Cost-effectiveness of nucleic acid test screening of volunteer blood donations for hepatitis B, hepatitis C and human immunodeficiency virus in the United States

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
Several screening protocols for reducing the risk of transfusion-transmission of hepatitis B virus (HBV), hepatitis C virus (HCV) and human immunodeficiency virus (HIV) in donated blood were examined. The strategies considered were:

- serological (antibody and antigen) screening (SS);
- SS plus minipool (MP) nucleic acid testing (NAT);
- SS plus MP-NAT without p24 antigen (-p24);
- SS plus individual (ID) NAT -p24;
- SS plus ID-NAT -p24/antibody to hepatitis B core antigen (anti-HBc), (but retaining hepatitis B surface antigen, HbsAg); and
- SS plus ID-NAT -p24/HBsAg (but retaining anti-HBc).

Type of intervention
Screening.

Economic study type
Cost-effectiveness analysis and cost-utility analysis.

Study population
The study population comprised a hypothetical cohort of volunteer blood donations, which included whole blood, red blood cells, platelet concentrates, frozen plasma and cryoprecipitate. Autologous blood donations and single donor platelets were excluded.

Setting
The setting was a clinical laboratory. The economic study was carried out in the USA.

Dates to which data relate
The effectiveness data were derived from studies published from 1993 to 2003. Some resource use data were derived from studies published in 2000 and 2001. The price year was not reported.

Source of effectiveness data
The effectiveness evidence was derived from a synthesis of completed studies and authors' assumptions.
Modelling
A decision tree model was constructed to assess the clinical and economic impact of the alternative screening protocols for reducing the risk of transfusion-transmission of HBV, HCV and HIV. The model consisted of three parts. First, blood was donated, screened, then processed and transfused. Second, the total number of transfusion recipients who developed HBV, HCV, and HIV infections was calculated. Third, the model outcomes were estimated. The structure of the tree was not reported. Three cohorts of patients were considered: 27 years, 54 years, and 76 years. The time horizon of the model was lifetime.

Outcomes assessed in the review
The outcomes derived from the literature were:

- the annual blood donations and transfusions in 1999;
- the number of transfused components per donated unit;
- the ratio of transfused units to transfused patients;
- the age distribution of the whole cohort;
- the incidence of infection;
- factor to adjust for increased risk of incident cases in first-time donors for HBV, HCV and HIV;
- the ratio of repeat to first-time donors;
- the incidence of HBV adjusted for all donors;
- the windows periods;
- the residual risk estimates per 1 million donations;
- survival;
- the utility adjustments for quality-adjusted life-years (QALYs); and
- disease-specific inputs such as latent periods, life expectancy and lifetime QALYs.

Study designs and other criteria for inclusion in the review
It was not stated whether a systematic review had been carried out to identify relevant studies. Not all of the study designs were reported. Some of the sources consisted of US statistics life tables and published models.

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
Not stated.
Number of primary studies included
Twenty-five primary studies provided the evidence used in the decision model.

Methods of combining primary studies
In general, each study provided a series of estimates. Only a few studies appear to have been combined to derive the primary estimates. A narrative method appears to have been used.

Investigation of differences between primary studies
Not stated.

Results of the review
The annual blood donations and transfusions in 1999 were 13,900,000.

The number of transfused components per donated unit was 1.45.

The ratio of transfused units to transfused patients was 3.3.

The age distribution of the whole cohort was 15% for 27-year-old individuals, 25% for 54-year-old individuals, and 60% for 76-year-old individuals.

The infection incidence per 100,000 person-years was 4.46 for HBV, 2.24 for HCV, and 1.72 for HIV.

The factor to adjust for increased risk of incident cases in first-time donors was 4.5 for HCV and 2.5 for HIV.

The ratio of repeat to first-time donors was 80:20.

The HBV incidence adjusted for all donors per 100,000 person-years was 6.69.

The windows period with SS was 59 days for HBV, 70 days for HCV, and 16 days for HIV.

The residual risk estimates per 1 million donations with HBV, HCV and HIV were, respectively:
10.81, 7.31 and 0.98 with SS;
8.98, 0.94 and 0.61 with SS plus MP-NAT; and
6.96, 0.73 and 0.43 with SS plus ID-NAT.

In the cohorts of 27-, 54- and 76-year-old individuals, the post-transfusion mortality rates were, respectively:
0.105, 0.271 and 0.382 in year 1;
0.029, 0.088 and 0.190 in year 2,
0.013, 0.057 and 0.139 in year 3;
0.007, 0.047 and 0.153 in year 4; and
0.010, 0.044 and 0.149 in year 5.

