Cost-effectiveness of transfusion of platelet components prepared with pathogen inactivation treatment 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
The use of the Intercept Blood System (IBS) for pathogen inactivation treatment in single-donor apheresis platelets (AP) and random-donor pooled platelets concentrates (PC). This was compared with AP and PC platelet transfusions performed without the IBS, in specific patient populations.

Type of intervention
Primary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
Four reference patients were used to represent the patient groups that accounted for the majority (76%) of platelet use in the USA. They were a 10-year-old boy undergoing haematopoietic progenitor cell transplant (HPCT) for acute lymphocytic leukaemia, a 50-year-old man undergoing HPCT for non-Hodgkin's lymphoma, a 60-year-old man undergoing coronary artery bypass grafting and a 70-year-old woman undergoing hip arthroplasty.

Setting
The setting was secondary care. The economic study was carried out in the USA.

Dates to which data relate
The risk and outcome data used to populate the model were obtained from 18 published studies and Internet resources. The publication and Internet access dates for these resources ranged from 1992 to 2003. The price year was 2001.

Source of effectiveness data
The effectiveness data were derived from a review of completed studies and some authors' assumptions.

Modelling
A decision analytic model was used to assess the economic costs and clinical outcomes associated with the use of the IBS in platelet transfusions. The model relied on a published study (Lopez-Plaza et al. see Other Publications of Related Interest). The structure of the tree was depicted graphically in the paper.

Outcomes assessed in the review
The model used data from published studies to incorporate the risks of being infected (as a result of transfusion) with human immunodeficiency virus, hepatitis B or C, human T-cell lymphotropic virus (HTLV-1) or bacteria. The seven
disease outcomes of transfusion-related sequelae in the model were:

AIDS-related complex/acquired immune deficiency syndrome,
chronic hepatitis,
cirrhosis,
hepatocellular carcinoma,
fulminant hepatitis,
adult T-cell lymphoma/HTLV-1 associated myelopathy, and
death.

Study designs and other criteria for inclusion in the review
The review was not systematic. The authors did not state on what basis the studies were selected for incorporation into the model.

Sources searched to identify primary studies
The authors used existing published studies that were primarily indexed in MEDLINE. They also incorporated data on file at Baxter Healthcare Corporation (Chicago, IL) and Cerus Corporation (Concord, CA).

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

Methods used to judge relevance and validity, and for extracting data
Not reported.

Number of primary studies included
Twenty studies were used to establish the risk of acquiring transfusion-transmitted pathogens. The same studies were also used to provide estimates of the probabilities of developing the seven disease outcomes.

Six studies were used to estimate the annual mortality rates and quality-adjusted life-year (QALY) weights of the pre-existing medical conditions. Twelve studies were used to estimate annual mortality rates and QALY weights for transfusion-acquired sequelae.

Methods of combining primary studies
The estimates were used as inputs into the model. The method by which the value entered in the baseline analysis was created was not specified.

Investigation of differences between primary studies
Not reported.

Results of the review
The probability used as the baseline value of developing each of the disease outcomes (and the range from the literature) was:
1.00 (range not applicable) for AIDS-related complex/acquired immune deficiency syndrome;
0.85 (range: 0.69 - 0.88) for chronic hepatitis C;
0.10 (range: 0.02 - 0.20) for chronic hepatitis B;
0.20 (range: 0.05 - 0.35) for cirrhosis;
0.05 (range: 0.01 - 0.20) for hepatocellular carcinoma;
0.10 (range: 0.001 - 0.010) for fulminant hepatitis; and
0.04 (range: 0.02 - 0.06) for adult T-cell lymphoma/HTLV-1 associated myelopathy (ALT/HAM)

Methods used to derive estimates of effectiveness
The authors made a key assumption, which was used in the decision model.

Estimates of effectiveness and key assumptions
The IBS was assumed to be 100% effective in the prevention of pathogens.

Measure of benefits used in the economic analysis
The health benefit was measured in QALYs. The authors used utility values from the literature to value health states. Up to six sources were used to apply utility values to the underlying disease processes and eight sources were used in relation to transfusion-acquired diseases. The sources used to derive the utility weights were not described. A 3% annual discount rate was applied to the QALYs.

Direct costs
The cost/resource boundary of the study was not stated. The direct medical costs included were those of AP and PC, the IBS treatment and the annual treatment of transfusion-related sequelae. The unit costs and the quantities of resources used were not reported separately. Twelve sources of cost data were referenced, with publication and Internet access dates ranging from 1992 to 2003. These were used to form a range of costs for the baseline and sensitivity analyses. The authors also made some assumptions about resource consumption. The costs were discounted at a rate of 3% per annum, which was appropriate as long-term costs were evaluated. All the costs were updated to 2001 values using the health care component of the US Consumer Price Index.

Statistical analysis of costs
A statistical analysis of the costs was not undertaken.

Indirect Costs
The indirect costs were not considered.

Currency
US dollars ($).

Sensitivity analysis
One-way simple sensitivity analyses were conducted to explore the impact on the estimated cost-effectiveness ratios of variations in:
the transfusion-transmission risk,
the cost of treatment for transfusion-related sequelae,
the cost of IBS,
the probability of disease outcomes,
eliminating the need for gamma radiation,
the potential benefit of a reduction in the risk of transmission of emerging pathogens, and
the possibility of increased platelet use.

A probabilistic sensitivity analysis (Monte Carlo simulation) using 10,000 iterations was conducted on all the variables for which a range in values had been obtained from the literature. These variables were concerned with:

- the risk of acquiring transfusion-transmitted pathogens and their associated outcomes;
- the excess annual mortality rates and QALY weights attributable to the subsequent outcomes of transfusion-related sequelae; and
- the cost parameters for AP, PC, platelet inactivation and the treatment of transfusion-related sequelae.

