Cost-effectiveness of transfusing virus-inactivated plasma instead of standard plasma

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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
Virus inactivated plasma compared to standard plasma in patients requiring blood transfusions.

Type of intervention
Secondary prevention.

Economic study type
Cost-utility analysis.

Study population
Patients who received Fresh Frozen Plasma (FFP) at a hospital clinic blood bank (Barcelona, Spain), were used to derive the probability distributions for age, sex and number of blood components transfused per recipient. Patients' ages ranged from 1-102 years and 55.5% were male.

Setting
Secondary care (hospital). The economic study was conducted in Barcelona, Spain.

Dates to which data relate
Data for probability distributions of age, sex and number of transfusions were collected between July 1996 and June 1997. Cost data for treating transfusion-related viral diseases were taken from published studies and were converted to a price year of 1997. The year to which plasma costs relate was not stated. Risk figures for transmitting viruses during transfusion related to 1996. Sex adjusted life expectancy data were taken from a population survey conducted in 1994.

Source of effectiveness data
Effectiveness and epidemiological data were derived from a review of the literature plus authors estimates.

Modelling
A Markov Model was used to represent the possible costs and outcomes of simulated patients. Transition probabilities were time dependent, and the solution method used was Monte Carlo simulation. The model was used to simulate the evolution of patients through a series of possible health states and outcomes, represented by a decision tree. A variety of data were used to populate the model. For each scenario represented in the model the mean and standard deviation of 10 simulations with 10^7 patients per simulation were used.

Outcomes assessed in the review
The review determined the following outcomes: Probability of virus-transmission per 10^6 blood units transfused for hepatitis B virus (HBV), hepatitis C virus (HCV), HIV; fatal reactions after blood-component transfusion; Hepatitis
virus complications; quality adjustments for health states; and relative risk of mortality. <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
Not stated.

Number of primary studies included
13 studies were included in the review.

Methods of combining primary studies
Not reported.

Investigation of differences between primary studies
Not reported.

Results of the review
The results of the review were as follows (Ranges tested in the sensitivity analysis are shown in parentheses):

Virus-transmission per 10^6 blood units transfused: HBV = 15.87 (range: 6.8 - 32.25), HCV = 4.95 (range: 3.47 - 35.71), HIV = 2.02 (range: 0.36 - 4.95).

Fatal reactions after blood-component transfusion per 10^6 blood units transfused: packed RBCs = 10 (range: 1 - 20), FFP = 6.5 (range: 1 - 10), platelets = 4 (range: 1 - 10).

Hepatitis virus complications: acute symptomatic hepatitis after HCV transmission = 40% (range 25% - 100%); after HBV transmission = 100%; fulminant hepatitis if acute hepatitis (80% mortality) = 0.2%; chronic hepatitis after acute HBV 5% (range: 1% - 25%); symptoms if chronic HBV infection = 15% (range: 1% - 50%); interferon treatment if chronic hepatitis = 50% (range: 10% - 100%).

Quality adjustments for health states varied from 0.25 (range: 0.1 - 0.7) for AIDS to 1 without complications.

Relative risk of mortality: AIDS (males and females) = x20; decompensated cirrhosis (males) = x3.14 (range: x1.04 - x9.42); and (females) x2.84 (range: x1.00 - x8.52).

These data formed the principal inputs to the model.

Methods used to derive estimates of effectiveness
Authors estimates, based on data in the literature.

Estimates of effectiveness and key assumptions
It was assumed that 5% of patients infected with HBV would develop chronic hepatitis after 6-months, and that it
would be symptomatic in 15% of cases. The model also assumed that 50% of patients with chronic hepatitis would receive interferon therapy, and hence would incur the costs associated with this. These data also supplemented the inputs to the model described above.

**Measure of benefits used in the economic analysis**
Quality Adjusted Life Years (QALYs) were used as the primary outcome in the economic analysis. Quality adjustments to life expectancy were based on common estimates found in the literature; AuBuchon (1997), AuBuchon (1993) and Wong (1995). No additional details regarding the source(s) and valuation of these utilities were given.

**Direct costs**
Costs and utilities were discounted at a rate of 5% per year (varied to 3% in sensitivity analysis). Costs and quantities were not reported separately. Complications costs included: acute symptomatic hepatitis, interferon treatment for chronic hepatitis, follow-up of chronic hepatitis, decompensated cirrhosis, pre-AIDS low CD4 cell counts, AIDS (per year). The costs of treating complications were derived from published sources. The costs of treating transfusion related viral diseases were taken from published studies and were converted to 1997 US dollars, using a 10% annual inflation rate. The year to which plasma costs related was not stated.