The utility adjustments for QALYs were 0.92 for 27-year-old individuals and for 54-year-old individuals, and 0.81 for 76-year-old individuals.

The average latent period was 3 years for HBV, variable for HCV, and 5 years for HIV.
The average life expectancies per patient in the cohorts of 27-, 54- and 76-year-old individuals were, respectively:

19.79, 10.44 and 4.24 for HBV;
19.67, 10.38 and 4.21 for HCV; and
13.57, 11.66 and 6.53 for HIV.

The average QALYs per patient in the cohorts of 27-, 54- and 76-year-old individuals were, respectively:

15.54, 8.30 and 3.42 for HBV;
17.45, 9.32 and 3.84 for HCV; and
11.49, 9.90 and 5.58 for HIV.

Methods used to derive estimates of effectiveness
The authors made some assumptions that were used in the decision model.

Estimates of effectiveness and key assumptions
The size of the cohort of transfused patients was 6,107,576. The ratio of risk in donated units to risk of infections in transfused units was 1.0.

The factor to adjust for increased risk of incident cases in first-time donors was 3.5 (average between increased risk of incident cases for HCV and HIV).

The HCV incidence adjusted for all donors per 100,000 person-years was 3.81. The HIV incidence adjusted for all donors per 100,000 person-years was 2.24.

The windows period with SS plus MP-NAT was 49 days for HBV, 9 days for HCV, and 10 days for HIV.

The windows period with SS plus ID-NAT was 38 days for HBV, 7 days for HCV, and 7 days for HIV.

After 5 years, the mortality rates were assumed to follow the age-specific pattern for the general population.

Other assumptions on the techniques under evaluation were also reported.

Measure of benefits used in the economic analysis
The summary benefit measures used were survival and QALYs. Both were estimated using the decision model. An annual discount rate of 3% was applied. The estimated number of cases of HBV, HCV and HIV was also reported.

Direct costs
Discounting was relevant, owing to the long timeframe of the study, and a 3% discount rate was applied. The unit costs were not presented separately from the quantities of resources used. The health services included in the economic evaluation were screening tests and treatment costs for HBV, HCV and HIV. Screening tests covered materials, equipment, labour, donor notification and counselling, donor losses, and all supplementary, discriminatory, and confirmatory testing associated with the procedures. Treatment costs were presented as macro-categories. The cost/resource boundary of the health care system was taken. Resource use was estimated on the basis of authors’ assumptions (based on the frequency of tests) and published studies. The costs were derived from manufacturer's sources and published evidence. The price year was not reported.
Statistical analysis of costs
The costs were treated deterministically.

Indirect Costs
The indirect costs were not considered in the economic evaluation.

Currency
US dollars ($).

Sensitivity analysis
Univariate sensitivity analyses were performed to investigate the robustness of the estimated cost-effectiveness and cost-utility ratios to variations in some model assumptions. For example, the discount rate, blood-donation assumptions, the age distribution of the blood-recipient population, disease incidence rates, window periods, disease progression and treatment assumptions, and blood screening test costs. The choice of some alternative values used in the analysis was justified.

Estimated benefits used in the economic analysis
The total number of cases (HBV, HCV and HIV) was:

385 (218, 147 and 20) with SS,
212 (181, 19 and 12) with SS plus MP-NAT and with SS plus MP-NAT -p24, and
164 (140, 15, and 9) with SS plus ID NAT -p24.

The estimated life-years were:
52,979,000 with SS,
52,979,053 with SS plus MP-NAT and with SS plus MP-NAT -p24, and
52,979,063 with SS plus IDP NAT -p24.

In the secondary analysis, the estimated life-years were 52,979,063 with both SS plus ID-NAT -p24/anti-HBc and SS plus ID-NAT -p24/HBsAg.

The estimated QALYs were:
47,016,875 with SS,
47,016,977 with SS plus MP-NAT and with SS plus MP-NAT -p24, and

In the secondary analysis, the estimated QALYs were 47,016,991 with both SS plus ID-NAT -p24/anti-HBc and SS plus ID-NAT -p24/HBsAg.

Cost results
The estimated costs were:
$210,311,375 with SS,
$364,787,229 with SS plus MP-NAT -p24,

$404,124,229 with SS plus MP-NAT, and

$461,783,104 with SS plus ID-NAT -p24.

In the secondary analysis, the estimated costs were $431,203,117 with SS plus ID NAT -p24/anti-HBc and $448,717,104 with SS plus ID-NAT -p24/HBsAg.

