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| Citation | Hong Kong Medical Journal, 2015, v. 21 n. 6, Suppl. 6, p. S9-S12 |
| Issued Date | 2015 |
| URL | http://hdl.handle.net/10722/222550 |
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Generalised cost-effectiveness analysis for breast cancer prevention and care in Hong Kong Chinese

IOL Wong *, JWH Tsang, BJ Cowling, GM Leung

KEY MESSAGES

1. A state-transition Markov model was used to evaluate various interventions across different breast cancer stages based on the generalised cost-effectiveness analysis.
2. From all strategies considered, the optimal allocation of additional resources for breast cancer in descending order would be: 25% reduction in waiting time for postoperative radiotherapy (average cost-effectiveness ratio, US\$5000 per quality-adjusted life year [QALY]); enhanced, home-based palliative care (US\$7105 per QALY); adjuvant, sequential endocrine therapy (US\$17963 per QALY); targeted immunotherapy (US\$62092 per QALY); and

mass mammography screening for women aged 40 to 69 years (US\$72576 per QALY).

3. The generalised cost-effectiveness analysis for the full range of interventions for the same disease enables rational prioritisation and coherent allocation of resources.

Hong Kong Med J 2015;21(Suppl 6):S9-12

HHSRF project number: 09100921

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Introduction

Decisions on funding for interventions at different stages of specific conditions have often been made in isolation. For diseases such as breast cancer, budgetary allocation was proposed to be set at a higher level, given the local disease burden. We have used generalised cost-effectiveness analysis (GCEA)¹ to compare alternative breast cancer-related interventions throughout the disease course.² In the context of the Hong Kong public health care system, this study determined the optimal combination of screening, enhanced capacity for postoperative radiotherapy, adjuvant hormonal therapy with aromatase inhibitors (AIs), and targeted immunotherapy with trastuzumab (herceptin) [that has been excluded from the standard drug formulary in the public sector], and enhanced palliative services in order to maximise overall clinical benefits, subject to the constraints of a limited budget.

Methods

This study was conducted from September 2011 to August 2012. Data were extracted from local clinical, epidemiology and economic data, the US Surveillance, Epidemiology, and End Results database, and the literature and expert opinion whenever appropriate. Clinical effectiveness data from several breast cancer trials including the Early Breast Cancer Trialists' Collaborative Group overview of tamoxifen, the ATAC trial, and other

primary breast cancer trials including NSABP (trial B-31), NCCTG (trial N9831), HERA, and BCIRG (trial 006) were also used. Cost data were derived mostly from local sources such as the government gazette (public fees and charges) and publications of the Hospital Authority (patient-related group costs). To verify internal and external data consistency, the derived cost estimates were benchmarked with relevant overseas' data.

Based on our previous decision analytic model for the clinical course of breast cancer for Hong Kong Chinese women (Fig 1),³ the GCEA evaluated various interventions across different stages of breast cancer. The costs and benefits of alternative strategies were considered throughout the disease pathway (Fig 2). To identify the full range of possible interventions throughout the disease course, the literature on prevention and care of breast cancer appropriate for implementation in Hong Kong was reviewed. Relevancy of associated data to support a cost-effectiveness analysis was also considered.

Strategies studied were: (1) biennial mammography for women aged 40 to 69 or 79 years, (2) reduction in waiting time for postoperative radiotherapy by 15% or 25%, (3) neo-adjuvant treatment using newer and more expensive hormonal modulators AIs (such as anastrozole, letrozole, and exemestane) for postmenopausal hormonal-sensitive patients (upfront AI therapy or sequentially/switching with tamoxifen and AI), (4) targeted trastuzumab immunotherapeutics (ie

