIS were at an increased risk of developing invasive cancer compared with healthy women for the first 10 years. For women who were diagnosed with invasive cancer, we assigned a 1-year, breast cancer-specific mortality for the first year. Women who were diagnosed with stage I, II, and III cancer subsequently could develop metastatic recurrence and transition to the stage IV/metastatic health state. Except for treatment-related deaths that occurred during the first year after diagnosis, breast cancer deaths could occur only among women in the stage IV/metastatic state.

We compared the results from 2-view film mammography every 2 years, beginning at ages 40 years or 50 years and ending at ages 69 years or 79 years, with the results from no screening. We only evaluated biennial screening, because the 8 primary, randomized trials and subsequent systematic reviews did not report a consistent or significant survival difference in terms of frequency of screens within the tested range from 18 months to 33 months.[15] In our model, women who were diagnosed with invasive breast cancer would undergo annual mammography surveillance. It was assumed that all patients with cancer (including DCIS) would undergo prompt treatment on diagnosis.

Model outcomes were life expectancy, quality-adjusted life expectancy, and lifetime costs and were calculated using a 50-year time horizon. Comparative performance of the remaining screening strategies was measured by using the incremental cost-effectiveness ratio (ICER).[16] We adopted a societal perspective and discounted future costs and health effects at an annual rate of 3% for the reference case analysis.[17] All analyses were conducted using TreeAge Pro 2004 (TreeAge Software, Williamstown, Mass) and R (version 2.1.1; R Development Core Team, Vienna, Austria).

Clinical Data

Table 1 summarizes key parameter estimates. We obtained age-specific invasive breast cancer incidence and associated stage distribution from the Hong Kong Cancer Registry.[18] Because DCIS incidence is not recorded locally, we adopted the age-specific proportions of DCIS among all newly diagnosed breast cancer cases in the Surveillance, Epidemiology, and End Results (SEER) data in 1983 and 1998 for the unscreened and screened women in our model, respectively.[19,20] We estimated the increased risk of invasive cancer among patients with DCIS in the first 10 years after diagnosis using SEER data.[21,22] We abstracted local data on all-cause mortality.[23]

Benefits

We modeled the effectiveness of mammography by assuming that some cancers would be detected by screening at a less advanced stage compared with no screening. We applied the local stage distribution for newly diagnosed cancers in unscreened women and the stage distribution in SEER data[21] from the U.S. for newly diagnosed cancers in screened women to represent the stage shift caused by screening. We calibrated our model by varying the transition probabilities from early-stage disease to metastases until the 5-year relative survival probabilities generated by our model corresponded to the observed 5-year relative survival statistics from the SEER data for stages I, II, and III from the most recent 15 years.[21] For stage IV or metastatic disease, we derived cancer-specific death rates from the relative survival data from patients with stage IV disease. Then, we validated the model-predicted mortality reduction from screening by comparing our model outputs with empirical observations from the 8 primary, randomized controlled trials (Fig. 2).[15,24–27]

Costs

Costs adjusted to the 2005 level[28] are shown in Table 1. Four major categories of direct medical costs were included: 1) the cost of screening mammography, 2) the cost of evaluating abnormal results, 3) the 1-time cost of treating invasive cancer and DCIS, and 4) the cost of terminal care during the last 6 months before death. We derived cost estimates from local public sector costs[29,30] and private sector charges and further verified and calibrated these according to the report by Taplin et al.[31]

Quality-adjusted Life Years

To derive quality-adjusted life years (QALYs), we weighted time spent in each health state by health-related quality-of-life weights, in which a value of 1.0 was assigned to healthy (ie, breast cancer-free) women, and a value <1.0 was assigned to women with DCIS or invasive cancer (0.95, 0.9, 0.8, 0.7, and 0.3 for DCIS, stage I, stage II, stage III, and stage IV invasive cancer for the remaining time spent in stage IV/metastatic recurrence, respectively).[32] We assumed that productivity losses were accounted for by decrements in the utilities used to generate QALYs.[33]

In a comparison with a different geoethnic population, we respecified the base-case parameters on incidence and mortality[21] and costs[31,34,35] based on data from the U.S. Costs were expressed in 2005 dollars based on the U.S. Consumer Price Index for medical care.[36]

Sensitivity Analysis

We conducted a probabilistic sensitivity analysis, which involved specifying appropriate probabilistic distributions for clinical parameters[37] (Table 1) and employing a Monte-Carlo simulation with 1000 runs to select values at random from those distributions.[38] Based on the simulation results, we constructed cost-effectiveness acceptability curves to present the uncertainty in the ICER caused by sampling variation.[39]

To provide a better reflection of the age range of the population that is targeted for screening and to explore the potential impact of a multiple-cohort simulation on cost effectiveness,[40] we modified our single-cohort approach by specifying the initial cohort of women to match the age structure of the local population.[41] We specified 8 cohorts starting at 5-year intervals between the ages of 40 years and 79 years.

