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
The use of nucleic acid amplification testing (NAT) technology for human immunodeficiency virus (HIV), hepatitis C virus (HCV) and hepatitis B virus (HBV) in blood donations was assessed. Single-donation NAT and minipool NAT of pools of between 16 and 24 whole blood donations were considered in addition to current battery testing. Current battery testing included the detection of antibodies to HIV and HCV (using third-generation immunoassays), HBV, and the HBsAg and the HIV p24 antigen.

Type of intervention
Screening.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised people with a mean age of 60 years who were receiving blood component units.

Setting
The setting was not explicitly stated. The economic study was carried out in the USA.

Dates to which data relate
The effectiveness data were derived from studies published between 1987 and 2002. The resource use data were derived from studies published between 1993 and 2001, supplemented by authors' assumptions. The price year was not reported.

Source of effectiveness data
The effectiveness data were derived from a review or synthesis of completed studies.

Modelling
A Markov model was used to model the clinical impact and associated costs of the possible changes to the screening protocols. A published model based on the natural history of transfusion-associated viral illness was used. This was updated with disease incidence data from 2001. Assumptions were made during the construction of the model. For instance, whole blood donation resulted in a mean of 1.5 component units transfused, including red blood cells, plasma, and platelets. A 100% infectivity of all units from infected donors was also assumed.

Outcomes assessed in the review
The following model input parameters were identified:
the incidence of HIV, HCV and HBV infections in repeat donors; and

the window period of the current testing regimen, minipool NAT and single-donation NAT.

The window period was defined as the time between infection and the ability of a particular test to detect the virus.

**Study designs and other criteria for inclusion in the review**

Estimates of incidence were based on repeat donor incidence data for 2001, as collected by the American Red Cross (Dodd et al. 2002, see 'Other Publications of Related Interest' for bibliographic details). Estimates of the window period for serological tests were derived from the model of Schreiber et al. (see 'Other Publications of Related Interest' for bibliographic details), while those for NAT were derived using data collected in the Retrovirus Epidemiology Donor Study (Fiebig et al. 2000, Busch et al. 2000, and Peddada et al. 2000, see 'Other Publications of Related Interest' for bibliographic details).

**Sources searched to identify primary studies**

Not reported.

**Criteria used to ensure the validity of primary studies**

Not reported.

**Methods used to judge relevance and validity, and for extracting data**

The methods used to judge the relevance and validity of the studies were not reported. HBV incidence was adjusted upward by a factor of 2.8 to account for transient expression of HBsAg in acute infections.

**Number of primary studies included**

Seven primary studies were used to identify the model input parameters.

**Methods of combining primary studies**

Not reported.

**Investigation of differences between primary studies**

Not reported.

**Results of the review**

The following model input parameters were identified in the paper:

- incidence of HIV in repeat donors, $1.55 \times 10^{-5}$;
- incidence of HCV in repeat donors, $1.89 \times 10^{-5}$;
- incidence of HBV in repeat donors, $3.02 \times 10^{-5}$.

The serology window period was 16 days for HIV, 70 days for HCV, and 45 days for HBV.

The minipool NAT window period was 11 days for HIV, 10 days for HCV, and 39 days for HBV.

The single-donation NAT window period was 7 days for HIV, 7 days for HCV, and 20 days for HBV.
Methods used to derive estimates of effectiveness
The authors estimated the incidence in all blood donors, and then adjusted the incidence upwards to include the 20% of donations that came from first-time donors. They assumed a two-fold greater incidence rate for all three viruses among first-time versus repeat donors. The authors also calculated the risks of viral infection per 100,000 red blood cells units transfused, based on the assumption of 100% infectivity of all units from infected donors.

