The cost-effectiveness of screening for hereditary hemochromatosis in Germany: a remodeling study
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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 objective was to assess the cost-effectiveness of screening strategies for hereditary haemochromatosis in men in the general population. The current policy was generally supported. A genetic test after an elevated transferrin saturation test was more cost-effective, but the results were highly uncertain. On the whole, the methods seemed to be appropriate and were well reported. There were some limitations, but the conclusions appear to be appropriate.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
The objective was to assess the cost-effectiveness of different hereditary haemochromatosis screening strategies for men in the general population.

Interventions
The strategies were no screening; cascade screening, which was screening for men with a symptomatic parent only; and screening for all men. Screening was for asymptomatic men and was by two independent transferrin saturation tests (phenotypic testing); C282Y homozygosity (HFE) screening for a mutation (genetic testing); or a transferrin saturation test and HFE screening, using the same blood sample (phenotypic and genetic testing).

Location/setting
Germany/primary care.

Methods
Analytical approach:
A Markov model simulated the natural history of liver cirrhosis, associated with HFE homozygosity, using age-specific mortality rates multiplied by the relative risk of death for men with the mutation and liver cirrhosis. A cohort of men aged 30 years entered the decision analytic model and probability distributions were applied. The data were from published studies. The author stated that the perspective was that of the German Statutory Health Insurance.

Effectiveness data:
The effectiveness data were from published studies, including Whitlock, et al. (2006, see 'Other Publications of Related Interest' below for bibliographic details). More recent studies were identified by updating a search of PubMed to January 2008. The deoxyribonucleic acid (DNA) test sensitivity and specificity were from a study by Palomaki, et al. 2003 (see 'Other Publications of Related Interest' below for bibliographic details). The transferrin saturation test sensitivity and specificity were from published studies. The key clinical parameters included the probability of cirrhosis in men with the mutation, the effectiveness of preventive blood taking, the sensitivities and specificities of the DNA and transferrin saturation tests, the relative risk of death from cirrhosis, the age of cirrhosis, the prevalence of HFE homozygosity among non-Hispanic white men, and the adherence rate for screening.

Monetary benefit and utility valuations:
Not relevant.

Measure of benefit:
The primary benefit measure was the number of life-years gained (LYG) and these were discounted at an annual rate of 3%. The incremental cost per LYG was measured and life expectancy was estimated for the populations of men without the mutation, men with the mutation, and men with cirrhosis.

Cost data:
The cost categories included out-patient care, DNA test, blood taking, the average cost of liver cirrhosis, physician's practice information leaflets, and genetic counselling. Out-patient costs were from reimbursement rates, DNA test costs were from a German pilot study, and blood taking costs were from lump-sum reimbursement fees. The average costs of liver cirrhosis were from a published model (El-Serag, et al. 2000, see ‘Other Publications of Related Interest’ below for bibliographic details) and were in US dollars. These were inflated to 2004 values and converted to Euros (EUR) using the purchasing power parity rate. The cost of physician's practice information leaflets were estimated from the prices of a German print shop and German postage. All costs were in EUR and an annual discount rate of 3% was applied.

Analysis of uncertainty:
Deterministic one-way sensitivity analyses were performed on all the relevant parameters using appropriate high and low values from the literature and available data. The discount rate was varied between 0% and 10% as recommended by the Hanover Consensus. Probabilistic sensitivity analyses were performed on all the input parameters, using a Monte-Carlo simulation, based on 20,000 iterations, and the results were presented in cost-effectiveness acceptability curves (CEACs).

Results
Only the results of the non-dominated strategies were reported.

The total cost per patient was EUR 6.3518 for no screening, EUR 6.3539 for cascade phenotypic and genetic testing, EUR 6.7801 for population phenotypic and genetic testing, and EUR 6.8428 for population genetic testing.

The LYG per patient were 24.806433927 for no screening, 24.806433978 for cascade phenotypic and genetic testing, 24.806437415 for population phenotypic and genetic testing, and 24.806437803 for population genetic testing.

The incremental cost per LYG was EUR 41,425 for cascade phenotypic and genetic testing compared with no screening, EUR 123,996 for population phenotypic and genetic testing compared with cascade phenotypic and genetic testing, and EUR 161,248 for population genetic testing compared with population phenotypic and genetic testing.

The sensitivity analyses showed that the parameters with the highest impact on the incremental cost per LYG of screening were the discounting of LYG, the cost of genetic counselling, and the adherence to preventive blood taking. The CEACs showed that the results were very uncertain: at a threshold of EUR 50,000 per LYG the cascade phenotypic and genetic testing had a probability of 32.8% of being cost-effective.

Authors’ conclusions
The author concluded that the current German policy of screening men at risk was consistent with cost-effectiveness decision-making thresholds, but using a DNA test on the same sample after the first elevated transferrin saturation result was more cost-effective than a second transferrin saturation test, which was recommended by German guidelines. The author suggested that these results were highly uncertain and that further research should address how patients deal with results from genetic tests in the long term and how adherence to preventive blood taking could be enhanced in a cost-effective manner.

CRD commentary
Interventions:
The interventions were well described and relevant to the author's setting. The analysis compared several screening strategies among men in the general population.

Effectiveness/benefits:
A systematic review of the literature to identify the clinical effectiveness estimates was not reported, which means it is not possible to decide if the best available evidence was used. The effectiveness estimates appeared to be from reliable
published studies and more recent studies were identified in a search of PubMed. The study by Whitlock, et al. appears to have been a systematic review of hereditary haemochromatosis screening, but few details were given. Probabilistic sensitivity analysis was used to assess the parameter uncertainty.

Costs:
The costs were consistent with the perspective. Their sources were potentially good and discounting was appropriately applied. The costs of liver cirrhosis were inflated to 2004 prices and then converted from US dollars to EUR; this method has its limitations, which were acknowledged by the author. Changes in this parameter were tested in a one-way sensitivity analysis. The price year was not explicitly reported, but based on this calculation it was likely to have been 2004.

Analysis and results:
The analytic approach was well reported and the results of the non-dominated strategies were reported clearly and fully. A diagram of the model was presented. The issue of uncertainty was appropriately addressed in probabilistic sensitivity analyses, the results of which were presented in CEACs, and one-way sensitivity analyses on all the input parameters. The author acknowledged a number of limitations of this study, which included the fact that quality of life was not considered and this might have underestimated the expected benefits of preventing liver cirrhosis.

Concluding remarks:
On the whole, the methods seemed to be appropriate and were well reported. The study had some limitations, but the conclusions appear to be appropriate.

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