RESULTS

Effectiveness

A typical Chinese woman aged 40 years in Hong Kong has a 5.2% cumulative risk of developing breast cancer by age 90 years in our simulation (Table 2). For the no-screening scenario, if 100,000 women aged 40 years were never screened, then 2539 women would die of breast cancer, 1871 women would die of other causes after a diagnosis of invasive breast cancer, 141 who would die of DCIS, and 71,246 women would die of other causes without a history of known breast cancer over a 50-year period.

Under the different screening strategies, each woman would undergo an average of 10.1 to 19.1 mammograms and would have a 63.4% to 85.9% cumulative risk of having a positive screen result, and 98.8% of these would be false-positive results.

Applying biennial mammography from ages 50 years to 69 years would avert 80 deaths per 100,000 women compared with no screening. Extending the lower and/or upper age limits would save additional lives but also would result in more false-positive results.

Biennial screening from ages 50 years to 69 years would detect 3.4 times more DCIS cases (ie, 695 vs 206 per 100,000). However, this would not reduce breast cancer-related mortality; in fact, it would result in 7 more breast cancer deaths after a diagnosis of DCIS because of the much higher number of DCIS diagnoses with screening. Widening the age

TABLE 1
Clinical and Cost Parameter Estimates for the Base Case and Sensitivity Analyses

Parameter	Best estimate (plausible ranges) for Hong Kong model	Distribution ascribed in probabilistic sensitivity analysis	Best estimate (plausible ranges) for US scenario	Reference for Hong Kong model	Reference for US model
All-cause mortality: Age group, y				Hong Kong Census and Statistics Department, 2005[23]	SEER Program, 2002[21]
40–44	0.0008529	Log normal*	0.001803		
45–49	0.0013402		0.002629		
50–54	0.0018422		0.003787		
55–59	0.0029853		0.005910		
60–64	0.0049503		0.009276		
65–70	0.0086363		0.014581		
70–74	0.0152754		0.022927		
75–79	0.0264469		0.036839		
80–84	0.0469965		0.061618		
≥85	0.1397351		0.142513		
Invasive breast cancer incidence: Age group, y		Log normal*		Hong Kong Cancer Registry, 2006[18]	SEER Program, 2002[21]
40–44	0.000929		0.001158		
45–49	0.001244		0.001897		
50–54	0.001361		0.002489		
55–59	0.001315		0.003314		
60–64	0.001057		0.003973		
65–70	0.001204		0.004353		
70–74	0.000987		0.004454		
75–79	0.001371		0.004779		
80–84	0.001593		0.004526		
≥85	0.001494		0.003502		
Ratio of DCIS incidence compared with invasive breast cancer incidence					
Nonscreened group	0.040 (0.036–0.044)	β†	Same as Hong Kong model	Ernster and Barclay, 1997[19]	
Screened group	0.253 (0.229–0.277)	β†	Same as Hong Kong model	Ernster et al., 2002[20]	
No. of y DCIS patients remain at elevated risk for subsequent invasive cancer	10	Invariant	Same as Hong Kong model	Kerlikowske et al., 2003[22]	
Relative risk of invasive cancer in those previously diagnosed with DCIS	2.02	Invariant	Same as Hong Kong model	SEER Program, 2002[21]	
Invasive breast cancer stage distribution: AJCC stage classification: Nonscreened/screened		Dirichlet‡	Same as Hong Kong model	Hong Kong Cancer Registry, 2006[18]; SEER Program, 2002[21]	
I	0.316/0.521				
II	0.556/0.382				
III	0.099/0.057				
IV	0.029/0.041				
Five-y relative survival§: AJCC stage classification		Invariant	Same as Hong Kong model	SEER Program, 2002[21]	
I	0.980				
II	0.855				
III	0.675				
IV	0.312				
Annual rate of breast cancer-related death among women with stage IV invasive cancer	0.2331	β†	Same as Hong Kong model	SEER Program, 2002[21]	
Death within the first y after diagnosis of breast cancer: AJCC stage classification		Invariant	Same as Hong Kong model	SEER Program, 2002[21]	
I	0.002				
II	0.016				
III	0.039				

(*continued*)

TABLE 1
(Continued)

