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Department of Health and Ageing

# Screening Monograph No.9/2009

## BreastScreen Australia Evaluation

### Economic Evaluation and Modelling Study

May 2009



## **BreastScreen Australia Evaluation – Economic Evaluation and Modelling Study – May 2009**

Prepared by IMS Health Pty Ltd Australia for the Australian Government Department of Health and Ageing

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## LIST OF ABBREVIATIONS

<b>ABS</b>	Australian Bureau of Statistics
<b>ACER</b>	average cost-effectiveness ratio
<b>AHMAC</b>	Australian Health Ministers' Advisory Council
<b>AIHW</b>	Australian Institute of Health and Welfare
<b>AJCC</b>	American Joint Committee on Cancer
<b>AQoL</b>	Assessment of Quality of Life
<b>AR-DRG</b>	Australian Refined Diagnostic Related Groups
<b>AUD</b>	Australian dollars
<b>CBE</b>	clinical breast examination
<b>CEA</b>	cost-effectiveness analysis
<b>CEAC</b>	cost-effectiveness acceptability curves
<b>CENTRAL</b>	Cochrane Central Register of Controlled Trials
<b>C/E</b>	cost-effectiveness
<b>CI</b>	confidence interval
<b>CPI</b>	consumer price index
<b>DCIS</b>	ductal carcinoma in situ
<b>DES</b>	discrete event simulation
<b>DM</b>	Deutschmark
<b>DMIST</b>	Digital Mammography Imaging Screening Trial
<b>DoHA</b>	Department of Health and Ageing
<b>EAC</b>	Evaluation Advisory Committee
<b>EC</b>	European Community
<b>ECU</b>	European currency unit
<b>FF</b>	French franc
<b>FIM</b>	Finnish mark
<b>HYE</b>	healthy year equivalent
<b>IARC</b>	International Agency for Research in Cancer
<b>ICER</b>	incremental cost-effectiveness ratio
<b>ICUR</b>	incremental cost-utility rate

<b>IT</b>	information technology
<b>LY</b>	life year
<b>LYG</b>	life year gained
<b>LYS</b>	life year saved
<b>MAUI</b>	multi-attribute unity instruments
<b>MBS</b>	Medicare Benefits Schedule
<b>MCLYS</b>	marginal cost per life year saved
<b>MSAC</b>	Medical Services Advisory Committee
<b>NBCC</b>	National Breast Cancer Centre (now NBOCC)
<b>NBOCC</b>	National Breast and Ovarian Cancer Centre
<b>NCI</b>	National Cancer Institute (USA)
<b>NHMRC</b>	National Health and Medical Research Council
<b>NHS</b>	National Health Service (UK)
<b>NMP</b>	Norwegian Mammography Project
<b>NZD</b>	New Zealand dollars
<b>OECD</b>	Organization for Economic Cooperation and Development
<b>PBAC</b>	Pharmaceutical Benefits Advisory Committee
<b>PPP</b>	purchasing power parity
<b>QALY</b>	quality-adjusted life year
<b>QoL</b>	quality of life
<b>RCT</b>	randomised controlled trial
<b>RR</b>	relative risk
<b>SEER</b>	surveillance, epidemiology, end results
<b>SG</b>	standard gamble
<b>TNM</b>	tumour, node, metastasis
<b>TTO</b>	time trade-off
<b>USD</b>	United States dollars
<b>WHO</b>	World Health Organization
<b>WTP</b>	willingness-to-pay

## EXECUTIVE SUMMARY

Breast cancer is the most common invasive cancer among women in Australia. The lifetime risk of developing breast cancer before the age of 75 years is one in 11. The annual number of new breast cancer diagnoses increased from 5318 in 1983 to 12,027 in 2002 (AIHW and NBOCC 2006a).

Breast cancer is associated with a significant increase in mortality and is the leading cause of cancer deaths among women in Australia. Breast cancer five-year relative survival was 86.6% between 1998 and 2002. In 2004, there were 2641 deaths in Australian women due to breast cancer (AIHW and NBOCC 2006a).

As with some other cancers, diagnosis and treatment of breast cancer at earlier stages is associated with improved survival. Improved prognosis from early diagnosis and treatment is a key rationale for breast cancer screening programs.

