Original Article

Optimizing Resource Allocation for Breast Cancer Prevention and Care Among Hong Kong Chinese Women

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BACKGROUND: Recommendations about funding of interventions through the full spectrum of the disease often have been made in isolation. The authors of this report optimized budgetary allocations by comparing cost-effectiveness data for different preventive and management strategies throughout the disease course for breast cancer in Hong Kong (HK) Chinese women. **METHODS:** Nesting a state-transition Markov model within a generalized cost-effectiveness analytic framework, costs and quality-adjusted life-years (QALYs) were compared to estimate average cost-effectiveness ratios for the following interventions at the population level: biennial mass mammography (ages 40-69 years or ages 40–79 years), reduced waiting time for postoperative radiotherapy (by 15% or by 25%), adjuvant endocrine therapy (either upfront aromatase inhibitor [AI] therapy or sequentially with tamoxifen followed by AI) in postmenopausal women with estrogen receptor-positive disease, targeted immunotherapy in those with tumors that over express human epidermal growth factor receptor 2, and enhanced palliative services (either at home or as an inpatient). Usual care for eligible patients in the public sector was the comparator. **RESULTS:** In descending order, the optimal allocation of additional resources for breast cancer would be the following: a 25% reduction in waiting time for postoperative radiotherapy (in US dollars: $5000 per QALY); enhanced, home-based palliative care ($7105 per QALY); adjuvant, sequential endocrine therapy ($17,963 per QALY); targeted immunotherapy ($62,092 per QALY); and mass mammography screening of women ages 40 to 69 years ($72,576 per QALY). **CONCLUSIONS:** Given the lower disease risk and different age profiles of patients in HK Chinese, among other newly emergent and emerging economies with similar transitioning epidemiologic profiles, the current findings provided direct evidence to support policy decisions that may be dissimilar to current Western practice. ***Cancer* 2012;000:000–000.** © *2012 American Cancer Society.*

KEYWORDS: breast cancer, cancer care, Chinese, resource allocation, cost-effectiveness analysis.

INTRODUCTION

Decisions on funding for interventions at different stages of a specific condition often have been made in isolation. It has been proposed that budgetary allocations should be considered at a higher level. To optimize the allocation of scarce resources, it is useful to have comparative data on the cost-effectiveness of alternative interventions targeted throughout the disease course.

The World Health Organization (WHO) has advocated the application of generalized cost-effectiveness analysis (CEA)[1] to address this gap. Generalized CEA combines a "competing choice" decision model with a "shopping spree" analysis.[2] The former is a model in which several mutually exclusive strategies are compared, and the decision between strategies depends on whether the additional benefits are worth the additional costs when evaluated incrementally.[2] The latter refers to the analysis of a policy decision in which the objective is to maximize the total effectiveness of a selected range of independent interventions, subject to a constrained budget.[2]

In HK's tax-funded public health care system, which provides 95% of total bed-days, access to care is universal with minimal copayment at the point of care, except for certain newer, more expensive drug items or consumables.[3] Barring those who are socially indigent and subject to means testing, most patients with breast cancer are asked to self-purchase such treatments, including hormone modulators (eg, third-generation aromatase inhibitors [AIs], such as anastrozole, letrozole, and exemestane) and targeted immunotherapeutics (eg, trastuzumab).[4]

In the current study, we investigated whether, to increase the number of quality-adjusted life-years (QALYs) for breast cancer care overall, resources currently allocated elsewhere would be deployed more gainfully in paying for either or both types of these newer treatments or whether such a budget should be devoted to shortening postoperative radiotherapy queues.[5,6] Alternatively, we inquired whether secondary prevention by population-based mammography would be considered more cost-effective where HK does not currently operate a mass screening program.[7] Finally, we wanted to determine how enhanced palliative care toward the end of the disease process would compare with these other strategies. In a nutshell,