**Synthesis of costs and benefits**

Incremental cost-effectiveness and cost-utility ratios were calculated to combine the costs and benefits of the screening strategies. The incremental cost (in million) per life-year gained was $2.9 with SS plus MP-NAT -p24 over SS, and $10 with SS plus ID-NAT -p24 over SS plus MP-NAT -p24.

The incremental cost (in million) per QALY gained was $1.5 with SS plus MP-NAT -p24 over SS, and $7.3 with SS plus ID-NAT -p24 over SS plus MP-NAT -p24. The strategy SS plus MP-NAT was dominated by SS plus MP-NAT -p24 in both the cost-effectiveness and the cost-utility analyses.

The results changed in the secondary analysis where two additional strategies (SS plus ID-NAT -p24/anti-HBc and SS plus ID-NAT -p24/HbsAg) were considered.

The strategy SS plus MP-NAT was dominated by SS plus MP-NAT -p24, whereas SS plus ID-NAT -p24 was dominated by SS plus ID-NAT -p24/HbsAg.

The incremental cost (in million) per life-year gained was:

- $2.9 with SS plus MP-NAT -p24 over SS,
- $6.8 with SS plus ID-NAT -p24/anti-HBc over SS plus MP-NAT -p24, and
- $1,973 with SS plus ID-NAT -p24/anti-HBc over SS plus ID-NAT -p24/HbsAg.

The incremental cost (in million) per QALY gained was:

- $1.5 with SS plus MP-NAT -p24 over SS,
- $5.0 with SS plus ID-NAT -p24/anti-HBc over SS plus MP-NAT -p24, and
- $1,422 with SS plus ID-NAT -p24/anti-HBc over SS plus ID-NAT -p24/HbsAg.

The sensitivity analysis showed that the incremental cost per life-year saved with SS plus MP-NAT -p24 over SS ranged from $1.0 million to $2.1 million, while the incremental cost per QALY ranged from $3.1 million to $15.6 million.

**Authors’ conclusions**

A cost-effectiveness ratio in the range of $1 - 2 million per quality-adjusted life-year (QALY) gained, as in the case of adding minipool nucleic acid testing (MP-NAT) without p24 antigen (-p24) to serological screening (SS) protocols for donated blood, was not extraordinary in the context of established blood safety measures. The high values of the cost-effectiveness ratios were due to the fact that SS protocols had already reduced the risk of transmission of hepatitis B virus (HBV), hepatitis C virus (HCV) and human immunodeficiency virus (HIV) to very low levels. The cost-effectiveness of adding NAT to current screening improved in young age groups.

**CRD COMMENTARY - Selection of comparators**

The selection of the comparators reflected the existing and proposed screening protocols for reducing the risk of
transfusion-transmission of HBV, HCV and HIV in donated blood. You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness evidence was derived mainly from published studies. It was not stated whether a systematic review was carried out to identify relevant studies. Very limited information on the design of the primary studies was provided. Some estimates were derived from US statistics. The issue of validity and comparability of the primary sources was not addressed. Narrative methods appear to have been used to combine the primary estimates, when required, owing to the use of multiple sources. Some model inputs were based on authors’ assumptions. Most of the estimators were varied in the sensitivity analysis.

Validity of estimate of measure of benefit
The use of survival and QALYs as summary benefit measures was appropriate because they captured the impact of the interventions on the most relevant dimensions of patient health. Discounting was applied, as recommended in US guidelines. The use of alternative discount rates was tested in the sensitivity analysis. There was limited information on the source of the utility values. QALYs and survival are comparable with the benefits of other health care interventions.

Validity of estimate of costs
The authors stated explicitly which perspective was adopted in the study. As such, it appears that all the relevant categories of costs have been included in the analysis. However, the treatment costs were presented as macro-categories and a detailed breakdown of the cost items was not provided. This would make it difficult to replicate the study. The source of the data was reported for all items. The costs were treated deterministically, but some items were varied in the sensitivity analysis. The price year was not reported, thus making it difficult to perform reflation exercises in other settings.

Other issues
The authors compared their findings with those from other published studies that evaluated the cost-effectiveness of blood screening protocols. They stated that their model improved upon other analyses in several ways, including the lifetime horizon, multi-drug treatment regimens for HIV, combination therapy for HCV, and three cohort ages. Some limitations to the validity of the analysis were also noted. For example, the use of assumptions and the lack of some specific data. The issue of the generalisability of the study results to other settings was not addressed, although several sensitivity analyses were conducted. These increased the external validity of the analysis.

Implications of the study
The study results suggested that the addition of NAT strategies to common screening protocols for donated blood in the USA could represent a cost-effective strategy, despite the fact that the cost-effectiveness ratio appears outside the typical range for most health care interventions.

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