BreastScreen Australia actively targets all women aged 50–69 years; however, women aged 40–49 years and over 70 years are also eligible to attend.

In Australia, the mortality rate of breast cancer among women aged 50–69 years has declined from 66.5 per 100,000 women in 1991 (before introduction of the screening program) to 50.9 per 100,000 women in 2004 (AIHW 2007).

This decrease is likely to be attributable, at least in part, to the early detection of breast cancer in women.

### COST-EFFECTIVENESS LITERATURE REVIEW

A systematic review of cost-effectiveness studies of breast cancer screening strategies was conducted. This review collates prior international evidence on the cost-effectiveness of breast cancer screening and is used to inform the methods for the economic model presented in this report. A total of 25 studies were included in the final literature review by applying the criteria listed in **Table 2**.

The key findings of the literature review were:

- The modelling approaches are generally divided into three categories – non-modelled cost-effectiveness studies, Markov models and discrete event models. Markov modelling was the most commonly applied approach (19 studies) identified in the literature review, and microsimulation was the most commonly applied method of analysis.
- Markov modelling studies are considered to be most appropriate to the current research questions when incorporating the natural history of breast cancer and stage shift associated with early detection of disease attributable to screening.
- Most studies that incorporated the natural history of breast cancer in their modelling approach applied tumour size to define the relevant health states.

- The cost-effectiveness of breast cancer screening among younger women (aged 40–49 years) and older women (aged 70 years and above) is less favourable when compared with screening women aged 50–69 years.
- The cost-effectiveness of breast cancer screening decreased in favourability with a shorter screening interval and increased in favourability with a longer screening interval
- The most commonly reported ICER was in terms of cost/LYG.
- Results were dependent on key parameters such as age at start of first screen, age at last screen, participation, and screening intervals. These parameters varied by study setting and, therefore results also varied significantly among studies.
- Evidence on the cost-effectiveness of digital mammography screening compared to all-film mammography screening was limited.
- Only two Australian studies were identified in the literature review (Hall et al 1992, Carter et al 1993). Results from other international studies were not considered to be comparable to the current model because of differences in inter-country healthcare systems, disease incidence, prevalence, screening pathways, treatment patterns, and healthcare costs. Hall et al (1992) estimated ICERs associated with screening to be AUD\$7,190/LYS and AUD\$16,355/HYE compared with a scenario of no screening. Carter et al (1993) reported ICER estimates of four different policy options versus a policy of triennial screening of women aged 50–69 years. These estimates varied from AUD\$22,093/LYG (biennial screening for women aged 50–69) to AUD\$54,237/LYG (annual screening for women aged 40–49 years and biennial screening for women aged 50–69 years).

## **BREASTSCREEN AUSTRALIA PROGRAM AND EPIDEMIOLOGICAL DATA ANALYSIS**

The Economic Evaluation and Modelling Study of the BreastScreen Australia Evaluation compares the outcomes of the screening program with expected outcomes in the absence of the screening program. The preferred source of data for the economic evaluation is BreastScreen Australia. The approach used in the economic evaluation is to populate the economic model parameters with BreastScreen Australia data, where available. Where BreastScreen Australia data are not available, other Australian data are preferred over international data. Screening program data were obtained from the BreastScreen Australia Monitoring Report 2004–2005 (AIHW 2008) which summarises program data from 2004–2005. The breast cancer natural history component of the economic model is populated using published data external to BreastScreen Australia.

A review of randomised controlled trial (RCT) data identified seven studies. Of these seven studies, one study (Edinburgh) was considered to be neither adequately randomised nor able to provide reliable data, and was excluded from the Cochrane meta-analysis. A significant risk reduction was demonstrated at seven years in a meta-analysis of all six studies (RR 0.80; 95% CI: [0.70, 0.91]) and 13 years (RR 0.80; 95% CI: [0.73, 0.88]).

A Cochrane review did not find risk reduction in breast cancer mortality with screening at 13 years to be significant in a meta-analysis of the two adequately randomised studies (relative risk [RR] 0.93; 95% CI: [0.80, 1.09]). The IARC reported the relative risk of death from breast cancer to be 0.81 (95% CI: [0.65, 1.01]) in women aged 40–49 years and 0.75 (95% CI: [0.67, 0.85]) in women aged 50–69 years.