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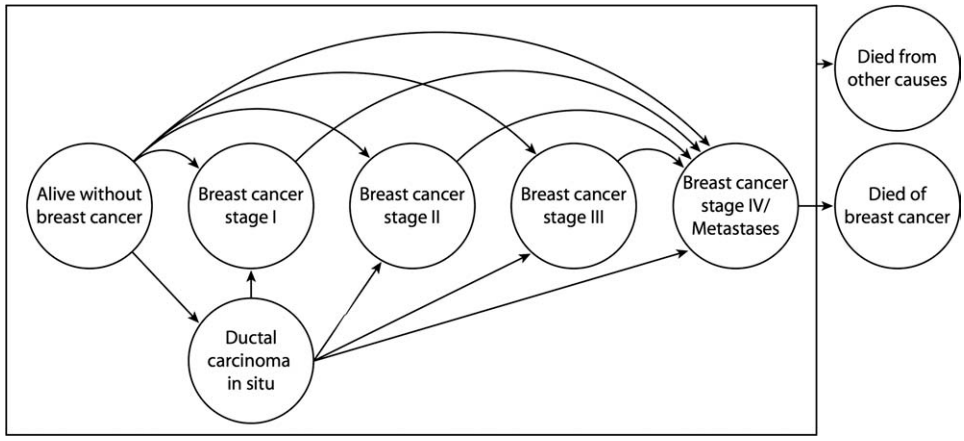

Figure 1. This illustration depicts the nested state-transition Markov model (adapted from: Wong IOL, Kuntz KM, Cowling BJ, Lam CLK, Leung GM. Cost-effectiveness of mammography screening for Chinese women. *Cancer*. 2007;110:885-895).

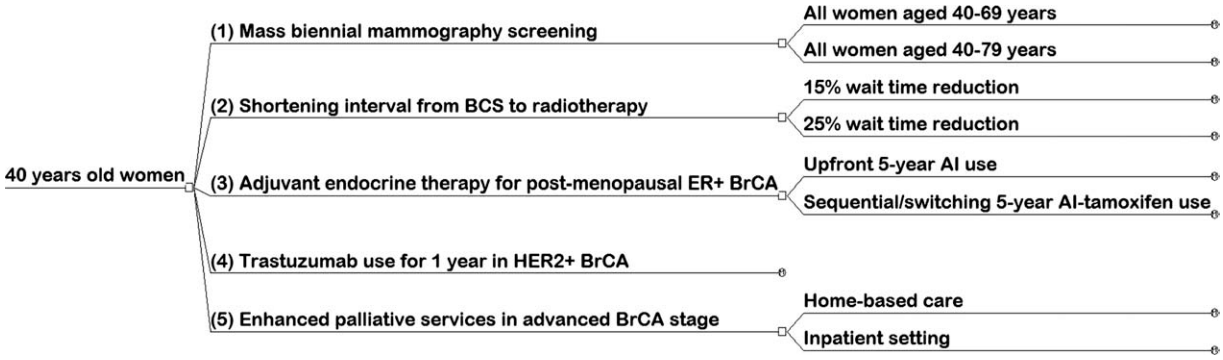

Figure 2. This is a decision tree for the breast cancer-related interventions that were assessed. BCS indicates breast-conserving surgery; AI, aromatase inhibitor; ER+, estrogen receptor-positive; BrCA, breast cancer; HER2+, over expression of human epidermal growth factor receptor 2.

subject to a spending cap, we wanted to determine the most cost-effective combination of the aforementioned strategies to minimize the overall breast cancer burden.

Previously we developed a decision analytic model to evaluate the cost-effectiveness of mass mammography.[7] Here, we applied this model to evaluate various interventions across different disease stages under the analytic rubric of a generalized CEA.

MATERIALS AND METHODS

Model

We extended a state-transition Markov model[7] (Fig. 1) to evaluate selected breast cancer-related interventions. The model was built to simulate biennial mammography, breast cancer diagnosis, treatment, and palliative care in a hypothetical cohort of HK Chinese women. The model tracks a cohort of cancer-free women aged 40 years over their lifetime. Each year, they may move to 1 of 5 breast cancer health states, including ductal carcinoma in situ (DCIS) and 4 American Joint Committee on Cancer (AJCC) invasive cancer stages, or they may could die or remain cancer-free. The model assumed that women with a history of DCIS had an elevated risk of developing invasive cancer compared with healthy women in the general population for the first 10 years. Among women who were diagnosed with invasive cancer, we specified a first-year breast cancer-specific mortality for the first year, whereas women with stage I to III cancer subsequently might develop a metastatic recurrence and transition to the stage IV/metastatic health state. We specified that breast cancer deaths could occur only among women with stage IV cancer, except for treatment-related mortality that occurred during the first year after diagnosis with invasive cancer at any stage.