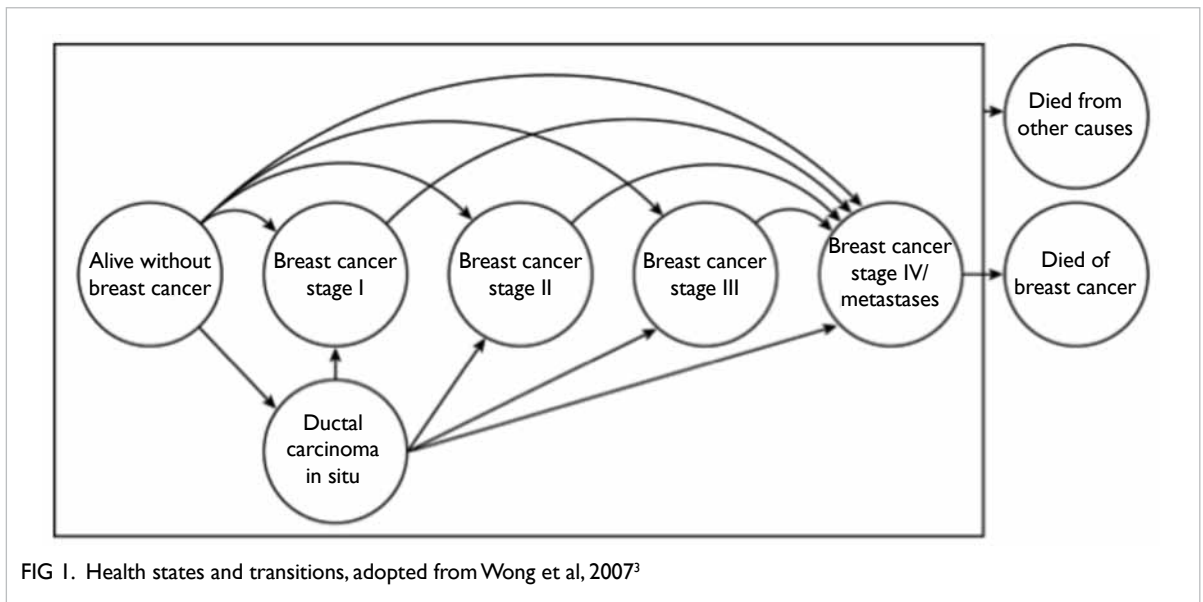


FIG 1. Health states and transitions, adopted from Wong et al, 2007³

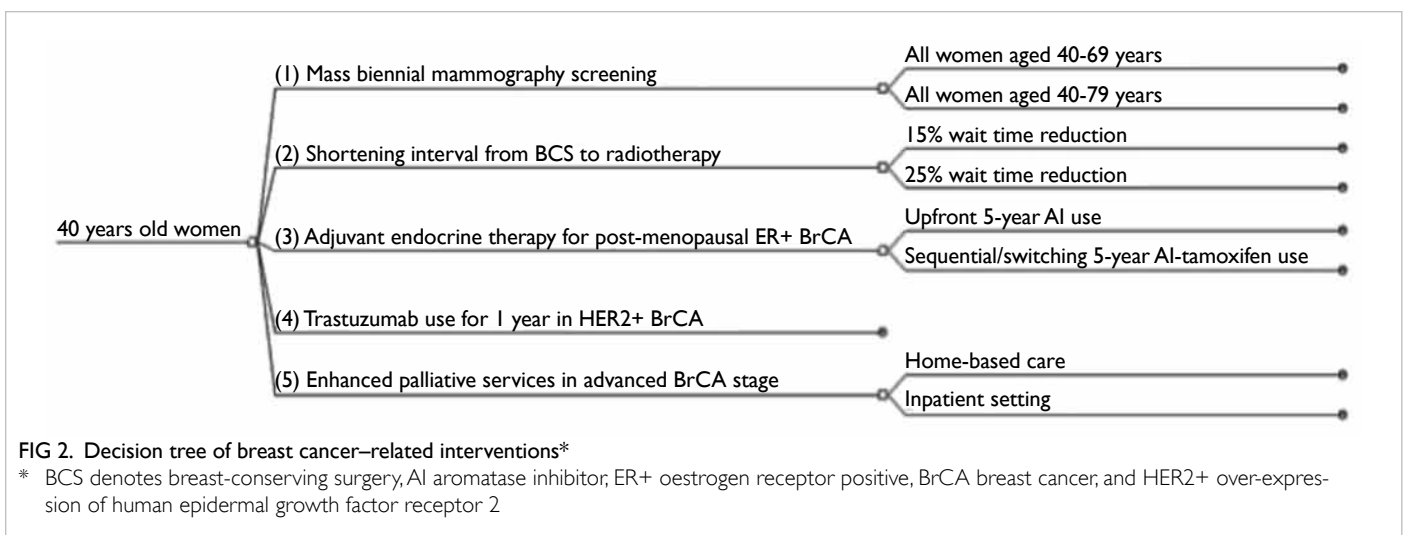


FIG 2. Decision tree of breast cancer-related interventions*

* BCS denotes breast-conserving surgery, AI aromatase inhibitor, ER+ oestrogen receptor positive, BrCA breast cancer, and HER2+ over-expression of human epidermal growth factor receptor 2