The individual and meta-analysed RCT data were not directly included in the model, but were used to make comparisons with breast cancer mortality risk reduction predicted by the economic model.

## MODELLED ECONOMIC EVALUATION

A modelled economic evaluation is presented that evaluates the cost-effectiveness of the current BreastScreen Australia program and various alternative screening scenarios compared with a hypothetical no screening scenario. The main objective of the economic model is to integrate and assess breast cancer mortality benefits of screening, breast cancer screening costs, and breast cancer treatment costs avoided due to increased cancer detection rates and the cancer stage shift associated with early detection through screening.

A Markov model incorporating a Monte Carlo simulation was applied as the appropriate modelling approach. The model is simulated over a woman's lifetime (women are assumed to survive to a maximum age of 100 years) using a cycle length of three months. The analysis was undertaken from the perspective of the Australian healthcare payer, and all direct healthcare costs were included in the analysis.

The incremental cost-effectiveness ratios were reported in terms of \$/life years gained. In addition to the total number of life years gained, the total numbers of additional cancers detected (screen detected cancers, interval cancers and cancers detected outside the program) and deaths avoided, are also determined using the model.

The model consists of two separate components; the natural history of disease component and the BreastScreen Australia screening pathway. The health states in the Markov model are defined as: no cancer; undiagnosed and diagnosed ductal carcinoma *in situ* (DCIS); undiagnosed and diagnosed cancers of 0–10 mm, 11–20 mm, > 20 mm diameters; breast cancer death; other death (attributable to non-breast cancer causes). In each cycle, the likelihood that a woman progresses between health states is based on transition probabilities associated with each health state. These transition probabilities vary between model cycles and women depending on the patient's age, disease history, and so forth. Breast cancer death is defined in the model as death attributable to breast cancer among women with either diagnosed or undiagnosed breast cancer. Other death is defined as death attributable to natural causes (all-cause mortality). In each model cycle, after determining whether the individual progresses to another health state, the individual moves through the screening pathway.

BreastScreen Australia program and epidemiological inputs include participation rates, DCIS and cancer detection rates (including screen detected cancers, interval cancers, and clinically detected cancers), breast cancer and other mortality, cancer dwell times, mammography sensitivity, and

DCIS/breast cancer incidence and prevalence rates. Two main cost components were included in the model: screening costs in the BreastScreen Australia program and annual treatment costs by tumour size.

The inputs associated with considerable uncertainty were varied in sensitivity analysis to determine the influence on cost-effectiveness results. A limited cost-utility analysis was also conducted by determining utility estimates associated with various diagnosed breast cancer health states.

## **RESULTS OF THE MODELLED EVALUATION**

The current policy of screening eligible women aged 40+ who participate, while specifically targeting women aged 50–69 years, yielded a cost-effectiveness estimate of \$38,302/LYG and \$23,713/LYG over a period of 20 and 40 years, respectively.

### **VARYING THE AGE RANGE IN THE BASE CASE CURRENT (TARGET AND ELIGIBLE) POPULATION (OPTIONS 1A–11A)**

Increasing the age range of the targeted group had varied results. In general, expanding the targeted age group resulted in only a slightly improved cost-effectiveness profile. Expanding the target age group to include women aged 40–49 years resulted in the least favourable cost-effectiveness estimate (\$52,318/LYG) compared with the base case (\$38,302/LYG). Including women aged 45–74 years in the target age group was found to be the most cost-effective strategy. The ICER estimate for this population was \$37,612/LYG compared with a policy of no screening.

Varying the frequency of screening from biennial to annual resulted in an ICER of \$55,411/LYG; whereas a policy of triennial screening resulted in an ICER estimate of \$30,602/LYG compared with no screening.

Despite variability in the ICER estimates, all policy options associated with increasing the target age group remained below \$55,000/LYG compared with a scenario of no screening. Furthermore, the ICER estimates associated with each policy option remained within the range of \$37,873/LYG to \$52,318/LYG compared with a scenario of no screening.

### **VARYING THE AGE RANGE IN THE BASE CASE TARGET POPULATION (OPTIONS 1B–11B)**

The analysis of the base case target population only (no eligibility for screening outside the target group) at a participation rate of 70% and a screening interval of two years yielded a cost-effectiveness estimate of \$45,576/LYG over 20 years.