Interventions

We reviewed the literature on the prevention and management of breast cancer to identify the full range of possible interventions throughout the disease course that would be

appropriate for implementation in the HK context (whenever additional funding may be available) and had relevant associated data to support a CEA. We evaluated the following interventions and their combinations (Fig. 2): 1) biennial mammography for women aged 40 to 69 or 79 years; 2) shortening the postoperative wait time to radiotherapy in women with stage I or II disease operationalized as a reduction of 15% and 25% from a baseline 6-week median waiting queue[8,9]; 3) adjuvant endocrine therapy, consisting of either upfront (ie, for patients with stage I-III disease vs restricted to patients with stage IV disease) AI for 5 years or sequentially with 2 to 3 years of tamoxifen followed by 2 to 3 years of AI in postmenopausal women with estrogen receptor (ER)-positive disease; 4) targeted immunotherapy with trastuzumab for 1 year in patients with human epidermal growth factor 2 (HER2) over expressed disease and enhanced palliative care in patients with stage IV disease (evaluated under 2 competing scenarios: home-based or inpatient setting, respectively); and 5) operationalized as increased costs of 12% and a QALY improvement of 2.25%, which were derived from a randomized, controlled trial of a home-based palliative care team[10] and on a mapping function of the Medical Outcomes Study 36-item short-form health survey (SF-36) to Euroqol EQ-5D scales[11] for QALY adjustment, or QALY improvement of 1.25% (by assuming no greater than 10% improvement compared with average utility scores of supportive institutional care with palliative chemotherapy/radiotherapy/surgery/hormone therapy for metastatic breast cancers[12]) that cost 25%[13,14] more than the base case incurred for stage IV disease. The base-case comparator was "usual care," which does not currently include any of the aforementioned strategies (ie, a "partial null scenario").

Clinical Effectiveness

Clinical parameters and assumptions are summarized in Table 1. Probabilities and utilities were derived and estimated from the published literature, when available, supplemented by local sources, internal reports, unpublished materials, and expert opinion whenever appropriate and necessary.

We derived QALYs regarding time spent in each health state adjusted by health-related quality-of-life weights. A utility 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 (the utility values were 0.95 for DCIS, 0.9 for stage I disease, 0.8 for stage II disease, 0.7 for stage III disease, and 0.3 for stage IV invasive cancer for the remaining time spent in stage IV/metastatic recurrence).[7] We assumed productivity losses were accounted for by decrements in the utilities used to generate QALYs.[7]

We assumed that the effect of screening was in the form of a stage shift.[7] That is, 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 US Surveillance, Epidemiology, and End Results[19] stage distribution for newly diagnosed cancers in screened women to represent the stage shift effected by screening.[7] In addition, we derived the clinical benefits of reducing postoperative delays to radiotherapy in terms of reduction in the local recurrence rate based on data from a retrospective study and a systematic review.[5,6]

We derived the additional benefits of AI for postmenopausal, ER-positive disease by comparing data from the Early Breast Cancer Trialists' Collaborative Group overview of tamoxifen[20]; the latest update on adjuvant endocrine therapy for women with hormone receptor-positive breast cancer by the American Society of Clinical Oncology clinical practice guidelines[22]; the most recent 10-year analysis of the Arimidex, Tamoxifen, Alone or in Combination (ATAC) trial for ER-positive early stage breast cancer[23]; and a meta-analysis of AI versus tamoxifen for women with ER-positive, advanced/metastatic breast cancer.[21] The overall survival data for patients with early stage, ER-positive breast cancer from the relevant trials were pooled by performing cumulative meta-analyses using fixed or random effects models (for the presence of heterogeneity). We used the nonparametric trim and fill method[27] of adjustment for publication bias whenever appropriate. We applied the same meta-analysis approach to estimate the pooled relative mortality risks among women with HER2 over expressed, early stage disease who received trastuzumab, mainly based on the findings from 3 primary breast cancer trials,[24] including a combined study by the National Surgical Adjuvant Breast and Bowel Project trial (NSABP) (trial B-31), the North Central Cancer Treatment Group (NCCTG) (trial N9831),[28] the Herceptin Adjuvant (HERA) trial,[29] and the Breast Cancer International Group (BCIRG) (trial 006).[30] The relative mortality benefits for patients with HER2 over expressing, advanced breast cancer was based on Slamon et al.[25] We also lowered the transition probabilities from stage I or II disease to stage IV disease among women with HER2-positive disease who received trastuzumab. The risk reduction was estimated by using the meta-analysis method based on 2 trial results[26] from the

