Comparative effectiveness of screening and prevention strategies among BRCA1/2-affected mutation carriers
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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.

CRD summary
This study assessed the cost-effectiveness of primary and secondary preventive interventions for breast cancer (BRCA) 1 and BRCA2 gene mutation carriers aged 30 years or older, with no cancer diagnosis. The authors concluded that bilateral salpingo-oophorectomy (BSO) was most cost-effective in quality-adjusted life-years, but prophylactic mastectomy and BSO was preferred, without quality adjustments. A conventional cost-effectiveness framework was used and the conclusions appear to be robust, but more details on the data sources are needed to objectively assess their validity.

Type of economic evaluation
Cost-effectiveness analysis, cost-utility analysis

Study objective
This study assessed the cost-effectiveness of primary and secondary preventive interventions available to breast cancer (BRCA) 1 and BRCA2 gene mutation carriers aged 30 years or older, who had no cancer diagnosis.

Interventions
The interventions were: prophylactic mastectomy, prophylactic bilateral salpingo-oophorectomy (BSO), prophylactic mastectomy and BSO (both surgeries), tamoxifen, mammography, mammography plus magnetic resonance imaging (MRI), and prophylactic BSO plus MRI.

Location/setting
USA/hospital and secondary care.

Methods
Analytical approach:
The analysis was based on a Markov cohort model, with a lifetime horizon. The authors did not state the perspective adopted.

Effectiveness data:
The clinical data were from a selection of relevant studies, including published reports, the US National Cancer Institute’s Surveillance, Epidemiology, and End Results (SEER) database for the period 1973 to 2004, and the Breast Cancer Prevention Trial. The authors selected the most appropriate estimate where multiple sources were available. Some assumptions were required. The incidence of ovarian or breast cancer was the key input for the model.

Monetary benefit and utility valuations:
The utility values were from published sources, which obtained the preferences for cancer and preventive treatment states, from a cohort of 236 mutation carriers receiving annual MRI and from women who were not known to be at high risk. All preferences were assessed using a time trade-off questionnaire.

Measure of benefit:
Quality-adjusted life-years (QALYs) and life-years were the summary benefit measures. A 3% annual discount rate was applied.
Cost data:
The economic analysis included the costs of screening, preventive treatment, cancer care, and treatment of other medical conditions. The authors stated that both the direct and indirect costs were considered. The drug costs were based on average wholesale prices, while other costs were from published literature and Medicare payments. The price year was 2009. All costs were in US dollars ($) and were discounted at an annual rate of 3%.

Analysis of uncertainty:
One-way sensitivity analyses were conducted on some of the model parameters and assumptions, such as the cost of MRI, the penetrance of ovarian or breast cancer, and the discount rate. Monte Carlo simulations were performed in a probabilistic sensitivity analysis.

Results
The expected costs for BRCA1 carriers were $150,986 with both surgeries, $153,396 with BSO, $167,607 with mastectomy, $170,893 with BSO and MRI, $172,353 with tamoxifen, $179,639 with mammography, and $192,429 with mammography and MRI. The QALYs (using the preferences of women with no known high risk) for BRCA1 carriers were 16.66 with both surgeries, 18.04 with BSO, 17.52 with mastectomy, 17.63 with BSO and MRI, 17.43 with tamoxifen, 18.08 with mammography, and 18.08 with mammography and MRI. After excluding dominated strategies, the incremental cost per QALY gained was $1,741 with BSO and $681,333 with mammography.

In BRCA2 carriers, the incremental cost per QALY gained was $4,587 with BSO, $88,104 with mammography, and $247,645 with mammography and MRI. When the preferences of mutation carriers were used, the incremental cost per QALY gained was $1,677 with BSO and $736,788 with BSO and MRI in BRCA1, and $4,535 with BSO and $236,867 with BSO and MRI in BRCA2 carriers. When using life-years as the summary benefit measure, both surgeries was the reference strategy and it dominated all other preventive options. The sensitivity analysis showed that the cost of MRI had to decrease by 75% (from $1,219 to $305) to make mammography plus MRI cost-effective.

Authors' conclusions
The authors concluded that BSO was most cost-effective in QALYs, but prophylactic mastectomy and BSO was preferred, without quality adjustments.

CRD commentary
Interventions:
The rationale for the selection of the comparators was clear, as the available strategies for ovarian and breast cancer prevention were analysed. The authors stated that MRI plus mammography was the strategy recommended by the American Cancer Society.

Effectiveness/benefits:
No details of a systematic search of the literature were reported and the data sources might have been selected from those known to the authors. A large database (SEER) and a clinical trial were used for the data on patient cancer stage distribution, but no information on the design and methods of the other data sources was given, reducing the possibility of making an objective assessment of the validity of the clinical inputs. Two sets of utility values were used and they were from studies that used a validated instrument (time trade-off). Both benefit measures were appropriate as they capture the impact of the disease on both survival and quality of life. These dimensions of health are relevant for cancer patients.

Costs:
The perspective was not stated and the types of costs included in the analysis were not clear. The authors mentioned both direct and indirect costs, but provided no information on their calculation. It appears that the analysis was conducted from the viewpoint of the third-party payer. The costs were presented as category totals and the patterns of resource consumption were not given, reducing the transparency of the analysis. Limited information on the data sources was given. The price year and discounting were explicitly reported.

Analysis and results:
The base-case results were extensively presented for both BRCA1 and BRCA2 carriers. An appropriate incremental
approach was used to synthesise the costs and benefits. The uncertainty was investigated, but the full results were given in an appendix. It was not clear whether a first- or second-order Monte Carlo simulation was conducted. The study appears to have been specific to the USA and might be difficult to replicate for other settings given the limited reporting of the costs.

Concluding remarks:
A conventional cost-effectiveness framework was used and the conclusions appear to be robust, but more details on the data sources are needed to make an objective assessment of the validity of the analysis.

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