Cost-effectiveness of recombinant human erythropoietin for reducing red blood cells transfusions in critically ill patients

MacLaren R, Sullivan P W

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 recombinant human erythropoietin (rHuEPO) for reducing red blood cell (RBC) transfusions in critically ill patients was evaluated.

Type of intervention
Primary prevention.

Economic study type
Cost-utility analysis.

Study population
The target population comprised critically ill adult patients (aged 18 years or older) who had already been in the ICU for 2 or more days and were expected to have an ICU stay of at least 3 days.

Setting
The setting was 'other' (an ICU). The economic study was carried out in the USA.

Dates to which data relate
The effectiveness data were gathered between 1997 and 2002. Two multi-centre studies were the main source of clinical data (Corwin et al. 1999 and 2002, see 'Other Publications of Related Interest' below for bibliographic details). The resource use data were also gathered between 1997 and 2002. The price year was 2002.

Source of effectiveness data
The effectiveness data were derived from a review of medical literature.

Modelling
Two decision trees were created to reflect differences in the methodology of the two main clinical studies used for the analysis. The purpose of the models was to compare the clinical and economic effects of patients receiving or not receiving rHuEPO, including the associated adverse effects of rHuEPO and RBC transfusions. The authors used TreeAge and Excel software.

Outcomes assessed in the review
The main outcomes estimated from the review of the literature were:

the deferral rate for allogeneic RBC transfusions,
the rHuEPO efficacy,

the reduction in allogeneic blood use, and

adverse effects of rHuEPO and RBC transfusions.

**Study designs and other criteria for inclusion in the review**
The chosen studies were included for reasons of sample size and methodological quality.

**Sources searched to identify primary studies**
The search strategy had been published elsewhere (MacLaren et al. 2004, see 'Other Publications of Related Interest' below for bibliographic details). No details were provided in this paper.

**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 6 studies were included in the review.

**Methods of combining primary studies**
Not stated. It appears that the two main clinical trials have been evaluated independently.

**Investigation of differences between primary studies**
Not stated.

**Results of the review**
The only clinically relevant benefit of using rHuEPO that was demonstrated in both studies was a reduction in transfusion requirements.

In the rHuEPO group, 45 to 50.5% of the patients required between 4.61 and 4.85 RBC units per patient.

In the no rHuEPO group, 55 to 60.4% of the patients required between 6.93 and 4.98 RBC units per patient.

These data formed the principal effectiveness and outcome parameters used in the analysis.

**Measure of benefits used in the economic analysis**
The measure of benefits used was the quality-adjusted life-years (QALYs). The EQ-5D tariffs (utility) for the ICU population were derived from published literature. The benefits were discounted at a rate of 3%.

**Direct costs**
The direct costs reported were those of the health service. The key resource use categories included were the average wholesale price for rHuEPO, administration costs for both rHuEPO and RBC units, and the costs of treating adverse...
events (e.g. deep venous thrombosis, thrombocytopenia and adverse events related to allogeneic RBC transfusions). Resource use was not reported separately from the costs. The unit costs were derived from published literature. Discounting was carried out at a rate of 3%. The price year was 2002.

**Statistical analysis of costs**
The costs were treated stochastically. The methods used for the statistical analysis of the costs were not reported in this paper.

**Indirect Costs**
Only the indirect costs of blood donor time appear to have been included in the analysis. Resource use was not reported separately from the costs. Discounting was carried out at a rate of 3%. The price year was 2002.

**Currency**
US dollars ($).

**Sensitivity analysis**
A probabilistic sensitivity analysis was performed using second-order Monte Carlo simulation. A series of univariate sensitivity analysis were also conducted for all input parameters, varying each of them by +/- 15% from the base-case value. A threshold analysis, in which the attributable risk of nosocomial infection was varied, was also conducted.

**Estimated benefits used in the economic analysis**
The mean number of discounted QALYs per average patient in the rHuEPO group was 10.49 in study 1 and 15.03 in study 2. The corresponding values in the no rHuEPO group were 10.43 (study 1) and 15.00 (study 2), respectively. The resulting QALY difference was 0.0563 in study 1 and 0.0305 in study 2, in favour of rHuEPO.