Parameter	Best estimate (plausible ranges) for Hong Kong model	Distribution ascribed in probabilistic sensitivity analysis	Best estimate (plausible ranges) for US scenario	Reference for Hong Kong model	Reference for US model
Stage progression transition probabilities		Invariant	Same as Hong Kong model	Calibration	
From I to IV	0.01				
From II to IV	0.08				
From III to IV	0.21				
Mammography test characteristics		β[†]	Same as Hong Kong model	Smith-Bindman et al., 2005[54]	
Sensitivity	0.77 (0.76–0.79)				
Specificity	0.90 (0.90–0.91)				
Discount rate	3% per y	Invariant	Same as Hong Kong model	Russell et al., 1996[17]	
Cost in US$					
Screening test (per test)		Uniform[‖]			
Mammogram	143		86		Farria and Feig, 2000[34]
Time (including travel time, waiting time and testing time–totaling 4 h)	25		61		
Evaluation of abnormal screens		Uniform[‖]			
Cost of further testing to work-up an abnormal mammogram	465[¶]		655		Farria and Feig, 2000[34]
Time	38		92		
Rate of abnormal results among all screens, %	10.1		11.0		Brown et al., 1995[35]
Aggregate treatment costs		Uniform[‖]			
DCIS	3411		17,356		SEER Program, 2002[21]; Taplin et al., 1995[31]
Invasive cancer: AJCC stage classification					
I	14,928		21,540		
II	16,632		23,999		
III	17,671		25,498		
IV	17,671		25,498		
Terminal care[#]	24,089		34,758		

SEER indicates Surveillance, Epidemiology, and End Results Program; DCIS, ductal carcinoma in situ; AJCC, American Joint Committee on Cancer.

All costs were adjusted to 2005 levels.

* Parameter mean of the distribution was equivalent to the base case value and the standard deviation was estimated based on the number of incidences or deaths by age group. Standard deviations were from 0.052778 to 0.120386 and from 0.012446 to 0.057364 for the incidence and mortality data, respectively.

† Parameters of the β distribution were derived based on the plausible ranges of the base case values.

‡ The Dirichlet distribution (a multivariate form of the β probability distribution that can be used to estimate the multinomial distribution) was applied to the stage distributions of nonscreened and screened groups. The parameter means of the distributions were equivalent to the sample size in each stage (Dirichlet [868,1622,329,114] in the nonscreened group, Dirichlet [1241,911,135,97] in the screened group).

§ Relative to the general population according to the US SEER Program.

‖ The plausible interval of the uniform distribution was specified as ±25% of base-case values.

¶ Assuming that, among women with an abnormal mammogram, 60.9% required repeat mammography, 27.9% required ultrasound, 4.4% required fine-needle aspiration, and 15.8% required open biopsy (see Elmore et al., 1998[55]). The respective costs of these procedures were $143, $109, $422, and $2112 (see Hong Kong Hospital Authority, 1996[30]).

Costs during the last 6 months before death.

interval for screening would yield between 53 and 111 more diagnoses of DCIS.

Cost Effectiveness

Compared with no screening, Hong Kong biennial mammography would save between 1590 and 3400 discounted life years per 100,000 women screened, depending on the starting and ending ages (Table 3). This is equivalent to an average increase in life expectancy of from 4.3 days to 9.3 days per woman. The concomitant cost would be increased by from US$117 million to US$242 million.

Of the 4 biennial screening strategies in Hong Kong that we considered, the least costly, nondominated option was to screen from ages 40 years to 69 years, with an ICER of $64,400 per LYS. By extending

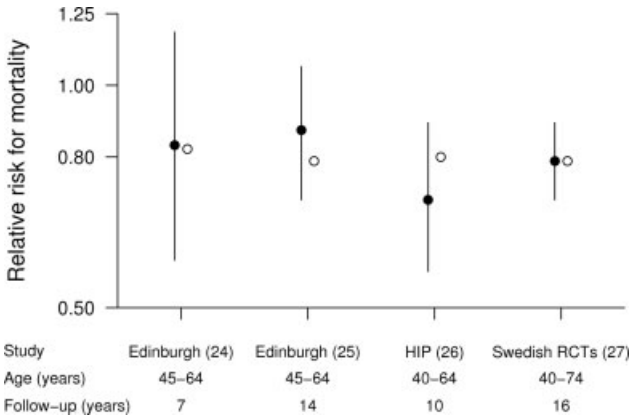

FIGURE 2. Empiric observations based on randomized controlled trials (RCTs)[15,24–27] (solid circles) with 95% confidence intervals compared with predicted mortality reduction predicted by the model (open circles). HIP indicates the Health Insurance Plan of New York.

screening until age 79 years, the ICER would increase 4-fold to $260,300 per LYS. When health-related quality of life was incorporated, the ICERs were more favorable (61,600 per QALY saved), because screening was effected through a stage shift in the model, and the quality-of-life decrements were less with earlier stages of cancer.

When we used U.S. all-cause mortality, age-specific cancer incidence, and costs as input parameters, the least costly, nondominated options were screening for women ages 50 years to 69 years at US$37,000 per LYS, followed by screening for women ages 40 years to 69 years ($47,800 per LYS), then screening for women ages 40 years to 79 years ($80,200 per LYS). This change in rank ordering most likely is accounted for by the different age dependency of cancer incidence between the 2 populations, in which cancer rates climb very steeply in the U.S. after age 40 years as opposed to a much slower rising plateau in Hong Kong (Fig. 3).