The inclusion of women aged 45–79 years was the most cost-effective option at \$40,741/LYG over 20 years; and inclusion of women aged 45–49 years was the least cost-effective option at \$67,652/LYG over 20 years. These results reflect increases in screening costs as additional populations participate at a rate of 70%, relative to the numbers of cancers detected in those age groups. In general, compared with the base case target (50–69 years) population, inclusion of other age groups of women resulted in less favourable cost-effectiveness estimates.

Variation in the frequency of screening to annual screening resulted in a less favourable cost-effectiveness estimate of \$47,520/LYG. Triennial screening resulted in a more favourable cost-effectiveness estimate of \$39,589/LYG.

### **VARYING PARTICIPATION RATES IN THE BASE CASE TARGET POPULATION (OPTIONS 1C–6C)**

Variation in the participation rate of the base case target population (50–69 years) when only the target population is eligible for screening resulted in an ICER of \$48,464/LYG. Increasing participation increases the numbers of cancers detected and the costs of screening and treatment. In general, when moving from a participation rate of 45% to 70%, cost-effectiveness improved.

### **EXTENDING THE PROGRAM TO INCLUDE SCREENING OF HIGH RISK WOMEN IN THE BASE CASE CURRENT (TARGET AND ELIGIBLE) POPULATION**

The extension of the program to include women with a family history of breast cancer resulted in a cost-effectiveness estimate of \$52,164/LYG. In the base case analysis (Option A), it was assumed that of those women with a personal history of breast cancer, 50% would be reinitiated for screening on an annual basis. In the scenario analysis, annual screening of all women (100%) with a personal history of breast cancer was simulated. This yielded the most favourable ICER estimate in this category of policy options (\$44,341/LYG) due to a higher cancer detection rate.

The scenario evaluating inclusion of women with significant symptoms of breast cancer and their diagnostic work up through a 'one-stop-shop' service in the public healthcare system resulted in an ICER estimate of \$50,052/LYG. In the scenario where diagnostic work up was conducted via a fee-for-service private provider arrangement, the ICER estimate remained at \$50,052/LYG. However, an incremental out-of-pocket cost of \$64 would be borne privately by women. The policy option to investigate the effect of discouraging women with significant symptoms of breast cancer from participating in the program also resulted in an ICER of \$50,052/LYG.

### **POTENTIAL VARIATIONS IN PROGRAM DELIVERY IN THE BASE CASE CURRENT (TARGET AND ELIGIBLE) POPULATION**

In each of the scenarios evaluating variations in program delivery, changes in cost-effectiveness were primarily attributable to variation in the per woman costs of screening. The use of digital mammography resulted in a cost-effectiveness estimate of \$40,650/LYG. This estimate was sensitive to the additional costs associated with implementing digital mammography. Other changes in work force, targeted to employ less specialised staff for all double mammogram reads, resulted in more favourable cost-effectiveness estimates ranging from \$36,043/LYG to \$36,405/LYG.

## SENSITIVITY ANALYSES

The results of the model were tested for robustness by varying some of the key model inputs and assumptions. The results of the model were sensitive with respect to the discount rate, the assumption regarding the total number of Medicare Benefits Schedule (MBS) funded mammograms that could be considered part of screening, and the assumption regarding progression from DCIS to invasive cancer.

As part of the sensitivity analyses indirect costs were also included to determine the effect on the cost-effectiveness estimate. The inclusion of indirect costs associated with the diagnosed breast cancer health states resulted in a negligible increase in cost-effectiveness. Therefore, it is reasonable to conclude that inclusion of indirect costs in the model, and the adoption of a societal perspective, does not impact on the ICER estimate.

A limited cost-utility analysis was conducted to estimate the ICER in terms of cost/QALY gained. Utility values for breast cancer treatment, specifically for women undergoing mastectomy or breast conserving surgery, were assigned to each diagnosed cancer health state to adjust for quality of life once diagnosed and treated for breast cancer. The results showed the incremental cost-utility ratio (ICUR) for the base case analysis to be \$39,700/QALY gained. The utility estimates were varied by 10% in both directions and these were included in the model to test variation in cost-utility estimates. The ICER estimates of \$40,613/LYG and \$38,864/LYG did not show significant variation from the base case estimate.

