Cost-effectiveness analysis of screening modalities for breast cancer in Japan with special reference to women aged 40-49 years
Ohnuki K, Kuriyama S, Shoji N, Nishino Y, Tsuji I, Ohuchi N

Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
Three modalities of screening for breast cancer (BC) were examined:

annual clinical breast examination (CBE) alone;

annual CBE and screening mammography (SMG) in combination; and

biennial CBE and SMG.

All screening strategies could be performed for 10 years in women aged from 30 to 79 years. The five different age groups considered were 30 to 39 years, 40 to 49 years, 50 to 59 years, 60 to 69 years, and 70 to 79 years.

Type of intervention
Screening.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised a hypothetical cohort of asymptomatic Japanese women aged 30 to 79 years. The base-case analysis focused on women aged 40 to 49 years.

Setting
The setting was secondary care. The economic study was carried out in Japan.

Dates to which data relate
The effectiveness data were derived from studies published between 1995 and 2003. The resource use data and costs were derived from a 1996 survey. The price year was unclear.

Source of effectiveness data
The effectiveness evidence was derived from a synthesis of published studies and authors’ opinions.

Modelling
A published modelling approach was used to determine the costs and benefits of the alternative screening strategies in hypothetical cohorts of 100,000 women for each option. Women underwent active screening for 10 years and were then followed for 5 years, while women undergoing no screening were followed for 15 years. Thus, the time horizon
of the model appears to have been 15 years. A structure of the decision model was provided. Women undergoing a screening strategy could test positive (true or false positive) or negative (true or false negative). Women with a negative test could either develop cancer with symptoms (false negative) or not (true negative) and receive a further screening the following years. Women with a positive test could either develop cancer (true positive) or not (false positive) and receive a further screening the following years. Cancer could be cured or lead to death. Thus, the accuracy of each screening approach determined the number of women in whom BC was detected and who underwent further examination.

Outcomes assessed in the review
The outcomes estimated from the literature were:

- the sensitivity, specificity, and proportion of early-stage BC associated with each screening approach;
- the incidence of BC;
- mortality from BC and from other causes;
- the life expectancy of the general population;
- the proportion of early-stage BC detected at outpatient clinics; and
- the 5-year survival for women with either early- or advanced-stage of disease.

Data on screening accuracy were presented for two sub-groups of women, those aged 40 to 49 years and those aged 50 to 69 years.

Study designs and other criteria for inclusion in the review
It was unclear whether a systematic review of the literature was undertaken to identify the primary studies. Thus, the primary studies might have been identified selectively. Data on screening accuracy came from studies conducted in a Japanese prefecture. Details of the periods covered by these studies (1995 to 1998) and the number of women involved were reported (a total of 15,271 women aged 40 to 49 years and 17,755 women aged 50 to 69 years). Similar sources were used to derive cancer incidence. Mortality was retrieved from Vital Statistics in Japan, while life expectancy came from Life Tables. Other data were obtained from the Ministry of Health and Welfare.

Sources searched to identify primary studies
Not reported.

Criteria used to ensure the validity of primary studies
Not reported.

Methods used to judge relevance and validity, and for extracting data
Not reported.

Number of primary studies included
Eight primary studies provided the clinical data.

Methods of combining primary studies
A narrative approach appears to have been used to combine the primary estimates. The 5-year survival and proportion of early-stage BC detected at outpatient clinics were calculated as average values after the exclusion of extreme
values.

Investigation of differences between primary studies
Not reported.

Results of the review
In women aged 40 to 49 years, the sensitivity with annual CBE was 0.873, the specificity was 0.918, and the proportion of early-stage BC was 0.620.

In women aged 40 to 49 years, the sensitivity with biennial CBE + SMG was 0.938, the specificity was 0.898, and the proportion of early-stage BC was 0.800.

In women aged 50 to 69 years, the sensitivity with annual CBE was 0.932, the specificity was 0.961, and the proportion of early-stage BC was 0.500

In women aged 50 to 69 years, the sensitivity with biennial CBE + SMG was 0.950, the specificity was 0.930, and the proportion of early-stage BC was 0.740.

The average proportion of early-stage BC for BC cases found at outpatient departments was 37.2% (range: 28 to 60).

The 5-year survival rate was 95.2% (range: 92 to 99) for women with early-stage BC and 73.8% (range: 60 to 82) for women with advanced BC.

Other data were not reported.

Methods used to derive estimates of effectiveness
The authors made some assumptions that were used in the decision model.

Estimates of effectiveness and key assumptions
Compliance with screening was assumed to be 100%, and the sensitivity of further examinations was assumed to be 100%.

Measure of benefits used in the economic analysis
The primary benefit measure used was the expected number of life-years (LYs) associated with each screening strategy. The LYs were derived using the modelling approach and were discounted at an annual rate of 3%. Survival duration was also reported as a model output.

Direct costs
The analysis of the costs was carried out from the perspective of the health care payer. It included the costs associated with the screening test, work-up examinations for recalled women, diagnostic tests for outpatients, initial treatment of BC and terminal care. The unit costs were not presented separately from the quantities of resources used. Costs and resource use data were estimated using a questionnaire survey commissioned by the Ministry of Health and Welfare in 1996 at 13 medical Japanese centres where BC screening had been actively conducted. Discounting was relevant, given that long-term costs were incurred, and an annual rate of 3% was used. The price year was not explicitly reported, but it could have been 1996.