The ranges of values used in the sensitivity analyses were derived from the review of the literature. The sensitivity analyses addressed variability in the data. They also explored the model in order to identify the most important contributory variables and uncertainties within the model.

Estimated benefits used in the economic analysis
The authors stated that the model estimated the incremental health benefit of using the IBS with AP and with PC, versus untreated AP and PC (i.e. no IBS). However the results were only reported in the synthesis with the cost.

Cost results
The model also estimated the incremental costs of using the IBS with AP and with PC, versus untreated AP and PC (i.e. no IBS). Again, these were only reported in the synthesis with the cost.

Synthesis of costs and benefits
The results of the analysis were reported as incremental cost-effectiveness ratios (ICERs), that is, the incremental cost per QALY gained in US$ for the year 2001.

In the base-case, across the four prototype patients, the incremental cost per QALY of using AP plus IBS versus untreated AP ranged from $1,308,833 to $4,451,650. The corresponding range for PC plus IBS, was from $457,586 to $1,816,060. When bacterial testing was also performed with AP plus IBS (base-case 2), the range changed to $4,759,401 to $22,968,066. In all three base-case scenarios the IBS was more cost-effective in the paediatric population than the adult populations.

The one-way sensitivity analysis identified three parameters that affected the results of the model. When the mortality rate due to bacterial contamination was increased from 2 deaths per million to 15 for AP and 62 for PC, the ICER decreased from $7,105,810 to $3,481,838. Also, when the IBS was assumed to increase the platelet yield reduction rate from 20 to 30%, the ICERs rose by approximately 30%. Conversely, decreasing the platelet yield reduction rate to 10% decreased the ICER by around 33%. Finally, the results of the model were altered when the benefits were included. Eliminating the need for gamma irradiation reduced the ICERs by 20 to 25% for the two immunosuppressed patients. Protection against emerging pathogens decreased the ICERs dramatically in all four patients. In the base-case, the ICER
ranged from $238,901 to $1,527,664 for AP plus IBS, and from $34,845 to $266,593 for PC plus IBS. When bacterial
testing was included, the ICER for AP plus IBS ranged from $234,807 to $1,811,903.

The probabilistic sensitivity analysis revealed that the results were sensitive to simultaneous changes in the multiple
parameters.

Authors’ conclusions
The cost of using the Intercept Blood System (IBS) was comparable to other accepted blood product safety systems.
IBS increases the safety of platelet transfusions and also offers protection against the threat of emerging pathogens.
This is achieved by preventing virus transmission and bacterial contamination, and it may make screening tests
superfluous in the future.

CRD COMMENTARY - Selection of comparators
Although no explicit justification was given for the comparator used, it would appear to represent current practice in
the authors’ setting. You should decide if the comparator represents current practice in your own setting.

Validity of estimate of measure of effectiveness
The authors did not claim to have undertaken a systematic review of the literature. Estimates of effectiveness from the
primary studies were combined to give a range of values. This range was then explored in the sensitivity analysis. The
authors did not report on the strengths and weaknesses of the original studies. They also did not adopt any weighting to
reflect differences in the sample size. The authors also made some assumptions that were explored in the sensitivity
analysis.

Validity of estimate of measure of benefit
The estimation of benefits was modelled. The instrument used to derive a measure of health benefit, a decision analytic
model, was appropriate. The use of QALYs makes it possible to capture the impact of the intervention on both the
quality and length of the patients’ life. In addition, QALYs represent a comparable benefit measure. However, the
estimated QALYs were not reported.

Validity of estimate of costs
The authors did not explicitly state their cost perspective. Insufficient detail was supplied to ascertain what costs were
included, as the authors simply stated that they included the costs of AP and PC, IBS treatment and transfusion-related
sequelae. The unit costs and the quantities of resources used were not presented separately. The indirect costs were not
considered and the authors stated that their inclusion would have favoured the study intervention. The price year was
reported, thus making reflation exercises in other settings possible. The costs and the quantities were treated
deterministically in the base-case, although a probabilistic analysis was carried out in the Monte Carlo simulation.

A sensitivity analysis of the prices was conducted. Discounting of the projected future costs was performed.

Other issues
The authors made appropriate comparisons of their findings with those from other studies. They noted that the cost per
QALY of IBS appeared high when compared with thresholds used in other medical fields. However, their findings were
comparable to ICERs reported in studies of accepted blood safety interventions. The issue of the generalisability of the
findings to other patient groups was not explicitly addressed. The authors do not appear to have presented their findings
selectively.

The results found that IBS was more cost-effective for paediatric acute lymphocytic leukaemia patients than for
orthopaedic, coronary artery bypass graft, or non-Hodgkin’s lymphoma patients. This reflected the favourable short-
term prognosis of the first two patients compared with high mortality in the first year for the coronary artery bypass.
graft and non-Hodgkin's lymphoma patients. In addition, the young age at transfusion increased the anticipated life expectancy of the paediatric acute lymphocytic leukaemia patients.

The authors reported that, as their intention was to produce conservative results, they did not include potential benefits such as the increased shelf-life of the platelet products, or the indirect cost benefits due to the avoidance of premature death or litigation.

**Implications of the study**
The authors suggested that blood banks, hospitals and other institutions administering platelet transfusions could increase the safety of transfusions and "insure" against the threat of emerging pathogens by using IBS.

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**Other publications of related interest**

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