Table 1. Clinical Parameter Estimates

Parameter	Best Estimate	Plausible Range	Distribution Ascribed in Probabilistic Sensitivity Analysis	Source
Proportion of ER+ invasive breast cancer	0.6667	0.6667-0.77	Beta	HK Breast Cancer Registry 2009[15]; local expert opinion[a]
Proportion of HER2 over expressed invasive breast cancer	0.25	0.25-0.30	Beta	Slamon 1987[16]; Slamon 1989[17]
Proportion of patients undergoing breast-conserving treatment	0.61		Invariant	HK Breast Cancer Registry 2009[15]
Proportion of HER2 patients with immunohistochemistry score of 2+, thus proceeding to FISH testing	0.42		Invariant	Local expert opinion[b]
Invasive cancer stage distribution (unscreened/screened)			Dirichlet[c]	HK Cancer Registry 2008[18]; SEER 2002[19]
Stage I	0.316/0.521			
Stage II	0.556/0.382			
Stage III	0.099/0.057			
Stage IV	0.029/0.041			
Proportional mortality reduction resulting from				
Adjuvant hormone therapy				
5-Y tamoxifen for invasive ER+ cancer vs no tamoxifen[d]	0.31	0.25-0.37	Beta	Early Breast Cancer Trialist Collaborative Group 2005[20]
AI for ER+ stage IV cancer vs tamoxifen only[e]	0.12	0.04-0.2	Beta	Gibson 2009[21]
HR for overall survival for				
5-Y primary AI for ER+ stage I-III cancer vs tamoxifen only	0.9	0.82-0.98	Beta	Burstein 2010[22]; Cuzick 2010[23] (a meta analysis of trials, including ATAC and BIG 1-98)
5-Y sequential AI-tamoxifen for ER+ stage I-III cancer vs tamoxifen only	0.73	0.59-0.89	Beta	Burstein 2010[22] (a meta analysis of trials, including ABCSG-8, ITA, and ARNO 95)
Targeted immunotherapy				
HR for overall survival resulting from				
Trastuzumab for stage I-III cancer with HER2 over expression	0.77	0.67-0.88	Beta	Costa 2010[24] (a meta analysis of trials for a joint analysis of NSABP B-31, NCCTG N9831, HERA, and BCIRG 006)
Trastuzumab for stage IV cancer with HER2 over expression	0.80	0.64-1.00	Beta	Slamon 2001[25]
HR for time-to-recurrence resulting from				
Trastuzumab for stage I-III cancer with HER2 over expression	0.55	0.47-0.64	Beta	Madarnas 2008[26] (a meta analysis of 2 trials for HERA and a joint analysis of NCCTG and NSABP B-31)
Reduction in delays to postoperative radiotherapy				
HR for local recurrence in stage I-II breast cancer	1.005/d	1.001-1.009	Log normal	Punglia 2010[5]

Abbreviations: +, positive; ABCSG-8, Austrian Breast and Colorectal Cancer Study Group trial 8; AI, aromatase inhibitor; ARNO 95, Arimidex-Novadex 95 trial; ATAC, Arimidex, Tamoxifen, Alone or in Combination; BCIRG 006, Breast Cancer International Research Group trial 006; BIG 1-98, Breast International Group trial 1-98; ER, estrogen receptor; FISH, fluorescence in situ hybridization; HER2, human epidermal growth factor receptor 2; HERA, Herceptin Adjuvant trial; HK, Hong Kong; HR, hazard ratio; ITA, Italian Tamoxifen Anastrozole trial; NCCTG, North Central Cancer Treatment Group; NSABP B-31, National Surgical Adjuvant Breast and Bowel Project trial B-31; SEER, Surveillance, Epidemiology, and End Results Program of the National Cancer Institute.

[a] Clinical oncology.

[b] Local pathologists at a large public sector cancer center.

[c] The Dirichlet 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 distribution for stages I through IV: 868, 1622, 329, and 114, respectively, in the nonscreened group; and 1241, 911, 135, and 97, respectively, in the screened group).[7]

[d] Tamoxifen was given at a dose of 20 mg daily.

[e] AIs refer to 3 commonly prescribed AIs (anastrozole, exemestane, and letrozole).