herceptin) for breast cancer patients with HER2 over-expression, and (5) enhanced home- or inpatient-based palliative services. The current standard and protocol of care as per the Hospital Authority (with comparably high international standards in management and patient care) was the comparator. Model parameters and assumptions were based on best available data including local clinical, epidemiological, and economic data, as well as a comprehensive literature review. The costs, quality-adjusted life years (QALYs) saved, and average cost-effectiveness ratios of all strategies were compared. Budgetary thresholds were benchmarked against hypothetical scenarios of different funding levels. Guidelines from the World Health Organization's

WHO-CHOICE programme¹ were followed.

Five main direct medical costs were considered: (1) mammography screening, (2) evaluation of abnormal screens, (3) initial treatment of ductal carcinoma in situ and invasive cancer including diagnostic tests, procedures, surgery, drugs (standard formulary inclusive of tamoxifen), outpatient visits, and hospitalisation, (4) adjuvant hormonal AI therapy and immunotherapeutics (including trastuzumab, Herceptin, and FISH testing for HER2 expression, and cardiac monitoring), and (5) terminal care during the last 6 months of life. Other major non-health care costs were also considered such as transportation and time costs. All costs were adjusted to the 2010 level.

In the GCEA, the performance of alternative options of the same class of interventions (eg mass biennial screening for women aged 40 to 69 years vs 79 years) was first assessed under a ‘competing choice’ framework using the incremental cost-effectiveness ratio (ICER). Strategies that were less effective and more costly than an alternative strategy (strongly dominated) and strategies that had a higher ICER than a more effective alternative strategy (weakly dominated) were eliminated. This process was repeated for all classes of intervention where more than one alternative was considered. All strategies that remained from different classes of interventions were entered into a generalised league table and compared based on their average cost-effectiveness ratios. Independent interventions can be added to existing interventions, whereas mutually exclusive interventions must replace an existing intervention. Results of the interventions were then rank-ordered by their average cost-effectiveness ratios in the same league table.

Detailed clinical data, parameters, and model assumptions have been reported.² A societal perspective was adopted in the analyses. Future costs and QALYs were discounted at a rate of 3% per year.

A probabilistic sensitivity analysis was conducted to examine uncertainty surrounding choice of policy. Clinical and cost parameters were specified with appropriate probabilistic distributions, and cost-effectiveness results associated with selecting values at random from the distributions were entered in a Monte Carlo simulation of the model with 1000 runs. Cost-effectiveness acceptability curves were constructed to present the uncertainty of the ICER across different values of the decision thresholds or ceiling ratios that represents

acceptable willingness-to-pay thresholds.

Results

For the Hong Kong female population aged ≥40 in 2009 (accounting for 1 961 000), the incremental total annualised costs, QALYs saved, and average cost-effectiveness ratio of different strategies were compared (Table). The optimal allocation of additional funding for breast cancer in descending order would be: (1) 25% reduction in waiting time for postoperative radiotherapy (US\$5000/QALY); (2) enhanced home-based palliative care (US\$7105/QALY); (3) adjuvant sequential endocrine therapy (US\$17 963/QALY); (4) targeted immunotherapy (US\$62 092/QALY); and (5) mammography screening for women aged 40 to 69 years (US\$72 576/QALY).

In the probabilistic sensitivity analyses, the first three interventions were certain to be cost-effective at the conventionally adopted threshold of US\$50 000 per QALY saved (Figure not shown).