Sensitivity Analysis

Both costs and effects were lower when different age strata were accounted for at the beginning of the simulation (ie, the multiple-cohort approach) compared with a single inception cohort of women at the same starting age in the base case. This is because the mean age of individuals starting the multiple-cohort simulation is older than in the single-cohort simulation, whereas older age groups have fewer screening years remaining and, thus, accumulate lower costs and benefits of screening. This adjust-

TABLE 2
Health States and Cumulative Numbers of Mammograms Performed for a Single Simulated Cohort of 100,000 Hong Kong Chinese Women Aged 40 Years During the Next 50 Years

	No. of patients								Screening impact				
	Alive			Dead									
Screening strategy	No history of known breast cancer or DCIS	Alive with history of invasive breast cancer	Alive with history of DCIS	Total	No history of known breast cancer	Other causes after diagnosis of invasive breast cancer	Invasive breast cancer	Other causes after diagnosis of DCIS	Invasive breast cancer after diagnosis of DCIS	Total	No. of incremental deaths averted	Total no. of deaths averted	No. of mammograms	No. of false-positive results	Cumulative risk of positive screen, %
No screening	23,362	781	62	24,205	71,246	1871	2536	141	3	75,797					
Screening every 2 y: Age group, y															
50–69	23,238	862	184	24,284	70,892	2058	2256	501	10	75,717	80	80	10.1	94,683	63.4
50–79	23,179	891	242	24,312	70,758	2095	2187	637	10	75,687	30	110	14.1	135,093	76.0
40–69	23,185	897	237	24,319	70,730	2158	2112	667	15	75,682	5	115	15.1	144,683	78.4
40–79	23,125	927	295	24,347	70,595	2195	2044	803	15	75,652	30	145	19.1	185,092	85.9

DCIS indicates ductal carcinoma in situ.

TABLE 3
Lifetime Discounted Costs and Benefits of Different Screening Strategies for 100,000 Women in Hong Kong and the United States

	Hong Kong				United States			
			ICER*				ICER*	
Screening strategy	Discounted lifetime cost, million US$	Discounted life-years	Cost per life-year saved*	Cost per QALY saved†	Discounted lifetime cost, million US$	Discounted life-years	Cost per life-year saved	Cost per QALY saved†
Single-cohort model								
No screening	54.14	2,373,740			168.29	2,253,170		
Biennial screening: Age group, y								
50–69	170.75	2,375,330	Dominated‡	Dominated‡	294.65	2,256,590	37,000	33,200
50–79	201.99	2,375,450	Dominated‡	Dominated‡	325.01	2,256,970	Dominated‡	Dominated‡
40–69	265.38	2,377,020	64,400	61,600	396.85	2,258,730	47,800	46,800
40–79	296.62	2,377,140	260,300	178,800	427.19	2,259,110	80,200	55,400
Multiple-cohort model								
No screening	45.34	1,918,513			165.27	1,793,667		
Biennial screening: Age, y								
50–69	143.20	1,919,827	Dominated‡	Dominated‡	273.05	1,796,664	36,000	32,300
50–79	190.07	1,920,057	Dominated‡	Dominated‡	321.87	1,797,400	Dominated‡	Dominated‡
40–69	172.98	1,920,411	67,200	63,400	305.42	1,797,426	42,500	Dominated‡
40–79	219.72	1,920,723	149,500	100,900	353.81	1,798,334	53,341	38,700

ICER indicates incremental cost-effectiveness ratio; QALY, quality-adjusted life-years.All ICERs were rounded to the nearest 100.

* Options were compared with the next least expensive, nondominated strategy.

‡ This strategy cost more but was less effective than another strategy or combination of strategies and, thus, was dominated.

† Assuming health-related utilities of 0.95, 0.9, 0.8, 0.7, and 0.3, respectively, for ductal carcinoma in situ, stage I, stage II, stage III, and stage IV invasive cancer for the remaining time spent in the same state.

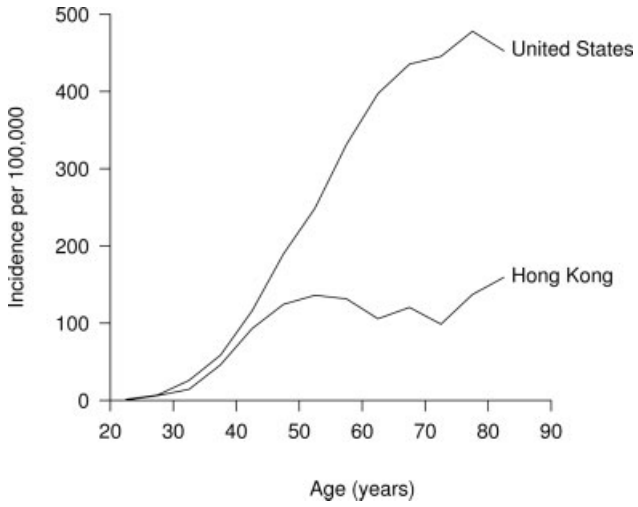

FIGURE 3. Age-specific breast cancer incidence for the U.S. and Hong Kong in 2002 (Sources: the U.S. Surveillance, Epidemiology, and End Results Program[21] and the Hong Kong Cancer Registry[18]).

ment, however, did not change our cost-effectiveness rankings (Table 3).

