A decision analysis model for diagnostic strategies using DNA testing for hereditary haemochromatosis in at risk populations

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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 examined the cost-effectiveness of deoxyribonucleic acid (DNA) testing in comparison with liver biopsy in people suspected of having haemochromatosis, and in comparison with phenotypic iron studies in family members of those diagnosed with haemochromatosis. The authors concluded that DNA testing was likely to be an effective and cost-saving strategy in clinical cases with iron overload and in the offspring of diagnosed patients. The study was based on valid methodology, which makes the authors’ conclusions more robust.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
This study examined the cost-effectiveness of deoxyribonucleic acid (DNA) tests compared with liver biopsy in people suspected of having hereditary haemochromatosis (HHC), and compared with phenotypic iron studies (biochemical tests) in family members of those diagnosed with HHC.

Interventions
In people suspected of having HHC, the two strategies were liver biopsy versus DNA testing in a hypothetical 45-year-old man. In siblings and offspring of people diagnosed with HHC, the two strategies were biochemical testing versus DNA testing. Biochemical tests consisted of transferring saturation (TS) and serum ferritin (SF). Those patients with TS over 45% and SF over 300μg/L were treated, while the remaining patients were monitored to see if the iron level increased.

Location/setting
UK/clinical laboratory.

Methods
Analytical approach:
This economic evaluation was based on two decision analytic models with a short time horizon, which was the testing and treatment period. In one model, individuals suspected of having haemochromatosis were analysed and, in the other, family members of those diagnosed with haemochromatosis were analysed. The authors stated that the perspective was that of the National Health Service (NHS).

Effectiveness data:
The clinical data were collected from systematic reviews and systematic searches supplemented by expert opinions. The design and other characteristics of the primary studies were not reported, except for a few studies. UK studies were selected, when available, and non-UK sources were adapted to the local context by means of expert opinions. The key clinical endpoint was the accuracy of the strategies.

Monetary benefit and utility valuations:
None.

Measure of benefit:
The summary benefit measure was the number of cases detected.
Cost data:
The health service costs were those of the DNA test, iron test, venesection treatment, liver biopsy, nurse visit, and surgical consultation. The unit costs were presented and were derived from national sources, such as the UK Genetic Testing Network website, as well as primary data reported in published studies. The resource use data were based on the authors’ opinions. The price year was not explicitly reported and all costs were in UK pounds sterling (£).

Analysis of uncertainty:
A deterministic univariate sensitivity analysis was carried out on the model inputs using alternative published estimates whenever possible. A probabilistic sensitivity analysis was also performed by means of a second-order Monte Carlo simulation, with probabilistic distributions assigned to the model inputs.

Results
The efficacy of the relevant strategies was similar in all simulations. The number of cases detected per 100 people tested was 75.1 with both strategies for people suspected of having HCC, 19 with both strategies in the sibling model, and 3.5 with both strategies in the offspring model.

In the simulation of 100 people suspected of having HCC, the total cost was £83,068 with liver biopsy and £73,823 with DNA testing. Thus, DNA testing saved £92.5 per person tested in comparison with liver biopsy.

In the model of 100 siblings, the total cost was £23,628 with the biochemical test and £27,423 with DNA testing. Thus, DNA testing resulted in an incremental cost per case detected of £200 compared with the biochemical test.

In the model of 100 offspring, the total cost was £46,753 with the biochemical test and £18,638 with DNA testing. Thus, DNA testing saved £7,982 per case detected in comparison with the biochemical test.

The results of the sensitivity analysis confirmed that the base-case findings were robust. The most influential model inputs in the primary simulation were the proportion of patients with a positive DNA test for the C282Y mutation, the specificity of the TS test, and the cost of liver biopsy. For siblings, the most influential inputs were the cost of the DNA test and the cost of monitoring. A reduction of 40% in the cost of the DNA test or if those who were monitored were retested twice (instead of once) would make this strategy cost-saving. For offspring, the key inputs were the number of times the offspring were monitored and the penetrance of disease.

The probabilistic sensitivity analysis changed the magnitude of savings or additional costs, but did not alter the base-case findings.

Authors' conclusions
The authors concluded that DNA testing was likely to be an effective and cost-saving strategy in clinical cases with iron overload and in the offspring of diagnosed patients. These findings support the UK guideline which recommends the use of DNA testing.

CRD commentary
Interventions:
The authors justified their choice of the comparators, which appear to have been the relevant interventions for the two patient populations. All the strategies were extensively described. The authors provided a justification for the exclusion of magnetic resonance imaging as an alternative diagnostic tool, which was that it was not widely available in all medical centres.

Effectiveness/benefits:
The identification of the primary sources for the data was by systematic search and review. The methods and conduct of this approach were not reported in this publication, which was a short version of a more comprehensive health technology assessment. More information on the search criteria, characteristics of the primary sources of data, and methodology used to pool the published data were available from the full report. Appropriate UK sources were used when available. The authors justified their selection of a disease-specific benefit measure. In effect, the detection rate represented the outcome of most interest to clinicians and medical providers.
Costs:
The analysis of costs was consistent with the perspective. The authors reported the categories of costs together with their unit prices. The sources of costs reflected the perspective and the UK NHS accounting system. The resource use data appears to have been based on authors’ opinions. Nevertheless, the use of alternative economic estimates was investigated in the sensitivity analysis. The price year was not reported.

Analysis and results:
The authors used an incremental approach in order to synthesise the costs and benefits of the alternative strategies. The issue of uncertainty was appropriately investigated in the sensitivity analyses, the methods and findings of which were clearly presented. The authors justified the relatively short-term horizon of their study on the grounds of the poor quality of long-term published evidence and the consequent need for assumptions which would have increased the uncertainty of the analysis. The authors acknowledged that complications related to liver biopsy were not taken into account, thus biasing the study findings against DNA testing.

Concluding remarks:
The study appears to have been based on valid methodology, which makes the authors’ conclusions more robust.

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