A health economic analysis of autologous transfusion
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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
The use of autologous versus allogeneic blood transfusion, carried out postoperatively after elective surgery.

Type of intervention
Treatment.

Economic study type
Cost-utility analysis.

Study population
The study population consisted of a hypothetical cohort, of composite gender and race, comprising 65-year-old patients undergoing elective total hip replacement surgery.

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

Dates to which data relate
The effectiveness rates were adopted from studies published between 1979 and 2001. The costs were derived from literature published between 1995 and 2001. The costs were adjusted to 2000 prices.

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

Modelling
A Markov simulation model was used to compare the two types of transfusion in terms of the costs and complications. The model included possible health states following the transfusion. For example, transfusion reaction, postoperative bacterial infection, HIV infection, acquired immune deficiency syndrome (AIDS), and hepatitis B, C and non-A non-B non-C (fulminant, acute and chronic), potentially followed by cirrhosis and hepatocellular carcinoma. The time horizon of the model was the remainder of the patients' life. The model was a modification of a model published elsewhere (see Other Publications of Related Interest).

Outcomes assessed in the review
The outcomes assessed in the review included:

the utilities of patients in the long-term health states of the Markov model, expressed as quality-adjusted life-years (QALYs);
the probabilities of transfusion and units of blood needed (for initial and additional transfusions) by patients undergoing total hip replacement;

the probabilities of transfusion reactions;

the risks of postoperative infections without or after transfusion (e.g. HIV, hepatitis B, C, non-A non-B non-C, and bacterial infections);

the transition probabilities between the health states of the model;

the excess mortality rates at these health states; and

age-specific mortality rates for patients of composite gender and race.

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
Approximately 15 primary studies were included in the review.

Methods of combining primary studies
The results of the primary studies were combined in a narrative. In some cases, when the results of the primary studies differed, an average value was estimated and used in the model.

Investigation of differences between primary studies
Not reported.

Results of the review
The QALYs of the long-term health states were 0.77 for symptomatic HIV infection, 0.79 for AIDS, 0.94 for chronic hepatitis, 0.92 for compensated cirrhosis, and 0.49 for hepatocellular carcinoma.

The probability of transfusion in elective hip replacement was 0.89, with an average of 2.8 units of allogeneic blood transfused and 2.4 units of autologous blood transfused. The probability of additional allogeneic transfusion to autologous patients was 0.36, with 1.1 units of blood required.

The probabilities of minor or major allogeneic transfusion reaction were 0.0039 (minor) and 0.000113 (major), respectively. The corresponding probabilities for autologous transfusion reaction were 0.0013 (minor) and 0 (major), respectively.
The risk per unit of screened blood was $1.9 \times 10^{-6}$ for HIV infection, $1.6 \times 10^{-5}$ for hepatitis B, $9.7 \times 10^{-6}$ for hepatitis C and $9.6 \times 10^{-7}$ for hepatitis non-A non-B non-C.

The probability of hospitalisation was 0.033 for post-transfusion hepatitis B and 0.025 for post-transfusion hepatitis C.

The probability of fulminant hepatitis was 0.047 if hospitalised for hepatitis B and 0.20 if hospitalised for hepatitis C.

The probability of chronic hepatitis was 0.075 after acute hepatitis B and 0.85 after acute hepatitis C.

The annual rate of cirrhosis was 0.054 after chronic hepatitis B and 0.011 after chronic hepatitis C.

The annual rate of hepatocellular carcinoma was 0.0033 after chronic hepatitis B and 0.0009 after chronic hepatitis C.

The annual probability of developing AIDS after HIV infection was 0.006 (after a 3-year period of zero risk).

The probability of postoperative bacterial infection without transfusion was 0.037. The relative risk of postoperative bacterial infection after allogeneic transfusion was 1.85.

Mortality from elective hip arthroplasty was 0.005, from fulminant hepatitis 0.75, and from postoperative infection 0.26.

The excess annual mortality rate due to chronic hepatitis was 0.028, cirrhosis 0.117, hepatocellular carcinoma 0.56 and AIDS 0.285.

Age-specific mortality rates and utilities following infection were not presented.

**Methods used to derive estimates of effectiveness**

The author made some assumptions about the estimates of effectiveness.