Table 2. Cost Parameter Estimates[a]

Parameter	Best Estimate, $US	Distribution Ascribed in Probabilistic Sensitivity Analysis	Source
Screening (per test)			Wong 2007[7]; local gazetted fees
Mammogram	172	Uniform[b]	
Time (including travel time, waiting time and testing time; totaling 4 h)	28		
Evaluation of abnormal screens		Uniform[b]	Wong 2007[7]; local gazetted fees
Cost of further testing to work up an abnormal mammogram[c]	541		
Time (totaling 6 h)	42		
Aggregate treatment		Uniform[b]	Wong 2007[7]
Ductal carcinoma in situ	3752		
Invasive cancer			
Stage I	16,421		
Stage II	18,295		
Stage III	19,438		
Stage IV	19,438		
Terminal care[d]	26,498		
Hormone therapy		Uniform[b]	Local gazetted fees
Anastrozole, per y	1755		
Letrozole, per y[e]	1701		
Targeted immunotherapy		Uniform[b]	
Trastuzumab by injection per every 3 wk	3162		Local expert opinion[f]
HercepTest	131		Local expert opinion[f]
FISH	261		Local expert opinion[f]
Cardiac monitoring[g]	1292		Kurian 2007[33]; Tan-Chiu 2005[34]
Time (including travel time, waiting time, and testing time; totaling 4 h) for each visit	26		

Abbreviations: FISH, fluorescence in situ hybridization.
[a] All costs were adjusted to 2010 levels.
[b] The plausible interval of the uniform distribution was specified as ±25% of base-case values.
[c] This is based on the assumption that, among women with an abnormal mammogram, 60.9% required repeat mammography, 27.9% required an ultrasound, 4.4% required fine-needle aspiration, and 15.8% required an open biopsy (Wong 2007[7]). The respective costs of these procedures were $172, $180, $464, and $2,323. We estimate that the rate of abnormal results among all screens was 10.1%.
[d] These are costs during the last 6 months before death.
[e] Letrozole 1 mg daily.
[f] Clinical oncologist and pathologists.
[g] These are the average costs of echocardiograms and gated blood pool scans performed every 3 months during trastuzumab treatment.

HERA trial study (2-year follow-up data) and a joint analysis of the NCCTG trial (1.5-year) and NSABP trial B-31 (2.4-year) for which time-to-recurrence data were available. Thus, we conservatively assumed that there was a 5-year carry-over effect for the time-to-recurrence benefit.

Costs

Costs, adjusted to the 2010 level,[31,32] are presented in Table 2. Five major categories of direct medical costs were included: 1) mammography screening, 2) evaluation of abnormal screens, 3) initial treatment of DCIS and invasive cancer (including diagnostic tests, procedures, surgery, drugs [according to a standard formulary, inclusive of tamoxifen], outpatient visits, and hospitalizations), 4) terminal care during the last 6 months of life, and 5) adjuvant hormone therapy (ie, AIs) and immunotherapeutics (including trastuzumab, HercepTest (Dako, Carpenteria, Calif) and fluorescent in situ hybridization (FISH) testing for HER2 expression, and cardiac monitoring).

We derived estimates for the first 4 categories from relevant gazetted costs and fees in the local public[7] and private sectors. The costs were then verified and calibrated according to the trajectory of US cancer costs.[35] We also obtained cost estimates for AIs and trastuzumab and for testing HER2 expression, including HercepTest and FISH, based on gazetted fees in the local public sector.

Costs of cardiac monitoring with echocardiograms every 3 months during targeted immunotherapy were estimated pro rata.[33,34] In the absence of local data, we estimated that inpatient palliative care cost approximately the same in HK as a proportion of total spending on breast cancer care as in the US Medicare program (25%[13,14]; ie, we assumed that enhanced palliative care during the advanced stage of cancer cost an additional 25%). We applied the same discount factor in the conventional exponential discount function with a different time factor to account for health care dollars spent earlier resulting from the reduced wait for postoperative radiotherapy. Patient time costs (in US dollars) were valued using the current median personal monthly wage in HK ($1282), assuming a 44-hour work week. Round-trip travel costs were estimated on survey-based, mean travel distance between home and a regional cancer center by public transportation.

Cost-Effectiveness

The model outcomes were quality-adjusted life expectancy and lifetime costs and were estimated on a 50-year time horizon. To reflect the uncertainty inherent in the scenarios, a probabilistic sensitivity analysis was performed, which involved specifying appropriate probabilistic distributions for clinical parameters and using Monte-Carlo simulations with values selected at random from the prespecified distribution.[2] Cost-effectiveness acceptability curves were constructed based on results from the multivariable probabilistic uncertainty analysis. We adopted a societal perspective and followed the recommendations from the WHO "Choosing Interventions that are Cost-Effective" (WHO-CHOICE) program on a generalized CEA.[1] Future costs and QALYs were discounted at a rate of 3% per year.