## FINANCIAL IMPLICATIONS ANALYSIS

The financial implications of implementing the BreastScreen Australia program for the next decade (2008 to 2017) in Australia were estimated for both eligible and target populations. These estimates were based on the numbers of participants under different screening policies and the unit cost per woman screened. Results from the screening program financial implications analysis illustrate that:

- under the current policy (Option A—screening women aged 40–44, 45–49, 50–69 and 70 years and above biennially at current program participation rates [2004–2005]), total screening costs in Year 1 (2008) are estimated to be \$124 million, increasing to \$147 million in Year 10 (2017)
- holding all other factors constant, the costs of implementing the screening program will increase over time as a consequence of increased population sizes
- increasing targeted participants' age ranges leads to increased screening program costs because of greater numbers of eligible women
- increasing (or decreasing) the screening interval would reduce (or increase) total program costs
- increasing (or decreasing) screening participation rates among the eligible and/or target populations would result in increased (or decreased) total screening program costs.

The economic modelling analysis in **Section 5** demonstrates that the screening program increases numbers of cancers detected, and hence, increasing the numbers of cancers treated. Breast cancer treatment leads to productivity losses (indirect costs) as a consequence of absences from paid work by women undergoing treatment (**Section 5**). Increasing the numbers of cancers detected, and hence, women who require breast cancer treatment, increases indirect costs associated with breast cancer treatment. The financial implications analysis also provides estimates of anticipated additional indirect costs associated with breast cancer each year with availability of the screening program. Results from the indirect cost analysis demonstrate that:

- under the current policy (Option A – screening women aged 40–44, 45–49, 50–69 and 70 years and above biennially at the current program participation rates [2004–2005]), the total indirect costs of breast cancer treatment in Year 1 (2008) are estimated to be \$679,352, increasing to \$1.5 million in Year 10 (2017)
- including women aged 40–44 and 45–49 years in the target population leads to increased indirect costs; inclusion of women aged 70 years and above in the target population has negligible impact on indirect costs
- increasing (or decreasing) screening intervals reduces (or increases) total indirect costs
- increasing (or decreasing) screening participation rates in the target population (50–69 years) results in an increase (or decrease) in total indirect costs.

Overall, additional indirect costs associated with breast cancer treatment as a consequence of implementation of the screening program are small compared with screening program costs.

## CONCLUSIONS

The main findings of the modelled economic evaluation were:

- Expanding the target age group to include women aged less than 50 years and 70 years and above (Options A–9A) produced ICER estimates between \$37,612/LYG and \$52,318/LYG.
- Varying the frequency of the screening interval to triennial screening, using the current BreastScreen Australia program as the base case, resulted in an ICER of estimate of \$30,602/LYG compared with a no screening scenario. Annual screening resulted in an ICER of \$55,411/LYG.
- Expanding the current target age group of women (50–69 years) to include women aged less than 50 years and 70 years and above without maintaining the eligible age group of women, and assuming a 70% participation rate, resulted in ICER estimates from \$40,741/LYG to \$67,652/LYG.
- Variation of the screening participation rate in the target age group of women aged 50–69 years only did not lead to large variations in incremental cost-effectiveness.
- Annual screening of women with a family history of breast cancer and biennial screening of women with symptoms resulted in ICER estimates greater than \$50,000/LYG. The exception was a policy to screen annually all women with a personal history of breast cancer which resulted in an ICER estimate of \$44,341/LYG.
- Total screening costs associated with the current policy were estimated at \$124 million in Year 1, increasing to \$147 million in Year 10. The increase in costs over time is likely due to an increasing population size.
- A decrease in the frequency of screening resulted in a decrease of total program costs and an increase in screening increased total program costs.
- Total indirect costs of treatment associated with the current policy as a result of productivity losses (workplace absences) as women undergo treatment for breast cancer were estimated at \$679,352 in Year 1, increasing to \$1.2 million in Year 10.
- Including women aged 40–44 and 45–49 years in the current target population (50–69 years) leads to an increase in indirect costs; inclusion of women aged 70 years and above has a negligible impact on indirect costs.