Screening blood donors for hereditary hemochromatosis: decision analysis model comparing genotyping to phenotyping

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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 blood donors for hereditary hemochromatosis.

Type of intervention
Screening.

Economic study type
Cost-utility analysis.

Study population
The study population was a hypothetical cohort of 10,000 voluntary blood donors and 50 siblings of the identified homozygotes.

Setting
Hospital and primary care. The study was carried out in Ontario, Canada.

Dates to which data relate
Effectiveness data were derived from a 1995 database of 170 hemochromatosis homozygotes and from studies previously published between 1996 and 1998. Resource use and cost data were derived from a 1995 source. The price year was 1998.

Source of effectiveness data
A single study was used to derive clinical, biochemical, pathological and long-term survival data along with a review of previously published studies and authors' assumptions.

Link between effectiveness and cost data
In the single study element the costing was undertaken retrospectively on the same patient sample as that used in the effectiveness analysis.

Study sample
170 patients with hemochromatosis consisting of symptomatic probands and asymptomatic family members.

Study design
This was a prospective case series, carried out at a single centre. The data collection related to a period of 30 years.
Analysis of effectiveness
Analysis of effectiveness was based on intention to treat. The primary health outcomes measured included the prevalence of life-threatening complications and the rates of progression to life-threatening complications.

Effectiveness results
43% of men and 28% of women will develop life-threatening manifestations of hemochromatosis if unscreened.

Clinical conclusions
As indicated in the above findings from the database.

Modelling
A decision tree was constructed to estimate costs and benefits.

Outcomes assessed in the review
The review element assessed the sensitivity and specificity of the screening tests.

Study designs and other criteria for inclusion in the review
Not stated.

Sources searched to identify primary studies
Not stated.

Criteria used to ensure the validity of primary studies
Not stated.

Methods used to judge relevance and validity, and for extracting data
The data were extracted by means of summary statistics.

Number of primary studies included
At least 6 studies were included.

Methods of combining primary studies
Not combined.

Investigation of differences between primary studies
Not stated.

Results of the review
The genetic test had a sensitivity value of 85%.

Methods used to derive estimates of effectiveness
Estimates of effectiveness were also based on authors’ assumptions.

**Estimates of effectiveness and key assumptions**
Threshold levels for transferrin saturation were 50% for women and 60% for men and for ferritin were 150 micro.g/L for women and 200 micro.g/L for men. In the phenotyping screening model, 4.6 donor homozygotes are missed and in the genotyping screening model, 4.5 donor homozygotes are missed.

**Measure of benefits used in the economic analysis**
Quality-adjusted life years (QALYs) were used as the measure of benefit. Utility estimates were derived from quality of life studies in hemochromatosis at the authors’ centre. Utilities were discounted at an annual rate of 3%.

**Direct costs**
Direct costs were discounted at an annual rate of 3%. Quantities and costs were reported separately. Direct costs included the costs of life-threatening complications such as heart failure, cirrhosis, hepatocellular carcinoma, and diabetes. The quantity/cost boundary adopted was that of the health service. The estimation of quantities and costs was based on actual data. Unit costs were derived from the tertiary care centre. The price year was 1998.

**Statistical analysis of costs**
Not reported.

**Indirect Costs**
Not included.

**Currency**
US dollars ($).

**Sensitivity analysis**
Sensitivity analysis was performed on the following parameters: sensitivity of the genetic test, prevalence and penetrance rates.

**Estimated benefits used in the economic analysis**
Phenotypic screening identified 25.4 homozygous blood donors and 12.5 homozygous siblings. Genotypic screening identified 25.5 homozygous blood donors and 12.5 homozygous siblings. 6.5 homozygotes are missed with the combined strategy (phenotype, then genotype). Compared to the "no screening" strategy, 2.75 quality life days are saved per person screened.

**Cost results**
Lifetime expenditure relating to 30 unscreened homozygotes in the blood donor population amounted to $515,478. The cost of the phenotypic screening strategy combined with the cost of 4.6 missed homozygotes was $502,843. The cost of the genotypic screening strategy combined with the cost of 4.6 missed homozygotes was $2,031,727.

**Synthesis of costs and benefits**
Compared to the "no screening" strategy, genotypic screening generates a cost-utility of $20,042 per QALY saved. Cost savings are only apparent if the initial gene test costs less than $28 with a prevalence of hemochromatosis of 0.003. Decreasing the specificity to 0.97 markedly increased the cost to $3,533,815. The effect of varying the rate of
progression to life-threatening symptoms is to decrease the incremental cost savings.

**Authors' conclusions**
Population screening programmes for hemochromatosis have the potential to save money. Optimal strategies for screening include initial testing for iron overload (phenotyping) with confirmatory genetic testing, or initial genetic testing if the test is less than $28.

**CRD COMMENTARY - Selection of comparators**
The rationale for the choice of the comparator was clear. You, as a user of this database, should verify whether these health technologies are relevant to your setting.

**Validity of estimate of measure of benefit**
The effectiveness data input to the decision tree have been derived from database records and, what may have been, a non-systematic review of the literature. The internal validity of effectiveness estimates from the database records is likely to be high, although the data derived from the literature cannot be fully assessed given the limited information provided about the literature review and the quality assessment of the primary studies. It can be argued that the validity of the results may be limited given the numerous assumptions that the authors had to make. The rates of progression used in the model were based on patients presenting with clinical symptoms and may be an over-estimate of the penetrance of disease found under population screening. The authors noted that the natural history of patients who present with symptoms of hemochromatosis may be different compared with asymptomatic patients discovered through screening. The authors also conceded that the effectiveness estimates are not applicable to large urban centres with multicultural non-white populations or to other countries.

**Validity of estimate of costs**
The validity of the costs considered (i.e. those relating to life-threatening clinical outcomes) is likely to be high. The authors do point out, however, that the costs of non-life-threatening diseases, costs of conducting the screening process, and indirect costs such as earnings gained due to the prevention of hemochromatosis were not considered. Cost estimates were derived from local sources and are unlikely to be generalisable to other settings.

**Other issues**
Adequate comparisons with other relevant studies were made. The generalisability of the results to other settings or countries was discussed. The authors do not appear to have presented their results selectively. The study enrolled blood donors and this was reflected in the authors' conclusions.

**Implications of the study**
Future studies should explore the use of an inexpensive automated unbound iron-binding capacity as an alternative to transferrin saturation.

**Source of funding**
None stated.

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