Economic analysis of erythropoietin use in orthopaedic surgery
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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 erythropoietin (EPO) in orthopaedic surgery.

Type of intervention
Primary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
Patients undergoing orthopaedic surgery.

Setting
Hospital. The study was carried out at Ottawa Civic Hospital, Ottawa, Canada.

Dates to which data relate
Effectiveness data were derived from studies published between 1987 and 1997. Resource use and cost data were derived from studies published between 1988 and 1998. The price year was 1996.

Source of effectiveness data
Effectiveness data were based on meta-analyses from a systematic literature review and additional reviews of the literature.

Modelling
A decision analytic model was used to determine the lifetime costs and effects of the various preventive strategies.

Outcomes assessed in the review
The review assessed the quantity of transfusions received, risks of transfusion-related illness, and life expectancy.

Study designs and other criteria for inclusion in the review
Data on the quantity of transfusions received were derived from a meta-analysis based on a systematic review of published randomised trials. Data on the risks of transfusion-related illness were derived from a systematic review of the literature. Data on life expectancy with disease were obtained from a further detailed literature review.
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
Individual data and summary statistics from individual studies.

Number of primary studies included
At least 27 studies were included.

Methods of combining primary studies
Meta-analysis in some cases, narrative in others.

Investigation of differences between primary studies
Not stated.

Results of the review
The use of EPO was found to reduce exposure to allogeneic blood with odds ratios of 0.38 (95% CI: 0.24 - 0.63) for EPO alone and 0.42 (95% CI: 0.28 - 0.62) for EPO to augment PAD.

EPO alone reduced the mean number of units received by 57.5% (from 1.27 to 0.54 units per patient). EPO to augment PAD reduced the mean number of units received by 25.7% (from 0.35 to 0.26 units per patient).

For HIV, hepatitis B and hepatitis C, the base case risks per unit of allogeneic blood transfused were 2/1000000, 16/1000000 and 10/1000000. The risks of haemolytic transfusion reactions associated with all transfusions were 52.3/1000000 for a non-fatal reaction and 1.67/1000000 for a fatal reaction. These risks were assumed to be the same for both allogeneic and autologous blood.

The risk of a febrile reaction was estimated to be 1/100 units. For patients who did not contract any transfusion-related infections, the discounted life expectancy was estimated to be 13.04 years. The estimate of the discounted life expectancies for Canadian patients with HIV was 8.47 years, for hepatitis B was 12.97 years and for hepatitis C was 12.96 years.

These values were used as the principal input parameters to the model.

Measure of benefits used in the economic analysis
The measure of benefit was the number of life-years gained. Outcomes were discounted at an annual rate of 5%.

Direct costs
Direct costs were discounted at an annual rate of 5%. Quantities and costs were not reported separately. Direct costs included the costs of EPO, the costs of allogeneic and autologous blood collection and delivery, the costs associated with transfusion-related illnesses (hepatitis B and C, HIV, haemolytic reactions and febrile reactions). The quantity/cost boundary adopted was that of the health service. The estimation of quantities and costs was based on actual data. The list price of EPO was obtained from the pharmacy department of the Ottawa Civic Hospital. Other cost estimates were derived from published studies. The price year was 1996.
Statistical analysis of costs
Not reported.

Indirect Costs
Not included.

Currency
Canadian dollars (Can$).

Sensitivity analysis
The sensitivity analysis focused on assessing the cost-effectiveness of EPO under more favourable scenarios by changing the rates of transfusion in the control group, the risks of transfusion-related illnesses, and the costs, quality of life and life expectancy of transfusion-related illnesses. Analyses also explored the effects of secondary infection of partners by patients who developed transfusion-related illnesses and the cost-effectiveness of the use of EPO in a younger patient population. Threshold analysis was conducted to identify the value for various parameters required for the cost per life year gained from EPO to be lower than Can$100,000.

Estimated benefits used in the economic analysis
EPO alone increased life expectancy compared to no intervention by 0.000024 life years, while EPO to augment PAD increased life expectancy by 0.0000006 life years compared to PAD alone.

Cost results
EPO alone cost Can$1,857 per patient compared to Can$269 for no intervention and EPO to augment PAD cost Can$2,904 per patient compared to Can$968 for PAD alone.

Synthesis of costs and benefits
The incremental cost per life year gained for EPO compared to no intervention was Can$66 million. For EPO to augment PAD, the incremental cost per life year gained was Can$329 million. Sensitivity analysis did not reveal any circumstances in which the cost-effectiveness ratios reached a level generally considered attractive.

Authors’ conclusions
On the basis of cost-effectiveness, the use of EPO to reduce peri-operative allogeneic transfusions in orthopaedic surgery did not meet conventionally acceptable criteria.

CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparators was clear. You, as a user of this database, should verify whether these health technologies are relevant to your setting.

Validity of estimate of measure of benefit
A relevant measure of benefits was used. Effectiveness estimates were derived from systematic reviews of the literature and were pooled using meta-analytic techniques. The authors identified several caveats in the literature. First, the optimal dose of EPO is unknown (although the authors conducted sensitivity analysis in determining the optimal dosage not to be feasible). Second, it was unclear what impact the use of EPO by a small proportion of potential transfusion recipients would have on the total blood supply. Third, it is impossible to predict whether unknown infections will be transmitted by allogeneic blood. Fourth, peri-operative allogeneic transfusions may increase the frequency of post-
operative bacterial infection. This could improve the cost-effectiveness of EPO. The authors did not consider the potential effect on patients' anxiety about the possibility of receiving allogeneic blood.

**Validity of estimate of costs**
Only direct costs falling to the health service were considered. The costs of EPO administration, patient education and patient travel were excluded. Indirect costs such as those related to lost productivity, although potentially relevant, were not included. Sensitivity analyses were, however, performed to take into account the reasonable costs associated with HIV and hepatitis. Some cost estimates were derived from local sources and are therefore unlikely to be generalisable to other settings.

**Other issues**
The analysis was conducted in the context of the Canadian health care system and was limited to orthopaedic surgery. No comparisons with other relevant studies were made although the generalisability of the results to other settings and countries was discussed. The authors do not appear to have presented their results selectively. The study examined patients undergoing orthopaedic surgery and this was reflected in the authors' conclusions.

**Implications of the study**
Larger randomised trials are needed which take into account the potential effect of peri-operative allogeneic transfusions on the frequency of post-operative bacterial infection. The high cost-effectiveness ratios currently derived do not support the intervention of EPO in this patient population.

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**Other publications of related interest**


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