Assuming an additional annual expenditure for breast cancer screening, diagnosis, and treatment in Hong Kong totalling about US\$6.1 million, strategies including 25% reduction in waiting time for postoperative radiotherapy plus enhanced home-based palliative care should be adopted, thereby yielding 902.1 additional QALYs overall. If an additional US\$30 million were available, in addition to the above two strategies, sequential endocrine adjuvant therapy should also be adopted on a partial basis.

Discussion

Comparing cost-effectiveness of different strategies throughout the course of breast cancer provides a

TABLE. Generalised cost-effectiveness analysis for 1 961 000 Hong Kong Chinese women aged ≥40 years

| Strategy | Lifetime costs (million 2010 US\$)* | Lifetime quality-adjusted life years (QALYs) saved* | Average cost-effectiveness ratio (US\$ per QALY saved) | Cumulative costs (million 2010 US\$) | Cumulative QALYs saved |
|--|-------------------------------------|---|--|--------------------------------------|------------------------|
| 25% reduction in waiting time for postoperative radiotherapy (for women with stage I-II breast cancer) | 0.8 | 156.9 | 5000 | 0.8 | 156.9 |
| Enhanced home-based palliative care (for women with advanced cancer stages) | 5.3 | 745.2 | 7105 | 6.1 | 902.1 |
| Providing an aromatase inhibitor for 2 to 3 years followed by tamoxifen (for women with postmenopausal oestrogen receptor positive cancer) | 38.0 | 2118.0 | 17 963 | 44.1 | 3020.1 |
| 1-year trastuzumab use (for women with HER2 over-expressed cancer) | 448.1 | 7216.8 | 62 092 | 492.2 | 10 236.9 |
| Biennial mammography for women aged 40 to 69 years | 4879.0 | 67 226.5 | 72 576 | 5371.3 | 77 463.5 |
| Incremental from biennial mammography for women aged 40 to 69 years to women aged 40 to 79 years | 721.7 | 3530.0 | 204 444 | 6092.9 | 80 993.4 |

* Compared with the status quo scenario, which is the current standard and protocol of care as per the Hospital Authority

holistic value-for-money understanding of the full range of interventions, and thus enables rational prioritisation and coherent allocation of resources. The findings may also have implications for affordability of cancer medicines in the Hong Kong public health care system, and for societal values and financial consequences for patients and their families.

Of the additional interventions not currently covered in the public sector, mass mammography screening would be the least cost-effective, compared with a reduction in waiting time for postoperative radiotherapy, palliative services, or adjuvant endocrine and immunotherapy. This finding is consistent with two previous local studies: (1) a conventional cost-effectiveness analysis of mass mammography reported that the ICER was above that of broadly accepted thresholds,³ and (2) a GCEA of colorectal, cervical, and breast cancer screening in women suggested that routine regular mammography would be the least cost-effective compared with colonoscopy and cervical smears +/- human papillomavirus testing (ie the only other preventive screening programmes for common cancers in women).⁴ Underlying these findings is the relatively lower (albeit increasing)⁵ risk of breast cancer in Hong Kong Chinese women,³ compared with their western counterparts. 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 would be outweighed by the corresponding potential risk/harm induced by over-diagnosis, false positive screens, false reassurance, anxiety and psychological consequences.³ Screening the entire population would be very costly, where the benefits only accrue to a small number of women who develop cancer. The effectiveness of mammography screening would depend on the prevalence of undiagnosed disease. The effectiveness of cancer treatment would be largely similar across different populations.

A potential caveat was that the assumption of

perfect adherence to the interventions does not fully reflect the inherent heterogeneities and complexities of disease type, service delivery, individual behaviour, and patient preferences. The optimised benefits projected in our model may not be completely realised.

Given the current disease pattern and age profile of patients in the Hong Kong Chinese female population, the most cost-effective interventions are those that ensure women receive the most-intensive treatment and care after a diagnosis of breast cancer, rather than receive mammography screening at a younger age. Further studies are needed to understand how these decisions can be flexibly deployed to comply with various budgetary constraints, affordability of cancer medicines, and ethical considerations. Our results can further inform policy debates about resource allocation for service delivery regarding breast cancer prevention, diagnosis, treatment, and palliative care.

Acknowledgement

This study was supported by the Health and Health Services Research Fund, Food and Health Bureau, Hong Kong SAR Government (#09100921).

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