BRCA1 mutations in Southern England
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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
Screening for BRCA1 mutations for women diagnosed with breast cancer.

Type of intervention
Screening.

Economic study type
Cost-effectiveness analysis.

Study population
Women diagnosed with breast cancer.

Setting
Breast clinic and genetics clinic. The economic study was carried out in the United Kingdom.

Dates to which data relate
The period during which the effectiveness and resource use data were collated was not stated. The price year was unclear.

Source of effectiveness data
The evidence for final outcomes was derived from a single study.

Link between effectiveness and cost data
The costing does not seem to have been undertaken on the same patient sample as that used in the effectiveness analysis and it was unclear whether it was performed prospectively or retrospectively.

Study sample
Power calculations did not determine the sample size. A total of 230 women diagnosed with breast cancer were grouped according to three criteria:

Group 1 - 155 women diagnosed with breast cancer before 40 years of age were systematically ascertained through breast clinics in Wessex;

Group 2 - 45 women identified from the same clinics as group 1, but where the criterion for selection was the presence of bilateral breast cancer diagnosed after 39 years of age; and

Group 3 - 30 women presenting to a genetics clinic with a strong family history of breast and ovarian cancer or both.
Study design
This was a cohort study; the total number of centres (breast clinics and a genetics clinic) were not reported. Loss to follow-up was not reported. The basis (intention to treat or treatment completers only) used for the analysis of the clinical study was not stated. The primary outcome used in the analysis was the number of BRCA1 mutations detected.

Effectiveness results
Detectable mutations were found in 10/155 (6.5%) women in group 1, no women in group 2 and 8/30 (26.7%) in group 3.

Clinical conclusions
18 probands from all three groups had mutations detected in the BRCA1 gene, all of which were protein truncating.

Measure of benefits used in the economic analysis
The benefit measure was number of BRCA1 mutations detected.

Direct costs
Costs were not discounted in view of the short time frame of the study. Some quantities were reported separately from the costs. The following laboratory elements of the mutation analysis were costed both for analysing the entire gene and limited exons: reagents (PCR reactions), staff time and sequencing costs. The costings did not take overheads into account. The date of the price data was not explicitly specified.

Indirect Costs
Not included.

Currency
UK pounds sterling (€).

Sensitivity analysis
No sensitivity analysis was performed.

Estimated benefits used in the economic analysis
Based on an estimate of a highly penetrant breast cancer predisposition gene with a frequency of 0.003 in the general population and the observation that roughly one-third of hereditary breast cancer may be accounted for by BRCA1, one-third by BRCA2 and one-third by as yet undiscovered genes, the authors calculated that in order to detect one mutation (based on mutation analysis of entire gene) they would need to test 1,428 samples from the general population corresponding to a detection rate of 0.0007 (with a sensitivity of 70% for the technique used). The corresponding value for the mutation analysis of limited exons was 2,500 (corresponding to a detection rate of 0.0004). When the mutation analysis of limited exons was considered, the number needed to be screened in groups 1 (all cases under 40 years of age) and 3 (cases selected for strong family history) in order to detect 1 mutation were 15.4 and 3.7, respectively (corresponding to detection rates of 6.5% and 26.7%, respectively). The corresponding values for the mutation analysis of entire gene were less than 15.4 and less than 3.7.

Cost results
The total laboratory cost per case of analysing the entire gene was 105 and for analysing limited exons was 45.
Synthesis of costs and benefits
The costs per mutation detected in the general population were 114,240, in group 1 were less than 1,144 and in group 3 less than 328. Mutation analysis of limited exons resulted in cost-effectiveness ratios of 50,000 (general population), 308 (group 1) and 74 (group 3).

Authors' conclusions
The cost of screening the population for mutations in the entire BRCA1 gene is unacceptably high. However, the cost of screening a carefully selected patient cohort is low, the risk of misinterpretation much less and the potential clinical benefits clearer.

CRD COMMENTARY - Selection of comparators
No specific health technology was regarded as the comparator since the study was an attempt to find a rational approach to genetic testing.

Validity of estimate of measure of benefit
The estimate of benefit is likely to be internally valid. However, it is not clear whether the sample size was appropriate for the study question.

Validity of estimate of costs
Some resource quantities were reported separately from the prices. Insufficient details of methods of cost estimation were given. Cost results may not be generalisable to other settings or countries.

Other issues
The authors’ conclusions were justified given the uncertainties in the data. The issue of generalisability to other countries was not addressed. Appropriate comparisons were made with other studies.

Implications of the study
At present, such testing is unlikely to become a routinely used test for breast cancer clinics and general practice, but once the benefits have been better clarified it may be appropriate to consider more generally available testing of selected cancer patients.

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Funded by the Wessex Cancer Trust.

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