Figure 4 shows cost-effectiveness acceptability curves based on different values of the ceiling cost-effectiveness ratio. They reflect the uncertainty that is present potentially in the costs and life years or QALYs saved. For example, the probability of the ICER being below US$50,000 per QALY saved (LYS) was <39.1% (14.6%) for the least costly, nondominated option.

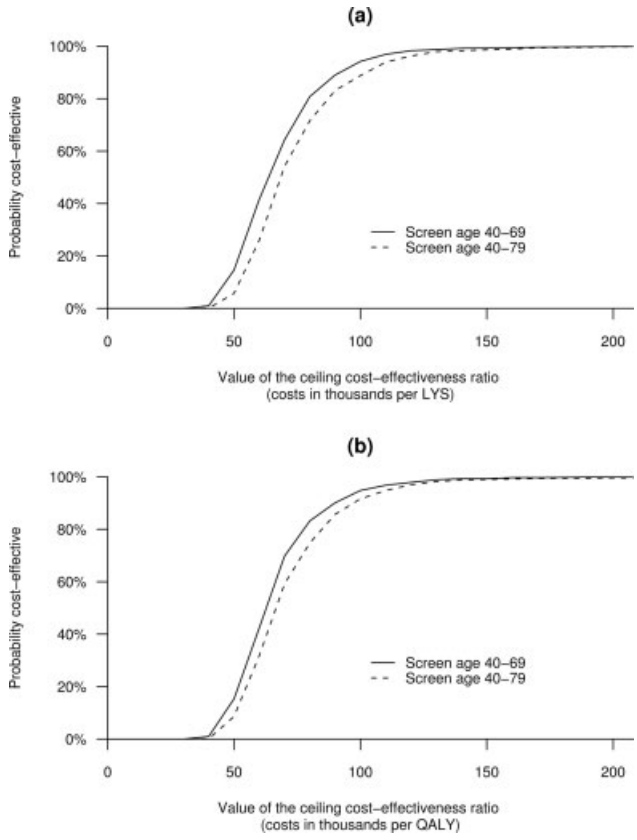

FIGURE 4. Cost-effectiveness acceptability curves for the nondominated screening strategies compared with no screening for the (a) cost per life-year saved (LYS) and (b) for the cost per quality-adjusted life year (QALY).

DISCUSSION

Although screening by mammography for the early diagnosis of breast cancer has become established practice in many western countries, there are no data regarding the efficacy, effectiveness, or cost effectiveness of mammography in Chinese women. Despite this lack of evidence, there have been widespread suggestions and unqualified recommendations for whole-population screening and the aggressive promotion of mammographic examination in East Asia. Currently, with the notable exception of the Singaporean breast screening program, which was launched before the conclusion of (and, thus, effectively invalidated) the Singaporean mammography trial,[42] there is no systematic screening program for breast cancer in the region, but an assortment of sporadic, opportunistic mammography screening services in both the private and public sectors proliferates. The current analyses provide insight concerning the cost effectiveness of mammography screening for Chinese and other East-Asian women with low baseline risk in this time of increasing concern regarding the cost of health care and heightened awareness of the need to live within budgets in the health sector.

Of the 5 strategies that we considered, our findings suggest that, although biennial mammography for all women ages 40 years to 69 years would be the least costly, nondominated screening option, the incremental cost (compared with no screening) of US$64,400 per LYS or US$61,600 per QALY is greater than the corresponding ratios in the West, as reported previously,[6–9] and seems to be slightly greater than the typical threshold used for new technology adoption by many advanced economies.[43–48] Although there is no consensus on what constitutes an acceptable ICER, the U.K.'s National Institute for Health and Clinical Excellence (NICE) typically has accepted technologies as cost effective if the ICERs are below US$36,000 to US$54,000 (US$1 = £0.55) per QALY, although NICE has (very rarely) accepted technologies (not related to screening) with larger ICERs up to US$90,000.[43] The Canadian Coordinating Office for Health Technology Assessment

considers US$50,000 per QALY as relatively unattractive for their therapeutics program.[48] In Australia, a threshold of between US$31,500 and US$57,000 (US$1 = AU$0.75) per LYS has been considered by the Pharmaceutical Benefits Advisory Committee for reimbursement.[47] Hong Kong's low cancer incidence, like that elsewhere in East Asia,[49] is the main driver for our result, as confirmed by the comparison with the modeled ICER using U.S. input data.