**Statistical analysis of costs**
No statistical analysis of costs was carried out.

**Indirect Costs**
Indirect costs were not considered.

**Currency**
US dollars ($).

**Sensitivity analysis**
The sensitivity of specific variables was analysed by calculating elasticities, that is the ratio of percentage change in cost-effectiveness to the percentage change in the relevant variables. Transmission rates, cost of virus-inactivation procedure, recipient's age and the rate of short-term mortality, were allowed to range from plus or minus 10% of the baseline value. The baseline probabilities, used in the model, were also varied according to the specified ranges (see review results) with several one-way sensitivity analyses being performed.

**Estimated benefits used in the economic analysis**
Baseline analysis showed that virus-inactivated plasma produced an average net benefit of 135.7 QALYs per million patients, this constituted a benefit of 1 hour 11 minutes per patient, or 9.8 minutes per plasma unit. This benefit was over the patient's lifetime.

**Cost results**
The increase in cost of virus-inactivated over standard plasma was estimated at $40, although sensitivity analysis varied this estimate between $30 and $50. Differences between groups for each component of cost were not reported. The gain in effectiveness from virus-inactivated compared to standard plasma was achieved at an incremental cost of $39.66 per unit of virus-inactivated plasma.

**Synthesis of costs and benefits**
Costs and benefits were combined to provide an estimate of the cost per QALY of alternative strategies. Incremental
costs and effects were calculated: transfusing virus-inactivated plasma instead of standard plasma produced an average net benefit of 135.7 QALY's per million patients, or 9.8 minutes per plasma unit. This benefit was achieved at a net incremental cost of $39.66 per unit. A cost-effectiveness ratio of $2,156,398 +/- $257,587 per QALY, for virus-inactivated compared to standard plasma was achieved.

The sensitivity analysis showed that the estimate of cost-effectiveness was very sensitive to the cost of virus-inactivation procedure - incremental cost per QALY gained increased by $54,410 per dollar invested in the procedure.

Cost-effectiveness estimates were also sensitive to recipient's age, and rate of short-term mortality. An increase in either of these parameters had a negative impact on the cost-effectiveness ratio.

The cost per QALY gained increased as virus transmission rates decreased; at very low transmission rates the cost-effectiveness increased for HIV, however for HCV and HBV the cost-effectiveness reached a plateau when transmission rates fell below 1:200,000 and 1:64,000 respectively.

Using 95% Confidence Intervals from the Retrovirus Epidemiology Donor Study, transmission rates for HIV, HBV and HCV were ranged from the lower to upper bounds, resulting in a ten fold increase in cost-effectiveness. When the cost of virus inactivation procedure was varied, the cost-effectiveness of plasma was found to be very sensitive to any changes, with the two parameters displaying a linear relationship. Cost-effectiveness was also sensitive to the patient's age and the rate of short term mortality due to underlying disease.

The quality of life after developing blood borne infection and the discount rate changes did not significantly change the estimates of the cost-effectiveness ratio. Two best case scenarios were also presented, in which relatively young patients received inactivated plasma for which transfusion can offer a cure.

Authors' conclusions
The authors concluded that, compared to other accepted medical procedures, virus inactivation of plasma produced little benefit at very high cost, and thus achieved a poor cost-effectiveness ratio.

CRD COMMENTARY - Selection of comparators
Standard plasma is the choice most commonly used in US hospitals for transfusion, therefore its choice, as a comparator, would seem valid.

Validity of estimate of measure of effectiveness
The estimates of effectiveness used in the model may have been derived from a non-systematic review of the literature with the possibility of selection bias being present. However, the authors did undertake extensive sensitivity analyses to account for potential variability in the data.

Validity of estimate of measure of benefit
QALYs were synthesised by the model, based on what appear to have been valid sources for the range of health states examined. Variability in the utility scores was examined in the sensitivity analyses over what appear to have been plausible ranges.

Validity of estimate of costs
The authors made the sources of all cost data explicit, and also stated the price year. Since the cost-effectiveness estimate largely depends on the cost of a unit of virus-inactivated plasma, more effort could have been spent on calculating an accurate cost for this. However, the results were subjected to a comprehensive sensitivity analysis.

Other issues
The authors compared their results with other interventions in discussing acceptable cost-utility thresholds. The population of patients used to derive probability distributions in this model was taken from a Hospital clinic blood bank in Spain, and the results of the cost-effectiveness analysis conducted using these data may not be easily generalisable to a UK setting. An interesting point raised by the authors is that socially accepted cost-effectiveness thresholds for interventions that limit transmission of infectious diseases, such as HBV, HCV and HIV, through blood transfusions appear to be much higher than other interventions.

**Implications of the study**
The authors did not include much discussion of the implications of the study, however they did conclude that virus-inactivated plasma would be unlikely to be rejected on economic grounds alone, and that emphasis could be placed on equally effective but less costly options.

**Source of funding**
None stated.

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**Other publications of related interest**


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