An economic evaluation of erythropoiesis-stimulating agents in CKD
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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.

CRD summary
The study assessed the cost-effectiveness of treating non-dialysis and dialysis patients with chronic kidney disease with erythropoiesis-stimulating agents (ESAs) to a low, intermediate or high haemoglobin level target. The authors concluded that targeting ESA treatment to high haemoglobin levels was not associated with overall clinical benefit and resulted in considerable additional costs. The study methodology was good quality. Methods and results were reported in detail. Given the scope of the study, the authors’ conclusions appear appropriate.

Type of economic evaluation
Cost-utility analysis

Study objective
The objective of the study was to assess the cost-effectiveness of treating non-dialysis and dialysis patients with chronic kidney disease with erythropoiesis-stimulating agents (ESAs) to achieve a low, intermediate or high haemoglobin level target.

Interventions
The study compared four interventions for non-dialysis and dialysis patients with chronic kidney disease: management of anaemia without ESAs; use of ESAs to attain a low haemoglobin level target (9 to 10.9g/dL); use of ESAs to attain an intermediate haemoglobin level target (11 to 12g/dL); and use of ESA to attain a high haemoglobin level target (>12g/dL).

Location/setting
Canada/Outpatient secondary care.

Methods
Analytical approach:
A decision Markov model was used to model the costs and clinical outcomes of the interventions. The time horizon was the lifetime of the patient. The authors reported that a healthcare payer perspective was adopted.

Effectiveness data:
The authors reported that clinical and effectiveness data were derived from several sources: systematic reviews and meta-analyses; previously published studies; and two Canadian cohort studies following dialysis and non-dialysis patients. The main parameter used in the model was the estimate of the effectiveness of managing patients with and without ESAs to achieve low, intermediate or high haemoglobin level targets. These data were derived from a meta-analysis by Tonelli et al. (see Other Publications of Related Interest) that was updated to include the TREAT trial (Trial to Reduce Cardiovascular Events with Aranesp Therapy, Pfeffer et al. 2009).

Monetary benefit and utility valuations:
Utility estimates were derived from previously published studies.

Measure of benefit:
Quality-adjusted life-years (QALYs) gained. Future benefits were discounted using an annual rate of 5%.

Cost data:
Direct costs included epoetin treatment, red blood cell transfusion, treatment of non-dialysis dependent chronic kidney
disease patients, haemodialysis and transplantation. Costs were derived from previously published studies. All costs were reported in Canadian dollars ($) and updated to 2006 prices using the consumer price index for healthcare goods in Canada. Future costs were discounted using an annual rate of 5%.

Analysis of uncertainty:
Scenario analyses were performed by varying utility estimates, risks of starting dialysis, costs and the impact that changes in haemoglobin had on quality of life. A Monte Carlo simulation was conducted to assess overall parameter uncertainty by fitting all model parameters with probability distributions.

Results
For dialysis-dependent patients the average QALYs gained ranged from 3.85 for no ESA to 4.48 with use of ESAs to attain a low haemoglobin level target. Mean costs ranged from $390,000 for no ESA to $461,000 with use of ESAs to attain a high haemoglobin level target.

For non-dialysis-dependent patients the average QALYs gained ranged from 2.92 for no ESA to 3.57 with use of ESAs to attain a low haemoglobin level target. Mean costs ranged from $245,000 for no ESA to $347,000 with use of ESAs to attain a high haemoglobin level target.

Costs and benefits were combined using an incremental cost-utility ratio (additional cost per QALY gained). When use of ESAs to attain a low haemoglobin level target was compared with no ESA, the incremental cost per QALY gained was $147,980 for non-dialysis dependent patients and $96,270 for dialysis dependent patients. Use of ESAs to attain a high haemoglobin level target was dominated by use of ESAs to attain a low haemoglobin level target (more costly and less effective). Use of ESAs to attain an intermediate haemoglobin level target was found to be extended dominated (less effective and less cost-effective than another option).

The scenario analyses showed that the results were robust to variations in all variables explored. The Monte Carlo simulation results showed that in 79% of simulations, the high-haemoglobin target strategy had worse clinical outcomes and higher costs than the low-haemoglobin strategy.

Authors' conclusions
The authors concluded that targeting ESA treatment to high haemoglobin levels was not associated with overall clinical benefit and resulted in considerable additional costs.

CRD commentary
Interventions:
The interventions under study were reported adequately. The rationale for selection of comparators was clear. The ESA strategies were feasible alternatives for treating anaemic non dialysis and dialysis patients and a strategy of no ESA was included.

Effectiveness/benefits:
Clinical and effectiveness data were derived from a large number of different published studies and references for all sources were provided. The main effectiveness measure for the model was derived from a previously published meta-analysis which was updated by the authors. As a result, it was likely that all relevant published evidence was considered when establishing the effectiveness of the interventions under study with estimates that were likely to be internally valid. QALYs were an appropriate benefit measure; they not only capture the impact of the disease on patients' health but also enable comparisons with the benefits of other health care interventions. The derivation of utility values used and their sources were reported adequately.

Costs:
The perspective adopted in the economic analysis was explicitly reported to be that of a publicly funded healthcare system. It appeared that all relevant cost categories for this perspective were included in the analysis. The sources from which unit costs were derived were adequately reported and were based on the Canadian setting. The authors explicitly reported the price year, time horizon, discount rate used and currency details.

Analysis and results:
The decision analytic Markov modelling approach was appropriate and had an adequate description and a diagram. The expected costs and benefits were presented clearly and synthesised appropriately using an incremental approach. The impact of uncertainty on the model's results was tested exhaustively using a series of scenario and probabilistic sensitivity analyses. As a main limitation to their study the authors reported that although much of the evidence used in the model was derived from cohorts of Canadian patients, effectiveness data were derived from North American and European studies.

Concluding remarks:
The quality of the study methodology was good. Methods and results were reported in detail. Given the scope of the study, the authors’ conclusions appear to be appropriate.

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