Costs and benefits of diagnosing familial breast cancer
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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
Two strategies for the identification of women at risk for inherited breast cancer were examined. The two strategies were cancer family clinics and the genetic testing of all incident breast and ovarian cancers for founder mutations in BRCA1.

Type of intervention
Diagnosis.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised women in families at risk for hereditary breast cancer. The women started the screening at an average age of 35 years and were followed for about 25 years (generally until 60 years).

Setting
The setting was a cancer family clinic. The economic study was carried out in Norway.

Dates to which data relate
No dates were reported for the effectiveness data. The data on resource use referred to 1995 and 1998. The price year appears to have been 1998.

Source of effectiveness data
The effectiveness evidence was derived from a review of the literature and from the authors' assumptions.

Outcomes assessed in the review
The outcomes assessed were the yearly incidence of detecting breast cancer using the cancer family clinic strategy at the authors' institution, and 5-year survival in familial breast cancer.

Study designs and other criteria for inclusion in the review
Not reported.

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
Two studies were included in the review.

Methods of combining primary studies
Not relevant as each estimate was derived from only one study.

Investigation of differences between primary studies
Not relevant as each estimate was derived from only one study.

Results of the review
The incidence of detection was 0.73%, in other words, 18.25% over 25 years.

The 5-year survival was 89% at an average of 48 years.

Methods used to derive estimates of effectiveness
The authors made some assumptions to derive the effectiveness estimates. Some of these were made on the basis of results from both published and unpublished studies.

Estimates of effectiveness and key assumptions
The authors stated that half of the genetic counsellings led to enrolment of the woman in the surveillance programme. This means that about one in two of the individuals receiving genetic counselling for breast cancer were enrolled in the follow-up programme (assumption based on unpublished data from authors' activity);

4% of the patients required fine needle aspiration and 1% required open biopsy;

the annual incidence of detection of BRCA1 mutation carriers was 0.02%, in other words, 50% over 25 years;

the median age of breast cancer diagnosis in the families was in the late forties, while life expectancy in healthy Norwegian women of 50 years of age was about 80 years; and
untreated breast cancer was assumed to be invariably fatal.

>From these data and the results of the review, the authors estimated a 75% cure rate and 30 extra years of life per woman cured. It was also assumed that:

breast cancer was five times as frequent as ovarian cancer;

the frequency of mutations in breast cancer was 0.6%;

there were 15 healthy relatives per family appearing for testing; and

one third of the counselees were mutation positive, thus one sixth of the women in the age group 35 to 60 years were mutation positive.
Measure of benefits used in the economic analysis
The benefit measures used in the economic analysis were the number of life-years saved with the interventions, and the number of cancers detected. These were calculated on the basis of the assumptions made by the authors.

Direct costs
Discounting was not reported, although it would have been methodologically relevant given the long time horizon of the analysis. The unit costs were reported separately from the quantities of resources used. The economic analysis included the costs of genetic counselling and follow-up for the cancer family clinic strategy, and the costs of molecular biology and clinical genetics for the founder mutation strategy. The follow-up costs included clinical examination, mammography, fine-needle aspiration and biopsy. The molecular biology costs included DNA extraction, polymerase chain reaction quick test, and sequencing to confirm families with founder mutation. The costs of clinical genetics included genetic counselling of proband pre/post-testing. The costs related to the establishment of cancer family clinics and laboratories, including the costs to train personnel, were excluded. The cost/resource boundary was that of the NIS. The source of the cost data was the Norwegian Radium Hospital in Oslo. The quantities of resources used were estimated from the authors' assumptions and the Norwegian Cancer Registry in 1995. The price year appears to have been 1998.

Statistical analysis of costs
No statistical analysis of the costs was carried out.

Indirect Costs
The indirect costs were not included in the analysis.

Currency
Euros.

