DNA testing for hypertrophic cardiomyopathy: a cost-effectiveness model

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 examined the cost-effectiveness of genetic versus clinical methods of screening for hypertrophic cardiomyopathy in the adult children of patients diagnosed with the disorder. The authors concluded that molecular genetic testing was cost-effective in diagnosing familial hypertrophic cardiomyopathy. The study was well carried out and the economic data were well described, but limited information was provided on the sources of the clinical data. The issue of uncertainty was appropriately investigated and the authors’ conclusions appear to be robust.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
This study examined the cost-effectiveness of genetic versus clinical methods of screening the adult children of patients diagnosed with hypertrophic cardiomyopathy.

Interventions
The conventional strategy consisted of a clinical history, a physical examination, and clinical tests by echocardiography and electrocardiogram. The genetic strategy included a clinical history, which was followed by screening of the four genes most commonly associated with hypertrophic cardiomyopathy, which were MYH7, MYBPC3, TNNT2, and TNNI3.

These two screening strategies were analysed as one-off screening or with repeated screening every five years for those who tested negative.

Each strategy assessed the risk of sudden cardiac death, due to hypertrophic cardiomyopathy, for the first-degree asymptomatic cascading family members (children aged between 18 and 22 years) of a patient diagnosed with hypertrophic cardiomyopathy.

Location/setting
UK/secondary care.

Methods
Analytical approach:
The economic evaluation was based on a decision-tree model with a lifetime horizon. The authors stated that the analysis was carried out from the perspective of the hospital.

Effectiveness data:
The clinical inputs were derived from a literature review, in medical and economic databases. Expert opinions were used when published data were not available. For example, no published randomised controlled trials were found that assessed the effectiveness of the treatment in preventing sudden cardiac death and this was therefore based on expert opinion. The accuracy of the screening tests (both clinical and genetic) was the key model input and it was from published studies and expert opinions.

Monetary benefit and utility valuations:
Not considered.
Measure of benefit:
Life-years (LYs) were the summary benefit measure and they were discounted at an annual rate of 3.5%.

Cost data:
The economic analysis included the costs of: finding a mutation for the parent and testing the children; contact with health care professionals; clinical tests; prevention, usually an implantable cardioverter defibrillator; surveillance; and follow-up. Assumptions for resource use were mainly based on discussions with experts and information from the Molecular Genetics Laboratory at the Churchill Hospital, Oxford. The unit costs came from official price lists, published literature, and primary data collection. A 3.5% annual discount rate was applied and the price year was 2007. All costs were reported in Euros (EUR).

Analysis of uncertainty:
A probabilistic sensitivity analysis, using Monte Carlo simulations, was undertaken to examine the uncertainty in the model inputs. Cost-effectiveness acceptability curves were constructed and a cost-effectiveness threshold of EUR 35,000 per LY saved was used. Conventional one-way sensitivity analyses were carried out to identify the most influential inputs. A scenario where the family consisted of only one child, aged 18 years, was analysed and a strategy with no screening was also considered.

Results
The lifetime costs were EUR 14,872 with clinical screening, EUR 19,459 with genetic screening, EUR 21,208 with five-yearly clinical screening, and EUR 21,803 with five-yearly genetic screening. The LYs were 43.61 with clinical screening, 43.93 with genetic screening, 43.91 with five-yearly clinical screening, and 44.04 with five-yearly genetic screening. Five-yearly clinical screening was dominated as it was less effective and more costly than another strategy. The incremental cost per LY gained, excluding the dominated strategy, was EUR 14,397 for genetic screening, compared with clinical screening, and EUR 21,561 for five-yearly genetic screening, compared with genetic screening.

Similar results were found in the scenario of a single child undergoing screening. The findings were generally robust and the most influential inputs were the discount rate, mortality of hypertrophic cardiomyopathy patients, proportion of mutation carriers at low or medium risk of sudden cardiac death, cost of defibrillator battery replacement and follow-up, and effectiveness of defibrillator treatment, but variation in these inputs did not alter the conclusions.

There was a 70% probability of the genetic screening strategies being cost-effective at a threshold of EUR 18,000 per LY. Genetic testing remained the optimal strategy compared with no screening.

Authors' conclusions
The authors concluded that molecular genetic testing was cost-effective in the diagnosis and management of familial hypertrophic cardiomyopathy.

CRD commentary
Interventions:
The two screening strategies were appropriately selected, as the new approach was compared against the usual one. No screening was also considered in the sensitivity analysis.

Effectiveness/benefits:
The clinical reporting was not complete, as the methods and conduct of the literature review were not described and few details of the sources of evidence were provided. This information would have been helpful in judging the validity of the clinical data. Other issues related to combining data from various sources were not discussed. The authors stated that expert opinion was required for many of the model parameters, due to a lack of valid published data. LYs were an appropriate benefit measure because death was the primary complication of the disease.

Costs:
The perspective was clearly stated and the analysis was consistent with this viewpoint. The unit costs and quantities of resources were reported, enhancing the transparency of the analysis, but the data sources were not clearly described. The price year was reported and the discount rate was consistent with the UK guidelines from the National Institute for...
Health and Clinical Excellence. The costs were varied in the sensitivity analysis.

Analysis and results:
The results were clearly reported and an appropriate incremental approach was used to synthesise the costs and benefits. Valid approaches were used assess the uncertainty, especially for the assumptions that were based on expert opinion. The structure of the decision model and a description of the key pathways were provided. The authors acknowledged some limitations of their analysis and these mainly related to the lack of valid clinical data and the need for assumptions.

Concluding remarks:
The study was well carried out and the economic data were well described, but limited information was provided on the sources of the clinical data. The issue of uncertainty was appropriately investigated and the authors’ conclusions appear to be robust.

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