The performance of alternative options of the same class of interventions (eg, mass biennial screening from ages 40 to 69 years vs age 79 years) was first assessed under a "competing choice" framework using the incremental cost-effectiveness (CE) ratio. Strategies that were less effective and more costly than an alternative strategy (strongly dominated) and strategies that had a higher incremental CE ratio than a more effective alternative strategy (weakly dominated) were eliminated. This process was repeated for all classes of interventions in which greater than 1 alternative was considered. All strategies that remained from different classes of interventions were entered into a generalized league table and compared based on their average CE ratios. Independent interventions could be added to existing interventions, whereas mutually exclusive interventions had to replace an existing intervention. Results of the interventions were then rank-ordered by their average CE ratios in the same league table. All analyses were performed using the statistical software packages TreeAge Pro 2005 (TreeAge Software, Inc., Williamstown, Mass), STATA version 10.1 (Stata Corp., College Station, Tex), and R (version 2.10.1; R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Estimates of the cost-effectiveness of mutually exclusive, competing choices are presented in Table 3. Nondominated options were entered into the generalized CEA, and the results are summarized in Table 4. The average CE ratios (lowest to highest) determined the rank order of the different interventions (from most CE to least CE). Subject to progressively higher, additional budgetary allocations beyond current spending, these extra interventions should be adopted in the resultant lexical order. We also could evaluate and identify the health-maximizing combination of interventions for any given budget by assuming that the options are divisible with proportional costs and effects and that any combination of interventions is feasible.

For instance, if there were an extra $6.1 M available, then a 25% reduction in wait time for postoperative radiotherapy plus enhanced, home-based palliative care should be adopted, thereby yielding 902.1 additional QALYs overall. However, if $30 M were available, then, in addition to reducing postoperative waiting for radiotherapy and enhancing home-based palliative care across the board, sequential endocrine adjuvant therapy also could be rolled out on a partial basis ($30.0 − $6.1 = 23.9 M remaining in the extra budgetary allocation, which would suffice for 23.9%/38% = 62.9% of all women with ER-positive, postmenopausal breast cancer who could benefit from sequential AI therapy).

Taking into account uncertainties in the costs and effects of the alternative strategies, Figure 3 provides the corresponding cost-effectiveness acceptability curves. Although there is no consensual, single threshold below which a strategy would be considered cost-effective, we previously used the threshold of $50,000 per QALY saved as a reference[7] based on decisions on the adoption of strategies in the United Kingdom[36] and Canada.[37] Three interventions—sequential AI therapy, a 25% reduction in wait time for postoperative radiotherapy, and enhanced, home-based palliative care—are certain to be cost-effective at this threshold, whereas targeted immunotherapy in HER2-over expressed disease has a high probability of

Table 3. Cost-Effectiveness Ratios for 4 Classes of Interventions Under a Competing Choice Framework for 100,000 Women in Hong Kong[a]

Strategy	Lifetime Costs, Million US$	QALYs Saved	Incremental CER, US$ per QALY Saved[b]
1) Biennial mammography strategies			
Status quo[c]	60.09	2,365,682	
Screen women ages 40-69 y	308.88	2,369,110	72,534
Screen women ages 40-79 y	345.60	2,369,290	204,444
2) Shortening waiting time to radiotherapy from BCS in early breast cancer			
Status quo[c]	60.09	2,365,682	
First scenario: Wait time reduction of 15%	60.12	2,365,686	Dominated[d]
Second scenario: Wait time reduction of 25%	60.13	2,365,690	5000
3) Adjuvant AI therapy			
Status quo[c]	60.09	2,365,682	
AI sequential[e]	62.03	2,365,790	17,636
AI primary[f]	63.26	2,365,770	Dominated[d]
4) Enhanced palliative care			
Status quo[c]	60.09	2,365,682	
Home-based	60.36	2,365,720	6750
Inpatient-care	60.66	2,365,700	Dominated[d]

Abbreviations: AI, aromatase inhibitor; BCS, breast-conserving surgery; CER, cost-effectiveness ratio; QALY, quality-adjusted life year.
[a] The 4 strategies were: 1) biennial mammography screening for women ages 40 to 69 years versus women ages 40 to 79 years; 2) shortening the time interval from BCS to radiotherapy in women with early breast cancer by 15% versus 25%; 3) primary (upfront) versus sequential adjuvant endocrine therapy; and 4) enhanced palliative care for advanced breast cancer (stage IV)—home-based care versus care in an inpatient setting.
[b] Options for strategies were compared with the next least expensive, nondominated strategy, except as otherwise stated.
[c] The "status quo" does not include any of the intervention strategies analyzed in the model and represents the current standard and protocol of care for eligible patients according to the Hospital Authority in Hong Kong.
[d] This strategy cost more but was less effective than another strategy or a combination of strategies and, thus, was dominated.
[e] AI sequential indicates the receipt of an AI for 2 to 3 years followed by tamoxifen in postmenopausal women with estrogen receptor-positive cancer.
[f] AI primary indicates the receipt of upfront 5-year AI in postmenopausal women with estrogen receptor-positive cancer.

