A cost-effectiveness analysis of angiotensin-converting enzyme inhibitors and angiotensin
receptor blockers in diabetic nephropathy

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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 objective was to examine the cost-effectiveness of angiotensin-converting enzyme inhibitors versus angiotensin-receptor blockers, in the prevention of end-stage renal disease, in patients with diabetic nephropathy. The authors concluded that angiotensin-receptor blockers were a cost-effective treatment. The analysis was generally well conducted and satisfactorily presented. The authors’ conclusions appear to be valid.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
The aim was to examine the cost-effectiveness of angiotensin-converting enzyme (ACE) inhibitors and angiotensin-receptor blockers (ARBs) as part of treatment to prevent end-stage renal disease (ESRD) in patients with diabetic nephropathy.

Interventions
Three comparators were considered: ARBs, ACE inhibitors, and no additional treatment.

Location/setting
Greece/secondary care.

Methods
Analytical approach:
This economic evaluation was based on a review of published studies. The time horizon was the patient’s lifetime. The authors stated that the analysis was carried out from the perspective of the third-party payer.

Effectiveness data:
The clinical data came from a systematic literature review of the PubMed (including MEDLINE) and EMBASE databases. The search details and inclusion criteria were reported. Randomised controlled trials (RCTs) with a minimum follow-up of one year were included. A total of 20 trials for ACE inhibitors and four trials for ARBs were found. The study quality was assessed using standard criteria. No head-to-head comparisons between ARBs and ACE inhibitors were found. A meta-analysis was carried out to pool the estimates from primary sources, using a random-effects model. The key clinical endpoint was the risk of developing ESRD.

Monetary benefit and utility valuations:
Not relevant.

Measure of benefit:
The summary benefit measure was the number needed to treat (NNT) to prevent one patient from developing ESRD.

Cost data:
The economic analysis included the costs of drugs and lifetime management of ESRD. Drug costs were derived from the Greek National Formulary and the data on drug consumption were based on published studies identified in the review. The costs and quantities associated with ESRD were obtained from a published study, the details of which were
not given. All costs were in US dollars ($) and were discounted at 3% per annum. The price year was 2006.

Analysis of uncertainty:
A sensitivity analysis was carried out by varying both the clinical and the economic data using a one-way approach. The ranges were derived from the literature and these sources were reported for the clinical, but not for the economic data. In an alternative scenario, US costs were used and these were taken from the US Renal Data System Annual Data Report in 2006.

Results
The NNT to prevent one patient from developing ESRD was 21 (95% CI 12.94 to 56.82) for ARBs, 333 for ACE inhibitors, and 65 for both agents. The mean lifetime cost of ESRD was $195,692. The mean weighted acquisition cost per patient per year was $763.50 for ARBs, $144.92 for ACE inhibitors, and $291.39 for both.

For patients receiving ARBs, the cost to prevent one patient from developing ESRD was $31,729 (95% CI 19,443 to 85,442) and given the lifetime cost of ESRD this would result in net cost savings per patient over three years of $7,770 (95% CI 1,940 to 13,631). For patients receiving ACE inhibitors, the cost to prevent one patient from developing ESRD was $189,190, which was very similar to the ESRD lifetime cost. For patients receiving ARBs or ACE inhibitors, the net cost savings were more than $2,000, but the results did not reach statistical significance.

When the analysis was performed using US data, the results were similar and showed the superior profile of ARBs. In general, the sensitivity analysis showed that the findings were robust; changes in the economic inputs did not alter the conclusions. The risk difference for ARBs was no longer significant when the inclusion criteria in the systematic review were changed.

Authors' conclusions
The authors concluded that ARBs were a cost-effective treatment for the prevention of ESRD, but a direct comparison of the two classes of agents was required to corroborate these findings.

CRD commentary
Interventions:
The selection of the comparators was appropriate as the authors compared two classes of agents that block the renin-angiotensin-aldosterone system.

Effectiveness/benefits:
The clinical analysis was carried out in a valid and transparent way and extensive details of the literature review were presented. The strict inclusion criteria should have ensured the selection of the best available evidence. Only RCTs were selected and the issue of heterogeneity among trials was investigated. The data were synthesised using a random-effects meta-analysis, which appears to have been an appropriate approach. In general, the clinical analysis was robust. The benefit measure was derived directly from the literature review. The authors stated that mortality and cardiovascular morbidity were not considered as relevant outcomes as they did not differ significantly between the treatment groups in two of the major trials found.

Costs:
The categories of costs were consistent with the perspective. The authors justified the exclusion of side-effect data from the costs due to the similar safety profile of the two treatments. In general, where potentially relevant cost categories were not included, a clear justification was provided. A broad perspective was considered in the sensitivity analysis, but the details of the derivation of indirect costs were not reported. The sources of drug-related data were reported. The ESRD costs were taken from a previous study, but its methodological characteristics were not described, which introduces some uncertainty into the analysis. In general, other details such as the price year, use of discounting, and statistical analyses were clearly presented.

Analysis and results:
The costs and benefits were clearly presented and synthesised. The external validity of the analysis was investigated using US estimates of costs to improve the generalisability of the results. The issue of uncertainty was only partially
investigated in a deterministic, univariate sensitivity analysis. The authors stated that their findings were in accordance with those from other publications. Some potential limitations of their analysis were pointed out, such as the lack of available RCTs and the need for an indirect comparison between ACE inhibitors and ARBs, using other agents as common comparators.

Concluding remarks:
The analysis was generally well conducted and satisfactorily presented. The authors’ conclusions appear to be valid.

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