In addition, the current mammography costs in Hong Kong are higher than in the U.S., whereas the treatment costs in Hong Kong are lower. This is because the cost of a local radiologist reading a mammogram is relatively high (physicians' fees generally are high in Hong Kong); whereas treatment and inpatient costs, including nurses, equipment, and overhead, can be kept much lower because of the local public sector's single-piped funding mechanism.

The policy corollary is that population-based, mass mammographic screening currently may be an inefficient appropriation of scarce public health dollars. Furthermore, although mass mammography would benefit only a small number of individuals, it would cause unnecessary distress to many women, because since approximately 4 in every 5 women enrolled in the program would end up with at least 1 positive screen during their lifetime, and most would turn out to be a false alarm. A positive screen inevitably leads to further confirmatory studies, ranging from a repeat mammogram, to a fine-needle aspiration biopsy, and, in some women, even to an open biopsy. The anxiety and psychological trauma associated with these interventions, which were unaccounted for in the current analysis (although these factors would be unlikely to alter the conclusions, because they would have been biased against screening), can be considerable albeit transient in nature. Moreover, nearly all women with mammography-detected DCIS would undergo major excision and potentially disfiguring (physically and psychologically) operations.[13]

It is noteworthy that the age-specific incidence pattern after age 40 years is a much slower rising plateau in Hong Kong and is very similar to that observed in Singapore,[50] with a clear cohort effect in which women who were born after 1945 have progressively higher incidence. In our previous study,[11] we also observed that the average annual increase in age-standardized breast cancer incidence was 1.2% from 1973 to 1999 and was driven largely by a cohort effect of westernization from the generation of the postwar migrants, who were the first generation of girls (and particularly adolescent girls) to experience in large numbers the more westernized lifestyle associated with socioeconomic development. The benefit of screening also will increase as the incidence increases. Therefore, notwithstanding our current findings, Hong Kong and other East-Asian health agencies must remain vigilant and periodically should revisit the question of population screening. In addition, the cost-effectiveness threshold is dynamic and needs to be adjusted over time when the community is willing to pay more collectively for health gains or, alternatively, to constrain health costs.[51] In fact, many have argued that the use of a single, universally applicable threshold can generate problems, and actual willingness to pay for health benefits often depends on the context of the health problem and the perspectives of decision makers.[52] There may be a role for empirical guidance based on contingent valuation studies of breast cancer prevention interventions.

Four other potential limitations that have not yet been acknowledged should be noted. First, we did not have aggregate, local stage-specific treatment costs for invasive breast cancer and, instead, relied on individual, itemized cost data. However, the results were insensitive to treatment costs on 1-way sensitivity testing. Second, we did not evaluate newer technologies to detect breast lesions, such as magnetic resonance imaging, ultrasound, full-field digital mammography, or computer-aided detection techniques. A recent systematic review concluded that there was insufficient evidence to support the use of any of those 4 methods for population screening.[53] Third, we did not consider the potentially differential effects of changing adjuvant treatment on breast cancer survival among the U.S. and Chinese populations in the model. However, there is no good evidence to assess whether there is differential response to adjuvant treatment by geoethnicity; however, to date, anecdotal experience has failed to identify nonequivalence between the U.S. and Hong Kong. Finally, when we had robust local data, we tried our best to use it fully; and, when we had to borrow from overseas (mostly the U.S.) because of a serious dearth of local data, we were very careful to calibrate the analysis to fit local empirical observations, thus remaining faithful to contextually specific epidemiology.

Our analysis has illustrated the potential danger of adopting, without careful economic appraisal, screening guidelines based on research in Western populations, on which all published randomized trials have been based. For Hong Kong, mammography may not be an efficient use of scarce public

health dollars currently. The verdict for the rest of Greater China and East Asia, which have lower breast cancer incidence and many more overriding health care priorities, is unequivocal.