These values were based on a life-time horizon.

**Cost results**
The mean discounted costs per average patient in the rHuEPO group were $3,846 (study 1) and $3,034 (study 2). The corresponding values in the no rHuEPO group were $1,928 (study 1) and $1,595 (study 2), respectively. The resulting incremental costs of rHuEPO compared with doing nothing were $1,918 for study 1 and $1,439 for study 2.

The authors also reported the incremental costs per allogeneic RBC unit avoided, which were $827 (study 1) and $11,072 (study 2). These values were based on a lifetime horizon.

**Synthesis of costs and benefits**
Incremental cost-effectiveness ratios (ICERs) were estimated.

The ICERs expressed the incremental costs of using rHuEPO per QALY gained compared with the do-nothing option.

From a societal perspective, the base-case scenario showed an ICER of $34,088 per QALY gained for study 1 and $47,149 per QALY gained for study 2.

The model was most sensitive to the attributable risk of nosocomial bacterial infections per RBC unit, but univariate sensitivity on the rest of parameters showed little impact on the results.

**Authors’ conclusions**
The probability of recombinant human erythropoietin (rHuEPO) being cost-effective was 0.52 at a threshold of $50,000 per quality-adjusted life-year (QALY). The use of rHuEPO for reducing red blood cell (RBC) transfusions in heterogeneous intensive care unit (ICU) patients would appear to be cost-effective, assuming that RBC transfusions increase the risk of nosocomial bacterial infections.

**CRD COMMENTARY - Selection of comparators**
A do-nothing option was used as the comparator, which seems appropriate for this type of analysis. You should decide whether this could be a valid comparator in your own setting.

**Validity of estimate of measure of effectiveness**
The effectiveness evidence was mainly derived from two randomised controlled trials. A more detailed explanation of the patient clinical characteristics and the comparability of the intervention and control groups would have been helpful. Although the ad hoc selection of studies to populate models is common practice, a more systematic approach is desirable to ensure that the best available evidence is used.

**Validity of estimate of measure of benefit**
A generic outcome measure was used for the analysis. The authors appropriately adjusted the mortality and quality of life of the general population, using national statistic lifetables, by the additional mortality rate and disutility associated with being admitted to an ICU unit.

**Validity of estimate of costs**
The authors explicitly identified the perspective adopted in the analysis. Whilst all relevant direct costs appear to have been included, it was not clear that all productivity losses were incorporated. In fact, it would appear that only the costs of blood donor time were included as indirect costs; the authors did not report a justification for this. Resource use was not reported separately from the costs. Discounting was appropriately carried out. The price year was reported, which will aid any future relation exercises.

**Other issues**
It was unclear whether the authors created two independent models with a different structure to reflect methodological differences of the two clinical studies, or if two alternative scenarios were run for each study using the same decision analytical model. The authors appropriately discussed the main limitations of their study and they compared their results in the context of the published literature.

**Implications of the study**
The authors recommended that further studies should focus on clinical outcomes other than RBC transfusion independence, a sub-group analysis of patients most at risk of developing anaemia in ICU, and the use of rHuEPO while incorporating a restrictive transfusion protocol. The authors made no explicit recommendation for changes in policy or implementation.

**Source of funding**
None stated.

**Bibliographic details**
Other publications of related interest


Indexing Status
Subject indexing assigned by NLM

MeSH
Adult; Anemia /economics /prevention & control /therapy; Cohort Studies; Cost-Benefit Analysis; Critical Care /economics /methods; Decision Support Techniques; Erythrocyte Transfusion /economics /utilization; Erythropoietin /adverse effects /economics /therapeutic use; Female; Health Care Costs; Humans; Intensive Care Units /economics; Male; Middle Aged; Outcome and Process Assessment (Health Care) /economics; Quality-Adjusted Life Years; Recombinant Proteins

AccessionNumber
22005007705

Date bibliographic record published
30/09/2006

Date abstract record published
30/09/2006