Cost-effectiveness of angiotensin-converting enzyme inhibitors in nondiabetic advanced renal disease
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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
This study assessed the cost-effectiveness of angiotensin-converting enzyme (ACE) inhibitors for the treatment of non-diabetic patients with proteinuria and advanced renal disease, with a serum creatinine level above 3.0mg per dL. The authors concluded that ACE inhibitor treatment saved money and lives, and was highly cost-effective. The structure of the analysis appears to have been robust, and the appropriate use of sensitivity analyses ensures the validity of the authors’ conclusions.

Type of economic evaluation
Cost-utility analysis

Study objective
This study assessed the cost-effectiveness of angiotensin-converting enzyme (ACE) inhibitors for the treatment of non-diabetic patients with proteinuria and advanced renal disease, with a serum creatinine level above 3.0mg per dL.

Interventions
The intervention was the ACE inhibitor benazepril 10mg twice a day. The comparator was no ACE inhibitor.

Location/setting
Germany/secondary care.

Methods
Analytical approach:
The analysis was based on a published Markov model, with a lifetime horizon. The authors stated that the perspective of the statutory health insurer was adopted.

Effectiveness data:
The clinical data were from a published review of available data in July 2001, and a search of the PubMed database for articles added after July 2001. This identified two randomised placebo-controlled double-blind trials, and their data were combined to produce estimated odds ratios, using the Mantel-Haenszel method. Averages were calculated, weighted by the sample sizes. This produced the event rates, which were the key inputs for the model. The placebo arms of the trials were used to estimate the baseline risk of events, such as end-stage renal disease. The intervention arms were used for the relative risks with ACE inhibitors. Mortality data were from a large community-based cohort study.

Monetary benefit and utility valuations:
The utility values were from a published survey that used the time trade-off approach, with US patients, and from a published systematic review of empirical studies that used time trade-off weights, based on patient preferences.

Measure of benefit:
Quality-adjusted life-years (QALYs) were the summary benefit measure and they were discounted at an annual rate of 3%.

Cost data:
The economic analysis included the costs of drugs, creatinine and potassium screening, end-stage renal disease (transplantation and dialysis), and the management of chronic kidney disease. The resource quantities were based on international recommendations and published studies. The reference price was used for benazepril. Other costs were from German sources and published studies. All costs were in Euros (EUR) and the price year was 2009. A 3% annual discount rate was applied.

Analysis of uncertainty:
One-way sensitivity analyses were carried out on all the variables, using published confidence intervals or a range of ±20% of their baseline values. A Monte Carlo simulation was performed, using predetermined probability distributions for the model inputs. Cost-effectiveness acceptability curves were generated. Short time horizons were considered.

Results
In the base case, the expected costs were EUR 205,200 without an ACE inhibitor and EUR 172,676 with an ACE inhibitor. The QALYs were 6.77 without the ACE inhibitor and 8.26 with the ACE inhibitor. The ACE inhibitor was dominant as it was less expensive and more effective than no treatment.

The superior economic and clinical profile of the ACE inhibitor held in the short-term simulations.

The most influential inputs were the efficacy of the ACE inhibitor, the discount rates for costs and benefits, and the cost of end-stage renal disease. The probabilistic analysis showed that the ACE inhibitor was dominant in 80% of simulations.

Authors' conclusions
The authors concluded that ACE inhibitor treatment saved money and lives, and was highly cost-effective for these patients.

CRD commentary
Interventions:
The two comparators were appropriately selected as they were the proposed and the conventional treatments for this patient population. The authors pointed out that the patients in both groups received other antihypertensive drugs, but no other renin-angiotensin system drugs.

Effectiveness/benefits:
The literature was appropriately searched to identify the relevant sources of evidence. The authors updated a literature review and reported the key methods and conduct of their own review. The inclusion of randomised controlled trials should ensure the validity of the clinical evidence, as they are considered to be robust sources. The patient populations and the meta-analytic approach used to pool these data were clearly reported. QALYs were a valid benefit measure, given the impact of the disease on survival and quality of life. The authors stated that time trade-off was the most common method for eliciting preferences for health conditions, but the data were from US patients and it is unclear whether these are transferable to German patients. Undiscounted life-years were reported, but were not combined with costs.

Costs:
The categories of costs appear to have reflected the perspective of German statutory health insurance, as those costs incurred by patients and productivity losses were not considered. Few unit costs and resource quantities were reported, with the costs generally presented as category totals. German sources were used and they are likely to have been appropriate, but were not extensively described. Other details, such as the price year and discount rate, were reported. The costs were varied in the sensitivity analyses.

Analysis and results:
The results were clearly reported. An appropriate incremental approach was used to synthesise the costs and benefits of the alternative treatments. Valid approaches were used to investigate the uncertainty, and the key findings were clearly presented and discussed. The authors stated that it was unclear whether their results that used clinical data from trials of enalapril and benazepril might be transferable to other ACE inhibitors. They acknowledged the limitations that data...
from a trial conducted in China, might not be transferable to the German population, and the transferability of the conclusion to other countries was limited given differences in costs, clinical management, and epidemiology.

Concluding remarks:
The structure of the analysis appears to have been robust, and the appropriate use of sensitivity analyses should ensure the validity of the authors’ conclusions.

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