Estimates of effectiveness and key assumptions
The incidence of HIV in all donors was 1.86 x10-5.
The incidence of HCV in all donors was 2.7 x10-5.
The incidence of HBV in all donors was 3.62 x 10-5.
The baseline risk of viral infection was (per 1,000,000) 0.82 for HIV, 4.3 for HCV and 4.5 for HBV.
The risk of viral infection after minipool NAT was (per 1,000,000) 0.56 for HIV, 0.62 for HCV and 3.9 for HBV.
The risk of viral infection after single-donation NAT was (per 1,000,000) 0.36 for HIV, 0.43 for HCV and 2.0 for HBV.
The authors assumed an additional mortality of 23% in the first year following transfusion.

Measure of benefits used in the economic analysis
The measure of health benefit used was the quality-adjusted life-years (QALYs). The evaluation of health states was taken from published studies. The authors reported that some of the quality of life adjustments were derived from patient surveys. The remaining values were determined by consensus of local clinicians and medical decision analysts after they had considered the published values. The health benefits were adjusted at a rate of 3% per annum.

Direct costs
The costs of processing donor blood and health care costs associated with subsequent infections with HIV, HBC and HCV were included in this study. The cost of testing included the lost revenue from discarded components and deferred donors because of false-positive test results. The unit costs of testing appear to have been estimated by the authors. The cost of minipool NAT was derived from actual expenses and charges at the two largest blood centre NAT programmes (American Red Cross and Blood Systems). The cost of single-donation NAT was estimated on the basis of projected manufacturer reagent pricing and 150% increased labour cost to perform single-donation NAT with semi-automated equipment. The unit costs and resource use associated with infection with one of the three viruses being screened were taken from published studies. The paper provided a partial breakdown of the unit costs and resource use data. No price year was reported. The future costs were discounted at a rate of 3% per annum.

Statistical analysis of costs
No statistical analysis of the costs was undertaken.

Indirect Costs
No indirect costs were included in this study.

Currency
US dollars ($).
Sensitivity analysis
A full sensitivity analysis was performed when the model was originally published. There were no details of how the ranges used in this analysis were derived. A comprehensive probabilistic sensitivity analysis was performed on age, each of the disease-specific mortality rates, and each of the disease-specific quality of life adjusters. These variables were simultaneously treated as normal distributions, each with a 20% coefficient of variation, and the model was run in Monte Carlo simulation mode. The discount rate was varied in the range of 0 to 5%.

Estimated benefits used in the economic analysis
A total of 62 QALYs were estimated to be gained following minipool NAT, compared with current practice (serological testing). Single-donation NAT resulted in a gain of 90 QALYs compared with current practice and 28 QALYS compared with minipool NAT.

Cost results
The total costs of the screening options were not reported in the paper.

Synthesis of costs and benefits
The incremental cost (millions) per QALY saved for each screening strategy was:

- $5.8 per QALY gained (range: 4.7 - 7.0) when adding minipool NAT testing for HIV and HCV;
- $8.4 per QALY gained (range: 7.6 - 9.2) when adding single-donation NAT testing for HIV and HCV;
- $7.6 per QALY gained (range: 5.7 - 10.6) when adding minipool NAT testing for HIV, HCV and HBV;
- $9.1 per QALY gained (range: 7.8 - 11.2) when adding single-donation NAT screening for HIV, HCV and HBV;
- $4.3 per QALY gained (range: 2.7 - 5.8) when adding minipool NAT testing for HIV and HCV, and discontinuing HIV p24 antigen;
- $7.3 per QALY gained (range: 6.2 - 8.4) when adding single-donation NAT testing for HIV and HCV, and discontinuing HIV p24 antigen;
- $6.1 per QALY gained (range: 3.8 - 9.5) when adding minipool NAT testing for HIV, HCV and HBV, and discontinuing HIV p24 antigen; and
- $7.3 per QALY gained (range: 5.5 - 9.9) when adding single-donation NAT testing for HIV, HCV and HBV, and discontinuing HIV p24 antigen and anti-HBc.

The sensitivity analysis showed that the model was sensitive to changes in the costs of screening and the infection probabilities. However, a sensitivity analysis over realistic ranges did not reduce the cost-effectiveness of the screening regimens to levels usually applied in other field of medical care (such as to the $50,000/QALY gained level).