Statistical analysis of costs
The costs were treated deterministically.
Indirect Costs
The indirect costs were not included in the economic analysis.

Currency
Japanese yen (JPY).

Sensitivity analysis
A univariate sensitivity analysis was carried out to assess the robustness of cost-effectiveness ratios to variations in the sensitivity and specificity of the alternative strategies, as well as the costs of screening. Alternative values were based on published sources.

Estimated benefits used in the economic analysis
In a cohort of 100,000 women aged 40 to 49 years, the number of LYs was 771.8 with no screening, 815.5 with annual CBE, 852.9 with annual CBE + SMG, and 833.8 with biennial CBE + SMG.

Survival duration was 15,963.9 years with no screening, 16,756.8 years with annual CBE, 17,434.2 years with annual CBE + SMG, and 17,098.0 years with biennial CBE + SMG.

Annual CBE + SMG was the most-effective strategy for all age groups.

Cost results
In a cohort of 100,000 women aged 40 to 49 years, the total costs (x10^6) were JPY 2,355.5 with no screening, JPY 5,265.3 with annual CBE, JPY 7,346.1 with annual CBE + SMG, and JPY 4,652.1 with biennial CBE + SMG.

Synthesis of costs and benefits
Incremental cost-effectiveness ratios were calculated in order to combine the costs and benefits of the alternative strategies in comparison with no screening.

In a hypothetical woman aged 40 to 49 years, the incremental cost per LY saved in comparison with no screening was JPY 66,536,600 with annual CBE, JPY 61,540,300 with annual CBE + SMG, and JPY 37,002,400 with biennial CBE + SMG.

The incremental cost per year of survival duration in comparison with no screening was JPY 3,669,900 with annual CBE, JPY 3,394,300 with annual CBE + SMG, and JPY 2,025,100 with biennial CBE + SMG.

Therefore, biennial screening was the most cost-effective strategy.

The same result was achieved in the other age groups, but higher cost-effectiveness ratios for all strategies were found for the age groups 30 to 39 years and 70 to 79 years.

The sensitivity analysis showed that the base-case results were robust to variations in the sensitivity of the screening tests. The cost-effectiveness ratio was reversed (annual CBE preferred strategy) when the specificity of annual CBE alone was at least 0.950 and that of biennial CBE + SMG was less than or equal to 0.700. Similarly, the cost-effectiveness ratios were altered when the screening cost of annual CBE was less than or equal to JPY 1,000, and that of biennial CBE + SMG was at least JPY 6,000.

Authors' conclusions
Biennial screening for breast cancer (BC) based on combined clinical breast examination (CBE) and screening mammography (SMG) was the most cost-effective strategy in asymptomatic Japanese women.
CRD COMMENTARY - Selection of comparators
The choice of the comparators under examination was appropriate and was justified by the authors. Different age groups and screening intervals were considered. You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness data were derived from the literature, although there was no indication of whether the review was conducted in a systematic manner. The authors selected national studies in order to populate the decision model with relevant epidemiological information. There was extensive information on most of the sources from which the clinical data were derived. For example, accuracy of screening was based on large samples of Japanese women. Data on mortality and cancer incidence were obtained from typical sources such as Vital Statistics and national databases. The authors did not address the issue of heterogeneity across the primary studies. The problem of uncertainty surrounding some clinical estimates was tested in the sensitivity analysis.

Validity of estimate of measure of benefit
The summary benefit measures were appropriate and reflected the most relevant dimension of health for women with BC (i.e. life expectancy). LYs have the further advantage that they can be compared with the benefits of other health care interventions.

Validity of estimate of costs
The analysis of the costs was consistent with the authors’ stated perspective. The categories of costs included in the analysis were reported, but a detailed breakdown of the cost items was not and this could limit the possibility of replicating the analysis in other settings. The sources of the data for unit costs and resource use were reported. Statistical analyses of the costs were not carried out, but the impact of varying the costs of screening was tested in the sensitivity analysis. The impact of changes in other costs or resource use data was not investigated. The price year was not reported clearly, although both the costs and resource use data were derived from a questionnaire that referred to 1996.

Other issues
The authors stated that their findings were consistent with those observed in three Japanese studies on the cost-effectiveness of SMG. Extensive details of these studies were reported in order to facilitate comparisons with the current economic evaluation. The issue of the generalisability of the study results to other settings was not explicitly addressed, although the sensitivity analysis investigated the impact of variations in some model estimates. The authors noted some limitations of their study. First, data on screening accuracy for women aged 40 to 49 years were also used for other cohorts because of the lack of published data. Second, the participation rate used in the analysis could not reflect actual compliance with screening patterns. Finally, some assumptions about the comparative accuracy of screening could have affected the results of the analysis. The difference between the participation rate assumed in the article (100%) and the real compliance rate in the Japanese context (12%) also appears to be a key issue of the analysis.

Implications of the study
The study results support the use of biennial BC screening based on CBE and SMG.

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