Toward optimal screening strategies for older women: costs, benefits, and harms of breast cancer screening by age, biology, and health status


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 breast cancer (BC) screening strategies for older women were examined:

- Biennial screening starting at age 50 years until death;
- Biennial screening starting at age 50 years and ending at age 70 years; and
- Biennial screening starting at age 50 years and ending at age 79 years.

Type of intervention
Screening.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised a hypothetical cohort of older women. The target population depended on the screening strategy under analysis.

Setting
The setting was primary care. The economic study was carried out in the USA.

Dates to which data relate
The effectiveness data were derived from studies published between 1982 and 2003. No dates for the resource use data were explicitly reported. The price year was 2000.

Source of effectiveness data
The effectiveness data were derived from a synthesis of completed studies and authors' assumptions.

Modelling
An event-driven continuous time Monte Carlo simulation model of the natural history of BC was used to assess the costs and benefits of different ages of screening cessation. The model began with a hypothetical cohort of women aged 50 and randomly assigned dates of death, preclinical and symptomatic breast cancer incidence, and uptake of first and subsequent screening mammograms. Women destined to get BC were assigned a date at which symptomatic illness would present (clinical presentation). If the tumour was detected before this time, the disease stage was calculated. Women developing BC were assigned an oestrogen receptor (ER) status and received treatment based on current...
patterns of care given age, stage at presentation and ER status. For women who did not develop cancer, the probability of a false-positive mammogram was calculated. The time horizon of the model was the women's lifetime.

**Outcomes assessed in the review**
The outcomes assessed in the review were:

- stage distribution for screen-detected and non-screen-detected BC cases;
- the annual transition probabilities;
- the sensitivity and specificity of mammography;
- mammography use;
- the proportion of ER positivity;
- the distribution of local treatment for women diagnosed with BC; and
- systemic treatment distribution.

**Study designs and other criteria for inclusion in the review**
The authors stated that the medical literature was reviewed to identify relevant estimates for model parameters. Most of data came from national sources, such as the Surveillance, Epidemiology, and End Results (SEER) registry, or life tables. Clinical trials were also used for some inputs.

**Sources searched to identify primary studies**
Not stated.

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

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

**Number of primary studies included**
Fourteen primary studies provided clinical evidence.

**Methods of combining primary studies**
The primary estimates were not combined since each source provided a series of inputs.

**Investigation of differences between primary studies**
Not reported.

**Results of the review**
The annual transition probabilities were:

\[0.714 \pm 0.452\] from ductal carcinoma in situ (DCIS) to DCIS;
0.286 (+/- 0.452) from DCIS to local cancer;
0.828 (+/- 0.377) from local cancer to local cancer;
0.172 (+/- 0.377) from local to regional cancer;
0.916 (+/- 0.201) from regional to regional cancer;
0.084 (+/- 0.201) from regional to distant cancer; and
1 from distant to distant cancer.

Dwell time was 2.1 years for women aged 50 - 59 years, 3 years for women aged 60 - 69 years, and 4.7 years for women over 70 years.

First-screen mammography sensitivity was 93.6% for women aged 50 - 59 years, 94.1% for women aged 60 - 69 years, and 91.2% for women over 70 years. First-screen mammography specificity was 92.9% for women aged 50 - 59 years, 92.6% for women aged 60 - 69 years, and 93.4% for women over 70 years.

The sensitivity of subsequent screens was 76.5% for women younger than 50 years and 73.8% for women older than 50 years. The specificity of subsequent screens was 98.1% for women younger than 50 years and 98.2% for women older than 50 years.

The median rate of mammography use (percentage of all women older than 65 having a reported mammogram in the past 2 years) was 73.7% (range: 56.5 - 83.6).

The rate of ER positivity was 72.0% (95% confidence interval, CI: 76 - 77) for women aged 50 - 64 years and 82.0% (95% CI: 78 - 86) for women aged 65 - 79 years.

BC stage distributions and distribution of local treatment depended on age and type of cancer, thus they will not be reported here.

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

**Estimates of effectiveness and key assumptions**
It was assumed that lobular carcinoma in situ and DCIS have the same history and survival. Women with carcinoma in situ that was destined to progress to invasive disease, or those with local stage who survived for 15 years without recurrence, would have survival after that time that was similar to their age-matched non-BC cohort. Screen and clinically detected cancers have the same survival.

**Measure of benefits used in the economic analysis**
The summary benefit measure used in the economic evaluation was life expectancy. This was estimated using the decision model and was discounted at an annual rate of 3%.

**Direct costs**
A societal perspective was adopted in the study. The direct costs included in the analysis were mammography (either normal or abnormal results) and the treatment costs for initial care, continuing care and terminal care. The costs of tamoxifen and adjuvant chemotherapy for initial treatment were also considered. The initial phase of care included all costs incurred by BC patients for the 12-month period following the date of diagnosis (e.g. initial diagnostic evaluation and staging, hospitalisations and surgery, and any adjuvant chemotherapy, medical visits and laboratory procedures). The continuing care phase included all costs incurred by BC patients after the initial phase up to the 12 months prior to
death (e.g. medical visits for surveillance, treatment of recurrences, hospitalisations, mammograms and laboratory procedures). The terminal care costs referred to all costs incurred by BC patients in the last 12 months of life (e.g. hospitalisations, chemotherapy, laboratory procedures and medical visits). The costs depended on age, stage and tumour location.