Sensitivity analysis
Several one-way sensitivity analyses were carried out to assess the robustness of the estimated cost-effectiveness ratios to variations in several assumptions made by the authors. In particular, the efficacy of the intervention, the uptake of testing and family size, intensified screening programmes, the penetrance and prevalence of founder mutations, laboratory and clinical fees, and screening for unknown mutations.

Estimated benefits used in the economic analysis
The number of life-years saved with each intervention and the number of cancers detected were not reported.

Cost results
The cost of surveillance was Euro 2,764 and was common to both strategies.

The cost to enrol a women in the programme was Euro 326 for the cancer family clinic strategy and Euro 6,596 for the founder mutation strategy.

The total cost per woman was Euro 3,090 for the cancer family clinic strategy and Euro 9,360 for the founder mutation strategy.

Synthesis of costs and benefits
An average cost-effectiveness analysis was carried out to combine the costs and benefits of the interventions.
The average cost per life-year saved was Euro 753 with the cancer family clinic strategy and Euro 832 with the founder mutation strategy.

The average cost per cancer detected was Euro 16,933 with the cancer family clinic strategy and Euro 18,720 with the founder mutation strategy.

The variables that mostly affected these cost-effectiveness estimates were the efficacy of the interventions, the uptake of testing, and the penetrance and prevalence of founder mutations.

Authors' conclusions
Both the cancer family clinic strategy and the founder mutation strategy for the detection of inherited breast cancer were cost-effective in Norway. The cancer family clinic strategy was slightly more convenient from the perspective of the NIS. "Inherited breast cancer may be managed effectively for the cost of Euro 750-1,600 per year earned."

CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparator was clear. The cancer family clinic strategy was the standard approach, while the founder mutation strategy represented a newer technique for the identification of inherited breast cancer. However, it should be noted that, as the authors stated, the current practice had, itself, not been evaluated sufficiently. This suggests the need for another comparator, possibly no surveillance, although this might be ethnically unacceptable. You should assess whether they represent widely used interventions in your own setting.

Validity of estimate of measure of effectiveness
The analysis of effectiveness was based largely on assumptions made by the authors, from two unpublished studies and the authors’ experience. The choice of the assumptions was justified only in a few cases. In addition, the studies were not obtained from a systematic review of the literature. Several sensitivity analyses were carried out to assess the robustness of the study conclusions to variations in the assumptions, but the ranges used were unclear. The estimated cost per life-year saved was also sensitive to some assumptions, thus caution is required when interpreting the study results.

Validity of estimate of measure of benefit
The life-years saved represented the benefit measure used in the economic analysis. It is a commonly used measure in the evaluation of interventions aimed at detecting cancer. However, few details were provided on the method used to derive this measure, and the results of the analysis were not reported.

Validity of estimate of costs
All the categories of costs relevant to the perspective adopted in the study were included in the analysis. The unit costs were reported separately from the quantities of resources used. In addition, the source of the cost data was given and the price year was reported. These factors enhance transparency and generalisability. However, the costs were treated deterministically and some costs, such as those related to the establishment of cancer family clinics and laboratories, were excluded. The authors stated that the impact of these items may be substantial. Finally, the cost-effectiveness was not based on an incremental analysis. The relevant decision-making criterion is the extra cost to go from standard to the new practice for the gain in benefit. This would make the new practice, in this case, more costly.

Other issues
The authors did not compare their findings with those from other studies. The issue of the generalisability of the study results to other settings was not addressed, although some sensitivity analyses were carried out. The analysis referred to a population of women at risk for inherited breast cancer, and this was reflected in the conclusions of the analysis. Although the authors underlined the assumptions used in the effectiveness analysis, the process used to derive the benefit measure was unclear. Finally, the authors have presented their results selectively.
Implications of the study
The conclusion that strategies for the identification of inherited breast cancer should be implemented needs to be viewed in the light of the limitations of the analysis. In particular, on the side of the effectiveness measures and the lack of an incremental analysis. The authors noted that the potential limiting economic factor on the clinical genetic side was represented by a manpower shortage in genetic counselling in Norway.

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