Decision analysis of prophylactic mastectomy and oophorectomy in BRCA1-positive or BRCA2-positive patients


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
Prophylactic mastectomy and oophorectomy in BRCA1-positive or BRCA2-positive patients.

Type of intervention
Prophylactic treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population consisted of Ashkenazi Jewish women and those from high-risk families who tested positive for BRCA1 or BRCA2 mutant genes and consequently had a significant risk of developing breast or ovarian cancer by the age of 70 years.

Setting
The setting was secondary care. The economic study was conducted in New York, USA.

Dates to which data relate
Various sources were used to identify probabilities of developing cancer, and death. The main study used was conducted between 1973 and 1992 and the two other main sources of data were published in 1995 and 1997.

Source of effectiveness data
Effectiveness data were derived from a synthesis of previously published studies.

Modelling
A Markov model was developed and Data 3.0 (TreeAge Software, Inc, Cambridge MA) software was used to estimate the cost-effectiveness of 4 alternative strategies for BRCA1 or BRCA2 positive patients: prophylactic oophorectomy, prophylactic mastectomy, prophylactic oophorectomy and mastectomy, and surveillance. The authors focussed on 4 health states: good health, breast cancer, ovarian cancer and death. Individuals were followed for 50 years (Markov cycles) starting at the age of 30 years.

Outcomes assessed in the review
Cumulative probabilities of developing breast cancer and ovarian cancer in each decade and probabilities of death were assessed.
**Study designs and other criteria for inclusion in the review**
The majority of data were extracted from 3 studies: 2 studies (design not stated) considered the cumulative risk of cancer and 1 study, a surveillance programme (SEER) conducted by the US National Cancer Institute between 1973 and 1992, considered probabilities of death.

**Sources searched to identify primary studies**
American Journal for Human Genetics, New England Journal Medicine, National Cancer Institute publications and the Journal of Clinical Oncology were the main sources searched to identify primary studies.

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

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

**Number of primary studies included**
Two studies on BRCA1/2 gene mutation and a surveillance programme implemented by the US National Cancer Institute were the main sources of data, but a total of 8 studies were reviewed.

**Methods of combining primary studies**
Meta-analysis was used to combine results of primary studies.

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

**Results of the review**
The cumulative risk of cancer by the age of 70 years in BRCA1 gene mutation carriers was found to be 85% for breast cancer and 63% in ovarian cancer.

For Ashkenazi Jewish women who tested positive for 3 mutations of BRCA1 and BRCA2, the cumulative risk was 56% for breast cancer and 16% for ovarian cancer by the age of 70 years.

Based on the literature review, the authors assumed that oophorectomy would reduce the risk of ovarian cancer by 50% among women with the BRCA1 and BRCA2 genes and that prophylactic mastectomy would reduce the risk of breast cancer by 90%.

**Methods used to derive estimates of effectiveness**
The authors also derived utilities for health states using a time trade-off technique and a questionnaire that described a scenario for each of 5 health states: well post-oophorectomy, well post-mastectomy and oophorectomy, breast cancer, ovarian cancer and metastatic disease. A convenience sample was used to develop community-based preferences. 54 participants (mean age 38 years, mean self-assessed pre-study health status 0.91) were asked how much time they would trade in each state to be as well as they were before their disability occurred. To estimate the quality of life of a given health state, the following formula was used (1 - T/L), in which T equals the time the respondent was willing to trade and L equals the health span assigned to the health state in the scenario. Validation of the quality-adjusted life years (QALYs) determined was performed through a comparison with 3 similar studies.
Estimates of effectiveness and key assumptions
QALYs saved were estimated.

Measure of benefits used in the economic analysis
The benefit measures were years of life saved and QALYs.

Direct costs
Direct health service costs were considered: Ambulatory care, mastectomy, breast surgery with reconstruction, oophorectomy, gynaecologic surgery and treatment of metastatic disease. Medicare payments from the Health Care Financing Administration for 1995 were used to proxy costs. Drug costs for chemotherapy were obtained from the 1996 Pharmacy Fundamental Reference. All costs were given in 1995 dollars.

Statistical analysis of costs
No statistical analysis of costs was performed.

Indirect Costs
Indirect costs related to loss of earnings or other medical conditions were excluded.

Currency
US dollars($).

Sensitivity analysis
Sensitivity analysis was performed on costs using values from fee- for-service or managed care insurance. The efficacy of oophorectomy and mastectomy were tested using values based on clinical experience. Sensitivity analysis was performed on quality of life utilities and the discount rate.