**Estimates of effectiveness and key assumptions**

The author made key assumptions about some of the input parameters of the model. The author assumed the following:

- patients receiving autologous blood after total hip replacement donated 3 units preoperatively;
- if chronic hepatitis developed, it would occur during the first year after acute hepatitis;
- the excess mortality rate for hepatitis C was the same as that for hepatitis B;
- all deaths from fulminant hepatitis occurred among patients hospitalised for hepatitis B or C.

Finally, the mortality from postoperative infection was calculated, based on the mortalities of specific postoperative infections (i.e. pneumonia, bacteraemia, deep wound infection). It was assumed that the relative proportions of postoperative specific infections in the model were the same as those reported for patients in four New Jersey hospitals.

**Measure of benefits used in the economic analysis**

The outcome measure used in the economic analysis was expressed as QALYs. It was obtained from the decision model. The future benefits were discounted at an annual rate of 3%.

**Direct costs**

The perspective of the study was not stated. However, it seems to have been consistent with that of a third-party payer. The costs were for transfusion (autologous and allogeneic), transfusion reaction and bacterial infection, acute and chronic hepatitis (treatment and hospitalisation), care for cirrhosis and hepatocellular carcinoma, and AIDS treatment.
The quantities and the unit costs were not reported separately. The costs were derived from data reported in the published literature or in hospital administrative databases. The total costs were derived using modelling. Discounting was carried out at an annual rate of 3%. This was appropriate since the study estimated the long-term costs resulting from transfusion. All the costs were adjusted to 2000 prices.

**Statistical analysis of costs**
No statistical analysis of the costs was undertaken. The costs were treated deterministically.

**Indirect Costs**
The indirect costs were not included in the analysis.

**Currency**
US dollars ($).

**Sensitivity analysis**
A sensitivity analysis was carried out to investigate whether the variability in published data had any impact on the results of the economic analysis. The parameters examined included:

- the cost difference between autologous and allogeneic blood,
- the relative risk of infection with allogeneic transfusion,
- the mortality and costs of infection,
- the risk of death and morbidity of autologous transfusion,
- the age of the patients, and the discount rate.

Moreover, the author examined the cost-effectiveness of autologous transfusion in other types of surgery. For example, total hip arthroplasty, coronary artery bypass graft, total abdominal hysterectomy, and transurethral resection of the prostate, which differed from elective hip replacement in terms of the units of blood donated preoperatively and the percentage of units transfused (autologous and additional allogeneic blood needed). One-way, two-way and threshold sensitivity analyses were performed. The threshold analysis was used to demonstrate cases in which the incremental cost-effectiveness ratio (ICER) reached $50,000/QALY, a value below which the intervention was deemed to be cost-effective. The range of values used in the other sensitivity analyses was based on author's assumptions and values reported in the literature.

**Estimated benefits used in the economic analysis**
The total benefits of each intervention were not presented separately. Only the incremental benefits were shown. Autologous transfusion resulted in 0.0523 additional QALYs per patient over allogeneic transfusion. This value had been discounted at 3% and accounted for the lifetime of the patient.

**Cost results**
The average total costs per patient were $1,395 for allogeneic transfusion and $1,539 for autologous transfusion. These costs had been discounted at 3% and referred to the lifetime of patient. Autologous transfusion incurred an additional (incremental) cost of $144 per patient.

**Synthesis of costs and benefits**
An ICER was calculated by combining the estimated costs and benefits of the two interventions. The ICER was...
$2,750/QALY. Thus, autologous transfusion incurred an additional cost of $2,750 per additional QALY gained.

The sensitivity analysis showed that the ICER was sensitive to the cost-difference between autologous (more expensive) and allogeneic blood. By ranging this parameter from $13 to $652 per unit of blood (base-case $66), the autologous transfusion either dominated ($13/unit) or exceeded $50,000/QALY ($652/unit), respectively.

The ICER was also highly sensitive to the relative risk of infection with allogeneic transfusion. If the relative risk was 1.0, then the ICER would be $2,545,000/QALY.

The threshold analysis showed that if the relative risk exceeded 1.10, then the ICER would be less than $50,000/QALY. If the ratio exceeded 2.39, then autologous transfusion dominated. In addition, autologous transfusion was cost-effective (ICER less than $50,000/QALY) if the mortality of infection exceeded 0.012, even if the additional cost of infection was 0. If the cost of infection exceeded $19,600, then autologous transfusion was the dominant strategy.

