Hereditary hemochromatosis screening: effect of mutation penetrance and prevalence on cost-effectiveness of testing algorithms
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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
The authors compared numerous screening scenarios for hereditary haemochromatosis in populations which represented varied prevalence and penetrance of HFE gene mutations. The authors concluded that population screening, using biochemical tests followed by genetic confirmatory tests, appeared to be a cost-effective option for the population in their setting. The lack of discounting and description of clinical data sources means that the authors’ conclusions should be treated with caution.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
The study compared 165 scenarios for population screening for hereditary haemochromatosis (HH) using two or three different biochemical screening tests on 91 simulated populations which represented the penetrance and prevalence of the HFE gene mutations. All scenarios were compared with no screening.

Interventions
The biochemical screening tests were serum transferrin saturation (TS), serum ferritin (SF), and unsaturated iron-binding capacity (UIBC). These were followed by genetic testing to detect the two important HFE gene mutations, which are C282Y and H63D. Various combinations of these tests were investigated using specific software.

Location/setting
Canada/primary care.

Methods
Analytical approach:
For each of the 91 simulated populations, varying by size, demographics, phenotypes and genotypes, the sampled patients passed through a decision tree where the time to events, and probabilities of events depended on the population characteristics. At the final branch of the tree, a total cost and life expectancy was attributed. The time horizon was the patients’ life expectancy from birth. The authors stated that the perspective was that of the Quebec public health care system.

Effectiveness data:
The effectiveness data were obtained from published studies. The main clinical parameters were prevalence and penetrance of combined HFE genotypes, sensitivity and specificity of the screening tests, complication rates, and therapeutic strategies used.

Monetary benefit and utility valuations:
Not relevant.

Measure of benefit:
\( \text{The measure of benefit was life expectancy from birth.} \)

Cost data:
The cost categories included the cost of the screening tests, of medical follow-up, and of the different treatment strategies used for different complications. The resource use and cost data were either derived from published literature or based on actual data from the province of Quebec (average prices obtained from administrative records). All costs were reported in Canadian dollars (CAD) for the price year 2004 and discounting was not performed. Administrative costs were included where relevant.

Analysis of uncertainty:
The confidence intervals around cost-effectiveness estimates were created and various scenarios were tested in sensitivity analyses. A set of simulations was conducted by restricting the complications to only cirrhosis and hepatocellular carcinoma. A two-way sensitivity analysis was performed by simultaneously varying the mutation prevalence and the HFE genotype biochemical penetrance. Finally, the uncertainty around the cost of HFE DNA testing was also investigated.

Results
For a hypothetical population with a HH prevalence of 2:1000, all population screening strategies were more effective and less costly compared with no screening.

The cost-effectiveness improved when the targeted age was extended to 50 years. A strategy of one-shot screening of people 20 to 25 years old every six years could be efficient, but the beneficial effects took up to 35 years to materialise.

The sensitivity analysis demonstrated that the results were very sensitive to variations in the prevalence and penetrance of disease mutations and the number and nature of HH complications.

The combination of UIBC and TS was the most robust strategy.

Authors' conclusions
The authors concluded that a population screening programme for haemochromatosis was cost-effective for the population in their setting.

CRD commentary
Interventions:
The interventions were clearly reported. The study was thorough in its coverage of alternative screening strategies and target populations.

Effectiveness/benefits:
The effectiveness data were derived from published studies, but no systematic search of the literature was reported. The sources were referenced, but were not described. It is not possible to judge the validity of the data from the information reported in this paper. The Uncertainty in certain parameters was investigated and the results were fully reported, which enhances the generalisability of the study findings. Life-years gained was an appropriate measure of benefit given the risk of mortality. However, quality of life is also likely to be important.

Costs:
The costs appeared to reflect the perspective stated. The resource use data and the unit costs were well reported and the cost data appeared to be appropriate for the study population and setting. The price year was reported, facilitating the revaluation of the results for future years. Although, discounting was relevant, given the long time horizon of the analysis, none was carried out. The uncertainty around the cost estimates was not investigated comprehensively; the analysis was restricted to the laboratory costs.

Analysis and results:
Part of the model structure was presented graphically along with all the details of the simulations. As the results were numerous, the authors selected the most important ones and presented them in full. The sensitivity analysis was restricted to the clinical parameters while variation in resource use and cost data was not investigated. The authors correctly acknowledged the variation in the cost data between settings as a major limitation to the generalisability of the findings to other settings.
Concluding remarks:
The lack of discounting and description of clinical data sources means that the authors’ conclusions should treated with caution.

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