Table 4. Generalized Cost-Effectiveness League Table for 1,961,100 Hong Kong Chinese Women Aged ≥40 Years

Strategy	Lifetime Costs, Million 2010 US$[a]	Lifetime QALYs Saved[a]	Average CER, US$ per QALY Saved	Cumulative Costs, Million 2010 US$	Cumulative QALYs Saved
Status quo (reference)[b]					
RTx 25% wait time reduction[c]	0.8	156.9	5000	0.8	156.9
PC home-based[d]	5.3	745.2	7105	6.1	902.1
AI sequential[e]	38.0	2118.0	17,963	44.1	3020.1
HER[f]	448.1	7216.8	62,092	492.2	10,236.9
SCR 40-69[g]	4879.0	67,226.5	72,576	5371.3	77,463.5
SCR 40-69–SCR 40-79[h]	721.7	3530.0	204,444	6092.9	80,993.4

Abbreviations: AI, aromatase inhibitor; CER, cost-effectiveness ratio; HER, human epidermal growth factor receptor; PC, palliative care; QALYs, quality-adjusted life-years; RTx, radiotherapy; SCR, screening.
[a] Compared with the status quo scenario.
[b] The "status quo" does not include any of the intervention strategies analyzed in the model and represents the current standard and protocol of care for eligible patients according to the Hospital Authority (with comparable high international standards in management and patient care) in Hong Kong.
[c] RTx 25% wait time reduction indicates shortening postoperative wait time to RTx by 25% in patients with stage I/II breast cancer.
[d] PC home-based indicates enhanced home-based PC for patients with advanced-stage cancer.
[e] AI sequential indicates giving an AI for 2 to 3 years followed by tamoxifen in postmenopausal women with estrogen receptor-positive cancer.
[f] HER indicates 1-year trastuzumab use for patients with HER2-over expressed cancer.
[g] SCR 40-69 indicates biennial mammography for women ages 40 to 69 years.
[h] SCR 40-69–SCR 40-79 indicates incremental from biennial mammography for women ages 40 to 69 years to women ages 40 to 79 years.

being cost-effective at this level. Biennial mammography screening would only have a high probability of being cost-effective at thresholds greater than $100,000 per QALY saved.

DISCUSSION

To the best of our knowledge, this is the first examination of the comparative cost-effectiveness of different preventive and management strategies throughout the disease

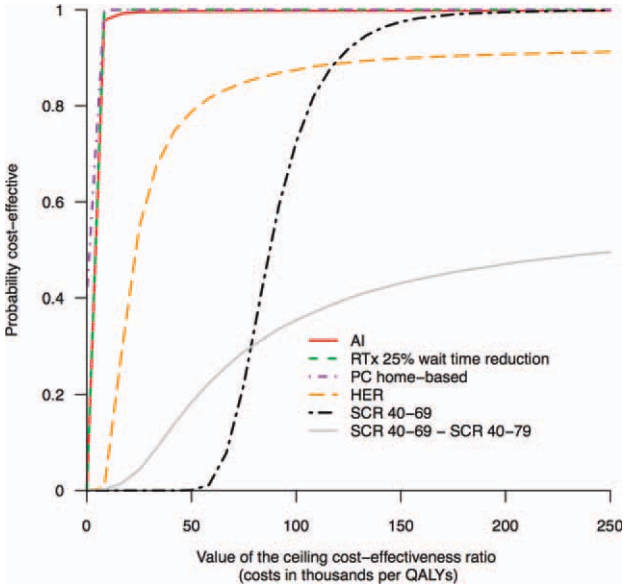

Figure 3. These are acceptability curves of breast cancer-related interventions compared with usual care, representing the current standard and protocol of care for eligible patients according to the Hong Kong Hospital Authority. AI indicates aromatase inhibitor therapy for 2 to 3 years followed by tamoxifen in women with postmenopausal, estrogen receptor-positive cancer; RTx 25% wait time reduction, shortening the postoperative wait time to radiotherapy by 25% in women with stage I/II breast cancer; PC home-based, enhanced, home-based palliative care in women with advanced stage cancer; HER, 1-year trastuzumab use for women with tumors that over express human epidermal growth factor 2; SCR 40-69, biennial screening mammography for women ages 40 to 69 years; SCR 40-69–SCR 40-79, incremental from biennial screening mammography for women ages 40 to 69 years to women ages 40 to 79 years.