Authors' conclusions
The introduction of nucleic acid amplification testing (NAT) can improve the safety of the US blood supply. However, its cost-effectiveness exceeds the cost-effectiveness ratios usually used as cut-off points in other medical interventions. The results suggested that the cost-effectiveness of NAT would be improved by lower NAT costs and/or eliminating certain redundant tests on blood donations.

CRD COMMENTARY - Selection of comparators
The comparator used in this study was chosen as it represented current practice in the study setting. You should consider how this relates to your setting before applying the results of this study.
Validity of estimate of measure of effectiveness

The clinical effectiveness data used in this study were derived from a model, the input parameters for which were taken from published studies. The identification of primary studies to provide information on the input parameters was not systematic. Details of the sources searched for relevant studies, criteria used to assess the primary studies, and methods used to combine the data from the studies were lacking. This limits the scope to assess and comment on the authors’ methods and thus the quality of the clinical effectiveness data used. In addition, the authors made several assumptions about the effectiveness. However, all model parameters and assumptions appear to have been varied in the sensitivity analysis, and this enhances the validity of the results.

Validity of estimate of measure of benefit

The estimation of benefits was modelled. The instrument used to derive the measure of health benefit (i.e. the Markov model) was appropriate. The measure of health benefits used in the economic analysis was the QALYs, which was appropriate for comparisons of the results of this study with those of different interventions. Since the benefits could be incurred during more than two years, future benefits were discounted using an appropriate discount rate. The discount rate was varied in the sensitivity analysis.

Validity of estimate of costs

The authors stated that they performed the cost analysis from a societal perspective, but no indirect costs were included. Therefore, it would appear that the economic perspective of the study was consistent with that of the health care system. In this respect, all the relevant costs appear to have been included in the study. The paper provided a partial breakdown of the unit costs and resource use data used but, whilst this assists the scope for generalising the results of this paper to other settings, a complete breakdown would have been more useful. No price year was reported, which will prevent any reflation exercises and, consequently, any comparisons with future studies. On a more positive note, a comprehensive sensitivity analysis of the unit costs, resource use data and other variables was undertaken to assess variability in the data used in the study. This strengthens the generalisability of the study findings. The costs were appropriately discounted to reflect the preference for current values.

Other issues

The authors did not compare their study with other similar studies. However, they did consider their findings in the cost-effectiveness context usually applied in the medical sector. The study was designed to be applicable across the USA, but the paper did not consider the scope to apply its results to other countries. Although the authors do not appear to have presented their results selectively, the paper was limited by incomplete information (especially the lack of total cost information). However, the authors' conclusions reflected the scope of the analysis.

The authors reported several further limitations. For example, the results were highly dependent on the predicted screening costs and the modelling of the window period would appear conservative. Thus, the cost-effectiveness of NAT may be poorer than reported in the present study.

Implications of the study

The authors did not make any specific recommendations for further research or changes to practice.

Source of funding

None stated.

Bibliographic details

Other publications of related interest


Fiebig E, Heldebrant C, Smith R, et al. HIV viremia preceding antibody (Ab) seroconversion (SC), detection by p24 antigen (Ag), minipool nucleic acid amplification test (Mp-NAT) and individual donations (ID-NAT). Transfusion 2000;40 Suppl:25S.


Indexing Status

Subject indexing assigned by NLM

MeSH

Blood Donors; Blood Transfusion /adverse effects; Cost-Benefit Analysis; HIV /genetics /isolation & purification; HIV Infections /transmission; Hepacivirus /genetics /isolation & purification; Hepatitis B /transmission; Hepatitis B virus /genetics /isolation & purification; Hepatitis C /transmission; Humans; RNA, Viral /blood; Reverse Transcriptase Polymerase Chain Reaction /economics

AccessionNumber

22003000893

Date bibliographic record published

31/08/2005

Date abstract record published

31/08/2005