The unit costs were not presented separately from the quantities of resources used. In general, macro-categories of costs were reported. However, the quantities of resource use depended on BC stages (local, regional and distant), and age-specific distributions of local treatment were reported as model parameters. The costs were estimated from Medicare reimbursement rates, average wholesale prices and published studies. Discounting was relevant and an annual rate of 3% was applied. The price year was 2000. All the costs were updated to 2000 using the medical component of the Consumer Price Index.

Statistical analysis of costs
Statistical analyses of the costs were not carried out.

Indirect Costs
The indirect costs associated with patient time were included in the analysis since a societal perspective was adopted. The source of the data was unclear. The costs came from time valued at current average US wage rates. The unit costs and the quantities of resources used were not reported separately. Discounting was relevant and an annual rate of 3% was applied. The price year was 2000.

Currency
US dollars ($).

Sensitivity analysis
Univariate sensitivity analyses were carried out to assess the robustness of the cost-effectiveness ratios to variations in several model inputs. Plausible ranges were used. A sub-group analysis was also performed to assess the relative cost-effectiveness of the screening strategies on women at different risk of developing BC. Finally, a cost-utility analysis was performed using the following health utility values:

- without cancer, 0.95;
- treatment for DCIS, 0.87;
- treatment for local and regional disease, 0.84;
- treatment for distant disease, 0.55;
- surviving cancer, 0.9; and
- living with metastatic disease, 0.55.

Estimated benefits used in the economic analysis
Life expectancy was 19.453 years with biennial screening from 50 to 70 years, 19.455 years with biennial screening from 50 to 79 years, and 19.456 years with lifetime screening.

Cost results
The estimated costs were $2,291.94 with biennial screening from 50 to 70 years, $3,488.17 with biennial screening from 50 to 79 years, and $2,628.11 with lifetime screening.
Synthesis of costs and benefits
Incremental cost-effectiveness ratios (ICERs) were calculated to combine the costs and benefits of the alternative screening strategies. Each ratio was calculated in comparison with the next least expensive strategy.

The incremental cost per life-year saved was $82,063 with biennial screening from 50 to 79 years (compared with biennial screening from 50 to 70 years), and $151,434 with lifetime screening (compared with biennial screening from 50 to 79 years).

In the sample of women in the top 25% of life expectancies for their ages, the incremental cost per life-year saved was $57,934 with biennial screening from 50 to 79 years (compared with biennial screening from 50 to 70 years), and $126,629 with lifetime screening (compared with biennial screening from 50 to 79 years).

The sensitivity analysis showed that only under certain circumstances might lifetime screening be cost-effective. For example, the ICER for screening to age 79 years was $62,842 for high-risk women. If survival data from the SEER database were used rather than data from clinical trials (where patients are followed in an idealised environment), the ICER for screening up to 79 years was $40,629. If the expected survival was quality-adjusted, then the optimal cessation age would be 70 years. The authors explained that the ICER, for screening to age 79 or for lifetime, compared with screening up to 70 years, were higher in the cost-utility analysis given that living with the knowledge of cancer lowers quality of life in the years that are gained.

Authors’ conclusions
It is cost-effective to conduct biennial screening until age 79 only at a threshold of cost-effectiveness of $80,000 per life-year saved. However, at a threshold of $60,000 per life-year saved, screening to age 79 was only cost-effective if limited to women with life expectancies in the top quartile for their ages.

CRD COMMENTARY - Selection of comparators
The authors justified the choice of the three biennial BC screening strategies included in the study and the exclusion of the no-screening option as a basic comparator. Current recommendations in the USA suggest biennial screening for women aged 50 - 70 years. You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The clinical evidence came from published studies, but the methods and conduct of the review of the literature were not reported. There was limited information on the studies used to estimate the clinical inputs. Similarly, the methods used to extract and then combine the primary estimates were not described. Thus, it was difficult to assess the validity of the studies included. Model assumptions were also made. Sensitivity analyses were carried out to address the issue of uncertainty.

Validity of estimate of measure of benefit
The use of life expectancy as the summary benefit measure was appropriate as this represents the most relevant dimension of health for women at risk of BC. Discounting was applied, according to US recommendations for economic evaluations. The impact of adjusting survival by quality of life was investigated in the sensitivity analysis.

Validity of estimate of costs
A broad perspective was adopted in the study. The indirect costs were included despite the fact that many older women are not in the workforce. The unit costs were presented only for some items. Other costs were presented as macro-categories, which represents a typical approach when assessing the lifetime costs. The source of the costs was reported for all items. However, the source of data on resource consumption was not stated clearly for all items. The price year was reported, which enhances the possibility of conducting reflation exercises in other time periods. The cost estimates were specific to the study setting but key cost items were varied in the sensitivity analysis.
Other issues
The authors stated that the findings were consistent with those from other studies that had concluded that BC screening of older women is cost-effective. The issue of the generalisability of the study results to other settings was addressed, and the authors stated that their findings should be limited to US screening policies. Some limitations of the analysis were noted. For example, the use of Medicare reimbursement rates as proxies for costs and the controversies surrounding the effectiveness of mammography. Also, the use of life expectancy corresponding to quartiles of health and age to measure the probability of death as a proxy for physiological age. A further limitation was the biennial interval for screening (as recommended in US guidelines). The study referred to women eligible for BC screening and this was reflected in the authors' conclusions.

Implications of the study
The study results support the BC screening programme until age 70. However, extending screening beyond age 70 could be considered, especially for women in the top 25% of life expectancy for their age.

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Other publications of related interest


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