course for breast cancer. Such an assessment provides a holistic, value-for-money understanding of the full range of interventions for the same disease, thus contributing to rational prioritization and coherent resource allocation. In HK, as China and other Asian countries rapidly transit through socioeconomic development and experience the attendant epidemiologic changes over the next few decades,[38] the population may serve as a reliable, sentinel, harbinger population in which to determine how best to allocate funding across breast-cancer related interventions over the disease course to maximize health benefits.

It is noteworthy that the empirically observed, optimal resource-allocation pathway confirms that, of all the possible additional interventions not currently covered in the public sector, mass mammographic screening would be the least efficient deployment of any extra resources compared with adjuvant radiotherapy, endocrine therapy, and immunotherapy or palliative services. This finding echoes 2 previous local studies of 1) a conventional cost-effectiveness analysis of mass mammography in which the incremental CE ratio was greater than that of broadly accepted thresholds,[7] and 2) a generalized CE analysis of colorectal, cervical, and breast cancer screening in women suggesting that routine mammography would be the least efficient mass screening program benchmarked against colonoscopy and cervical smears with or without human papillomavirus testing (ie, the only other preventive screening programs for common cancers in women).[39] Underlying these findings is the much lower (albeit increasing[40]) risk of breast cancer in HK Chinese women.[7] A lower incidence would mean a lower prevalence of disease at the time of screening, which, in turn, affects the performance of the mammography when evaluated at the population level. Any potential benefit of earlier detection in a low-risk population is easily outweighed by the corresponding risks induced by false-positive screens, especially in the event that confirmatory follow-up testing is invasive.[7] Screening the entire population would be very costly, and the benefits would accrue only to the small number of women who develop cancer, but those benefits are averaged over the population. Moreover, these results highlight an important distinction in the evaluation of interventions targeted at different disease stages. The effectiveness of mammography screening would depend on the prevalence of undiagnosed disease. In contrast, the effectiveness of cancer treatment would be largely similar across different populations.

Several caveats should be noted. Although randomized controlled trials remain the gold standard for evaluating the optimal combination of health care interventions, the wide availability of the various strategies under evaluation has rendered the conduct of such trials impractical. Decision modeling then becomes the most appropriate method to provide direct evidence to inform policy. Second, the simplistic assumption of perfect adherence to the interventions as stipulated, of course, does not fully reflect the inherent heterogeneities and complexities of disease type, service delivery, patient preferences, and individual behavior. Therefore, the optimized benefits projected in our model may not be completely realized. Nevertheless, the general direction of the findings, specifically, the rank ordering of the interventions, is unlikely to have been affected, because the aforementioned biases should be nonsystematic. Moreover, we did not include administrative costs associated with shortening postoperative wait time to radiotherapy, which may have underestimated the costs associated with this strategy. However, economies of scale because of increased staff capacity, the associated improved efficiency, and, thus, the resultant CE ratio, conversely, may have made this estimate conservative.

Third, we only considered primary and sequential adjuvant therapies. Extended, sequential endocrine therapy of, for instance, 5 years each of tamoxifen and AIs was not studied, because it has not demonstrated a significant overall survival benefit to date.[22] Fourth, our model may not fully reflect downstream effects on the reduced need and associated costs for palliative breast cancer care when there is an increase in funding for screening and treatment, leading to fewer patients who require palliative care. It also may be difficult in practice to increase funding for palliative care only for patients with breast cancer rather than for a range of patients with terminal illness, and this may affect the estimates of cost-effectiveness in our study, which focuses on breast cancer. Finally, we tried to parameterize our models with local data whenever available. For instances in which overseas sources were used, we were careful in calibrating the analyses to fit local empirical observations, thus remaining faithful to contextually specific epidemiology.

In conclusion, our findings provide direct evidence to support policy decisions regarding breast cancer diagnosis, treatment, and palliation that may be dissimilar to current Western practice, including mammography screening policy. These decisions can be deployed flexibly to fit various budgetary constraints and ethical considerations. Our analytic framework can be adapted for other disease entities in optimizing resource allocation along the entire spectrum of preventive and therapeutic activities.

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CONFLICT OF INTEREST DISCLOSURES

The authors made no disclosures.

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