Estimated benefits used in the economic analysis
QALYs saved were estimated. For a 30-year-old woman, according to her cancer risks, prophylactic oophorectomy improved survival by 0.4 to 2.6 years, mastectomy improved survival by 2.8 to 3.4 years and the two combined improved survival by 3.3 to 6 years when compared to surveillance. 0.5 QALYs were saved by oophorectomy and 1.9 for the combined procedures for the high-risk model.

Cost results
For well patients, the base-case costs for procedures and tests for surveillance were $1,700 (initial) and $677 (follow-up examination and tests per year).

For breast cancer patients, the base-case costs for procedures and tests for surveillance were $5,695 (initial), $1,200 (Tamoxifen each year for 6 years), $677 (follow-up examinations and tests per year).

For ovarian cancer patients, the base-case costs for procedures and tests for surveillance were $34,797 (initial) and $459 (follow-up examinations and tests per year).

For well patients, the base-case costs for procedures and tests for oophorectomy were $4,811 (initial) and $402 (follow-up examination and tests per year).

For breast cancer patients, the base-case costs for procedures and tests for oophorectomy were $5,695 (initial), $1,200 (Tamoxifen each year for 6 years), and $402 (follow-up examinations and tests per year).
For ovarian cancer patients, the base-case costs for procedures and tests for oophorectomy were $22,819 (initial) and $459 (follow-up examinations and tests per year).

For well patients, the base-case costs for procedures and tests for mastectomy were $7,726 (initial) and $607 (follow-up examination and tests per year).

For breast cancer patients, the base-case costs for procedures and tests for mastectomy were $2,424 (initial), $1,200 (Tamoxifen each year for 6 years), and $607 (follow-up examinations and tests per year).

For ovarian cancer patients, the base-case costs for procedures and tests for mastectomy were $34,797 (initial) and $389 (follow-up examinations and tests per year).

For well patients, the base-case costs for procedures and tests for mastectomy and oophorectomy were $12,537 (initial) and $332 (follow-up examination and tests per year).

For breast cancer patients, the base-case costs for procedures and tests for mastectomy and oophorectomy were $2,424 (initial), $1,200 (Tamoxifen each year for 6 years), and $332 (follow-up examinations and tests per year).

For ovarian cancer patients, the base-case costs for procedures and tests for mastectomy and oophorectomy were $22,819 (initial) and $389 (follow-up examinations and tests per year).

The base-case cost for procedures and tests for metastatic disease was $12,000.

**Synthesis of costs and benefits**

The discounted incremental cost per life-year saved was cost saving (denoting negative net costs and increased survival) for oophorectomy and the combined procedures and between $336 and $1,271 for mastectomy. By comparison, the incremental cost of bone marrow transplantation was $28,600 per life-year saved. Prophylactic surgeries were cost-effective compared to surveillance for life-years saved, but not for quality-adjusted life-years.

**Authors’ conclusions**

The authors stated that, among women who test positive for a BRCA1 or BRCA2 gene mutation, prophylactic surgery at a young age substantially improves survival. However, unless the genetic risk of cancer is high, no benefit exists for quality of life. Prophylactic surgery is cost-effective for years of life saved compared to other medical interventions deemed as cost-effective.

**CRD COMMENTARY - Selection of comparators**

The reason for the choice of the comparators was clear, as all four strategies (prophylactic oophorectomy, prophylactic mastectomy, prophylactic oophorectomy and mastectomy, and surveillance) are commonly proposed to treat patients who test positive for the BRCA1 and BRCA2 genes. You, as a database user, should consider if the same applies to your own setting.

**Validity of estimate of measure of benefit**

Life-years saved and QALYs were used as benefit measures and were suitable for the purpose of the study. Utilities were determined using the time-trade-off technique, a method that is more reliable than a scaling method. Utilities were determined based on the population of interest: young Ashkenazi Jewish women, or those from high-risk families who tested positive for BRCA1 or BRCA2 mutant genes.

**Validity of estimate of costs**

The costing methodology was presented comprehensively. The sources and values of costs were reported adequately.
Other issues
The costs may not be generalisable to other setting or countries and there may be limitations in the generalisability of
the benefits to other patient groups.

Implications of the study
An intensive surveillance programme for the women at risk would be preferable to the proposed prophylactic surgeries.

Source of funding
None stated

Bibliographic details
oophorectomy in BRCA1-positive or BRCA2-positive patients. Journal of Clinical Oncology 1998; 16(3): 979-985

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Other publications of related interest

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Subject indexing assigned by NLM

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