REFERENCES

1. Humphrey LL, Helfand M, Chan BK, Woolf SH. Breast cancer screening: a summary of the evidence for the U.S. Preventive Services Task Force. *Ann Intern Med*. 2002;137:347–360.
2. Gotzsche PC, Olsen O. Is screening for breast cancer with mammography justifiable? *Lancet*. 2000;355:129–134.
3. Freedman DA, Petitti DB, Robins JM. On the efficacy of screening for breast cancer. *Int J Epidemiol*. 2004;33:43–55.
4. Berry DA, Cronin KA, Plevritis SK, et al. Effect of screening and adjuvant therapy on mortality from breast cancer. *N Engl J Med*. 2005;353:1784–1792.
5. Dixon-Woods M, Baum M, Kurinczuk JJ. Screening for breast cancer with mammography. *Lancet*. 2001;358:2166–2167; discussion, 2167–2168.
6. Brown ML, Fintor L. Cost-effectiveness of breast cancer screening: preliminary results of a systematic review of the literature. *Breast Cancer Res Treat*. 1993;25:113–118.
7. Lindfors KK, Rosenquist CJ. The cost-effectiveness of mammographic screening strategies. [Erratum appears in *JAMA*. 1996;275:112.] *JAMA*. 1995;274:881–884.
8. Norum J. Breast cancer screening by mammography in Norway. Is it cost-effective? *Ann Oncol*. 1999;10:197–203.
9. Salzmann P, Kerlikowske K, Phillips K. Cost-effectiveness of extending screening mammography guidelines to include women 40 to 49 years of age. [Erratum appears in *Ann Intern Med*. 1998;128:878.] *Ann Intern Med*. 1997;127:955–965.
10. Hong Kong Cancer Registry. Hong Kong cancer statistics, 2002. Hong Kong: Hong Kong Cancer Registry, Hospital Authority. Available at URL: http://www3.ha.org.hk/cancereg/canstat2002.pdf Accessed February 1, 2006.
11. Leung GM, Thach TQ, Lam TH, et al. Trends in breast cancer incidence in Hong Kong between 1973 and 1999: an age-period-cohort analysis. *Br J Cancer*. 2002;87:982–988.
12. Parkin DM, Whelan SL, Ferlay J, Teppo L, Thomas DB, editors. Cancer Incidence in Five Continents. No. VIII. Lyon, France: International Agency for Research on Cancer; 2002.
13. Leung GM, Lam TH, Thach TQ, Hedley AJ. Will screening mammography in the East do more harm than good? *Am J Public Health*. 2002;92:1841–1846.
14. SEER Program, Cancer Statistics Branch, Division of Cancer Prevention and Control, National Cancer Institute. SEER Program: Comparative Staging Guide for Cancer. Version 1.1. NIH Pub. No. 93–3640. Bethesda, Md: National Institute of Health; 1993.
15. Kerlikowske K, Grady D, Rubin SM, Sandrock C, Ernster VL. Efficacy of screening mammography. A meta-analysis. *JAMA*. 1995;273:149–154.
16. Hunink MG, Glasziou PP, Siegel JE, et al. Decision Making in Health and Medicine: Integrating Evidence and Values. Cambridge, Mass: University Press; 2001.
17. Russell LB, Gold MR, Siegel JE, Daniels N, Weinstein MC. The role of cost-effectiveness analysis in health and medicine. Panel on Cost-Effectiveness in Health and Medicine. *JAMA*. 1996;276:1172–1177.
18. Hong Kong Cancer Registry. Hospital Authority, Hong Kong. Available at URL: http//www3.ha.org.hk/cancereg/ Accessed February 1, 2006.
19. Ernster VL, Barclay J. Increases in ductal carcinoma in situ (DCIS) of the breast in relation to mammography: a dilemma. *J Natl Cancer Inst Monogr*. 1997;22:151–156.
20. Ernster VL, Ballard-Barbash R, Barlow WE, et al. Detection of ductal carcinoma in situ in women undergoing screening mammography. *J Natl Cancer Inst*. 2002;94:1546–1554.
21. Surveillance, Epidemiology, and End Results (SEER) Program. SEER public use CD-ROM program. Bethesda, Md: National Cancer Institute, Division of Cancer Prevention and Control, Surveillance Program, Cancer Statistics Branch; 1973–2002.
22. Kerlikowske K, Molinaro A, Cha I, et al. Characteristics associated with recurrence among women with ductal carcinoma in situ treated by lumpectomy. *J Natl Cancer Inst*. 2003;95:1692–1702.
23. Census and Statistics Department. Hong Kong Life Table 1998–2033. Hong Kong: Census and Statistics Department; 2005.
24. Roberts MM, Alexander FE, Anderson TJ, et al. Edinburgh trial of screening for breast cancer: mortality at seven years. *Lancet*. 1990;335:241–246.
25. Alexander FE, Anderson TJ, Brown HK, et al. 14 years of follow-up from the Edinburgh randomised trial of breast-cancer screening. *Lancet*. 1999;353:1903–1908.
26. Shapiro S,Health Insurance Plan of Greater New York. Periodic Screening for Breast Cancer: The Health Insurance Plan Project and its Sequelae, 1963–1986. Baltimore, Md: Johns Hopkins University Press; 1988.
27. Nystrom L, Andersson I, Bjurstam N, Frisell J, Nordenskjold B, Rutqvist LE. Long-term effects of mammography screening: updated overview of the Swedish randomised trials. [Erratum appears in *Lancet*. 2002;360:724.] *Lancet*. 2002;359:909–919.
28. HKSAR Census and Statistics Department. Hong Kong Annual Digest of Statistics, 2003. Hong Kong: HKSAR Census and Statistics Department; 2003.
29. Finance Division, Hospital Authority. Breast Cancer Diagnosis and Management: Patient-related Groups Costing. Hong Kong: Hospital Authority; 1989–1999.
30. Hong Kong Hospital Authority. List of Charges. S. S. no. 4 to Gazette no. 44/1996. Hong Kong: Hong Kong Hospital Authority; 1996.
31. Taplin SH, Barlow W, Urban N, et al. Stage, age, comorbidity, and direct costs of colon, prostate, and breast cancer care. *J Natl Cancer Inst*. 1995;87:417–426.
32. Mandelblatt JS, Schechter CB, Yabroff KR, et al. Benefits and costs of interventions to improve breast cancer outcomes in African American women. *J Clin Oncol*. 2004;22:2554–2566.
33. Weinstein MC, Fineberg HV. Clinical Decision Analysis. Philadelphia, Pa: WB Saunders; 1980.
34. Farria D, Feig S. An introduction to economic issues in breast imaging. *Radiol Clin North Am*. 2000;38:825–842.
35. Brown ML, Houn F, Sickles EA, Kessler LG. Screening mammography in community practice: positive predictive value of abnormal findings and yield of follow-up diagnostic procedures. *Am J Roentgenol*. 1995;165:1373–1377.
36. US Department of Labor. Consumer Price Index. Available at URL: http://data.bls.gov/cgi-bin/surveymost?cu Accessed October 1, 2005.
37. Briggs AH, Goeree R, Blackhouse G, O'Brien BJ. Probabilistic analysis of cost-effectiveness models: choosing between treatment strategies for gastroesophageal reflux disease. *Med Decis Making*. 2002;22:290–308.