The results of a two-way sensitivity analysis using combinations of relative risk and cost of infection were presented graphically.

Concerning the risks of autologous transfusion, if the risk of death or morbidity exceeded 0.004 or 0.049 QALYs (18 quality-adjusted days), respectively, then the ICER would be higher than $50,000/QALY. If one of these parameters exceeded 0.0042 (death) or 0.052 (morbidity) QALYs, respectively, then autologous transfusion would be dominated by allogeneic transfusion.

The cost-effectiveness of autologous transfusion was not significantly affected by the patient's age (range: 35 - 85 years) or the discount rate (range: 0 - 10%).

The results of the analysis were found to be similar for the other surgical procedures considered, for which the percentage of autologous units transfused was relatively high (see 'Sensitivity Analysis' section). However, transurethral resection of the prostate TURP, for which the rate of use of donated autologous units was only 4%, showed an ICER for autologous transfusion exceeding $50,000/QALY.

The author concluded that postoperative bacterial infection (in terms of relative risks and costs) would be by far the most significant determinant of the cost-effectiveness of autologous transfusion.

**Authors' conclusions**

Autologous transfusion has a cost-effectiveness that compares favourably to well-accepted health interventions, if there is only a modest increase in the risk of bacterial infection following allogeneic transfusion.

**CRD COMMENTARY - Selection of comparators**

Although the comparators used were not explicitly justified, it was apparent that both interventions represented alternative methods of current practice in the USA. Allogeneic transfusion seems to have been the routine practice initially. However, it was eventually replaced by autologous transfusion, where applicable, following strong concerns about the risks of infection after allogeneic transfusion.

**Validity of estimate of measure of effectiveness**

The author did not state that a systematic review of the literature had been undertaken. The effectiveness estimates were combined using narrative methods. The author described, in detail, the methods used to derive the estimates of effectiveness. Potential differences between the primary studies were not investigated. However, the range of values derived from the review was explored in a sensitivity analysis. The author made some key assumptions that were also tested in the sensitivity analysis.

**Validity of estimate of measure of benefit**

The estimation of benefits was modelled using a Markov model. This model was appropriate since it included all
potential health states following blood transfusion. It also enabled the costs and benefits to be calculated over the lifetime of the patients, according to the study objective. The use of QALYs appears to have been appropriate since they are comparable with the benefits of other health care interventions. However, only incremental QALYs were reported.

**Validity of estimate of costs**
The perspective of the study was not stated, but it seems to have been consistent with that of a third-party payer. All the costs relevant to this perspective appear to have been included in the analysis. The costs and the quantities were not reported separately. Discounting was carried out, which was appropriate, as the costs were incurred over the lifetime of the patients. The price year was reported, thus facilitating reflation exercises in other settings. The costs were not treated stochastically in the base-case, although a sensitivity analysis of the costs was conducted for specific cost components (e.g. cost-difference between autologous and allogeneic blood, and the cost of postoperative bacterial infection).

**Other issues**
The author made appropriate comparisons of his findings with those from other studies. The issue of the generalisability of the results to other settings was not addressed. The author reported two factors not considered in the analysis, which might further increase the cost-effectiveness of autologous transfusion. One related to allogeneic transfusion-associated viral illnesses currently unknown, such as Creutzfeldt-Jacobs disease. The other was the "peace of mind" of patients receiving autologous blood, associated with the feeling that this procedure was "safe" in terms of possible virus infections. The author appears to have presented his results in full, and his conclusions reflected the scope of the analysis.

**Implications of the study**
Based on the study conclusions, it can be inferred that postoperative autologous transfusion could replace allogeneic transfusion, where applicable, in surgical procedures for which the percentage of donated blood transfused is relatively high. According to the author, the issue of costs and relative risk of postoperative bacterial infection was crucial to the cost-effectiveness of autologous blood transfusion, and by the time of publication this issue still remained unresolved. The author suggested that his analysis should be used as a framework for evaluating novel treatments designed to spare allogeneic blood transfusion (e.g. haematopoietic growth factors or blood substitutes).

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**Bibliographic details**

**Other publications of related interest**

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