Screening blood donors for hereditary hemochromatosis: decision analysis model based on a 30-year database

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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, diagnosis and treatment.

Economic study type
Cost-utility analysis.

Study population
Hypothetical cohort of 10,000 voluntary blood donors.

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

Dates to which data relate
The data for the prevalence and part of the effectiveness analysis were collected from 1965 to 1995. These data were supplemented with data from the literature "as necessary", from studies published between 1981 and 1993. The resource use data were collected during the same period. The price year was 1994.

Source of effectiveness data
A single study was used to derive clinical, biochemical, pathological and long-term survival (stored on the 'Clinical Haemochromatosis Database') plus a review of previously published studies and authors' assumptions.

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

Study sample
The Clinical Haemochromatosis Database, available to the authors, was used to derive input parameters for the model, based on data from 170 patients with hemochromatosis. Persons with anaemia, cirrhosis, diabetes requiring insulin, symptomatic coronary artery disease, gastrointestinal bleeding within 6 months, and viral infections are not eligible to become blood donors. No power calculations were reported.

Study design
This was a prospective case series, carried out at a single centre. The data collection relates to a period of 30 years. No loss to follow-up was reported.

**Analysis of effectiveness**
The principle (intention to treat or treatment completers only) on which the analysis of the clinical study was based was not reported. The primary health outcomes used included the prevalence of hereditary hemochromatosis, the cases of life-threatening disease manifestations, and the rates of organ dysfunction.

**Effectiveness results**
The prevalence of hereditary hemochromatosis was 0.003 in the population and 0.25 for siblings. 43% of males and 28% of females develop life-threatening disease manifestations. The rates of organ dysfunction varied between 0.045 for heart failure to 0.303 for cirrhosis.

**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 main outcomes assessed in the review were prevalence, symptom onset, symptom-specific survival, penetration of disease, sensitivity and specificity of transferrin saturation (TS), serum ferritin levels, and hepatic iron index.

**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 13 studies were included.

**Methods of combining primary studies**
Not combined.

**Investigation of differences between primary studies**
Not stated.
Results of the review
The unsaturated iron binding capacity (UIBC) test has a sensitivity of 0.92, a specificity of 0.93 and a positive predictive value of 86%. The serum percentage TS test combined with serum ferritin has a sensitivity of 0.94 and a specificity of 0.86, respectively. 22.1 donors with high TS and serum ferritin levels have a diagnostic percutaneous liver biopsy performed with hepatic iron determination. 90% of blood donors have positive screening results and consent to liver biopsy. The probability of intraperitoneal haemorrhage requiring transfusion is 0.002. The probability of blood donors dying from liver biopsy being performed is 0.0001. 20.4 donors with an elevated hepatic iron concentration are offered therapeutic venesections. Hepatocellular carcinoma develops in 25% of cirrhosis and is invariably fatal within one year. 10% of donors prefer venesections over liver biopsy.

Methods used to derive estimates of effectiveness
Authors’ assumptions were also used to derive estimates of effectiveness.

Estimates of effectiveness and key assumptions
The UIBC threshold value is set to select persons with a TS over 50%. The threshold values for serum percentage TS are more than 50% for females and 60% for males. 80% of donors with a high serum percentage TS and normal or low serum ferritin levels are followed up with repeat serum percentage TS and serum ferritin every 1-2 years. Donors with low or normal iron stores require six venesections and donors with high iron stores require 30 venesections. Donors with normal exchangeable body iron need maintenance venesections in 5 years. Compliance with follow-up is 80%. Probable homozygotes require further investigation followed by maintenance venesections within 5 years. 12.3 definite homozygotes are discovered among siblings. Removal of excess body iron does not affect the course of diabetes, and life expectancy is shortened. Patients with clinical manifestations require 52 venesections to deplete body iron stores and an average of 3 annual venesections to prevent iron reaccumulation.

Measure of benefits used in the economic analysis
Quality-adjusted life days (QALDs) were used as the measure of benefits. Utility was estimated by comparing symptom-specific global sickness impact profile scores with hemochromatosis and symptom-specific life expectancy. Benefits were discounted at an annual rate of 3%.

Direct costs
Costs were discounted at an annual rate of 3%. Quantities and costs were reported separately. Direct costs included costs of treating life-threatening conditions 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 University Hospital. The price year was 1994.

Statistical analysis of costs
Not reported.

Indirect Costs
Not included.

Currency
Canadian dollars (Can$), with Can$1=US$0.72.

Sensitivity analysis
A sensitivity analysis was conducted on the following parameters: prevalence rate, cost of screening test, inclusion of
siblings of donors, probability of life-threatening illness, sex of donors and siblings, sensitivity and specificity of the initial test, cost of venesection therapy, and discount rate.

**Estimated benefits used in the economic analysis**
The screening strategy generated an expected gain per person screened of 0.84 QALDS for donors, and 1.18 QALDs for donors and siblings.

**Cost results**
The screening strategy generated incremental cost savings per person screened of Can$3.19 for donors and Can$12.57 for donors and siblings.

**Synthesis of costs and benefits**
The screening strategy generated an incremental cost-utility per person screened of Can$4.082/QALDs for female donors. Sensitivity analysis showed that cost savings are evident for blood donors when prevalence rates are greater than 0.0026, probability of life-threatening disease is greater than 0.3 in males, initial test cost is greater than Can$8, sensitivity of serum UIBC equals 0.8, specificity of serum UIBC equals 0.8, the number of annual maintenance venesections equals 4 or the discount rate equals 5%.

**Authors' conclusions**
Screening blood donors for hemochromatosis has the potential to improve overall societal health status and decrease third-party payer health care costs over the long-term.

**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 have been derived from database records and, what may have been, a non-systematic review of the literature, to construct a decision tree. 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 authors conceded that the effectiveness estimates are not applicable to large urban centres with multicultural non-white populations or to other countries. The reported sensitivity of the UIBC test has not been validated.

**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. This relates to the perspective adopted (third-party payer).

**Other issues**
The authors conducted good sensitivity analyses on key parameters to deal with uncertainty in the data. Generalisability to the domain considered is likely to be high but see comments below.

**Implications of the study**
The authors pointed out that the model presented here cannot be extrapolated to ad hoc screening in an ambulatory care centre because of the higher mean age at presentation, the possible reduction in the specificity of the screening tests because of concurrent illness, and the possible higher cost of the initial screening test.
Source of funding
None stated.

Bibliographic details

Other publications of related interest


Indexing Status
Subject indexing assigned by NLM

MeSH
Adolescent; Adult; Aged; Blood Donors; Child; Costs and Cost Analysis; Decision Support Techniques; Decision Trees; Female; Ferritins /blood; Hemochromatosis /prevention & control /epidemiology /genetics; Homozygote; Humans; Information Systems; Iron /blood /metabolism; Life Expectancy; Liver /metabolism; Male; Mass Screening /economics; Middle Aged; Prevalence; Sensitivity and Specificity; Transferrin /analysis

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