38. Halpern EF, Weinstein MC, Hunink MG, Gazelle GS. Representing both first- and second-order uncertainties by Monte Carlo simulation for groups of patients. *Med Decis Making*. 2000;20:314–322.
39. Briggs A, Fenn P. Confidence intervals or surfaces? Uncertainty on the cost-effectiveness plane. *Health Econ*. 1998;7: 723–740.
40. Dewilde S, Anderson R. The cost-effectiveness of screening programs using single and multiple birth cohort simulations: a comparison using a model of cervical cancer. *Med Decis Making*. 2004;24:486–492.
41. Census and Statistics Department. Hong Kong Annual Digest of Statistics. Hong Kong: Census and Statistics Department; 2003.
42. Ng EH, Ng FC, Tan PH, et al. Results of intermediate measures from a population-based, randomized trial of mammographic screening prevalence and detection of breast carcinoma among Asian women: the Singapore Breast Screening Project. [Erratum appears in *Cancer*. 1998;83: 191.] *Cancer*. 1998;82:1521–1528.
43. Devlin N, Parkin D. Does NICE have a cost-effectiveness threshold and what other factors influence its decisions? A binary choice analysis. *Health Econ*. 2004;13:437–452.
44. Graham JD, Corso PS, Morris JM, Segui-Gomez M, Weinstein MC. Evaluating the cost-effectiveness of clinical and public health measures. *Annu Rev Public Health*. 1998;19: 125–152.
45. National Institute for Clinical Excellence. Orlistat for treatment of obesity in adults. Technology Appraisal Guidance no. 22. Available at URL: http://www.nice.org.uk/page.aspx?o=15725 Accessed August 1, 2005.
46. Weinstein MC. High-priced technology can be good value for money. *Ann Intern Med*. 1999;130:857–858.
47. George B, Harris A, Mitchell A. Cost-effectiveness analysis and the consistency of decision making: evidence from pharmaceutical reimbursement in Australia (1991 to 1996). *Pharmacoeconomics*. 2001;19:1103–1109.
48. Laupacis A. Inclusion of drugs in provincial drug benefit programs: who is making these decisions, and are they the right ones? *CMAJ*. 2002;166:44–47.
49. Leung GM, Lam TH, Hedley AJ. Screening mammography re-evaluated. *Lancet*. 2000;355:750–751.
50. Chia KS, Reilly M, Tan CS, et al. Profound changes in breast cancer incidence may reflect changes into a Westernized lifestyle: a comparative population-based study in Singapore and Sweden. *Int J Cancer*. 2005;113:302–306.
51. Ubel PA, Hirth RA, Chernew ME, Fendrick AM. What is the price of life and why doesn't it increase at the rate of inflation? *Arch Intern Med*. 2003;163:1637–1641.
52. Neumann PJ. Using Cost-effectiveness Analysis to Improve Health Care: Opportunities and Barriers. Oxford: Oxford University Press; 2005.
53. Irwig L, Houssami N, van Vliet C. New technologies in screening for breast cancer: a systematic review of their accuracy. *Br J Cancer*. 2004;90:2118–2122.
54. Smith-Bindman R, Chu P, Miglioretti DL, et al. Physician predictors of mammographic accuracy. *J Natl Cancer Inst*. 2005;97:358–367.
55. Elmore JG, Barton MB, Moceri VM, Polk S, Arena PJ, Fletcher SW. Ten-year risk of false positive screening mammograms and clinical breast examinations. *N Engl J Med*. 1998;338:1089–1096.