Pharmacoeconomic analysis of angiotensin-converting enzyme inhibitors in type 2 diabetes: a Markov model
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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 investigated the cost-effectiveness of treatment with or without angiotensin converting enzyme (ACE) inhibitors for patients with type 2 diabetes and normal albuminuria, microalbuminuria, or macroalbuminuria, in the USA. The authors concluded that ACE inhibitors were cost-effective and averted numerous events in patients with type 2 diabetes. The methods were appropriate and comprehensive and the authors’ conclusions appear to be reasonable for the analysis undertaken.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
The objective was to assess the costs and health effects of angiotensin converting enzyme (ACE) inhibitors for patients with newly diagnosed type 2 diabetes in the USA.

Interventions
This study compared treatment with and without ACE inhibitors for patients with type 2 diabetes and normal albuminuria, microalbuminuria, or macroalbuminuria. A hypothetical cohort of patients aged 45 years and older was modelled.

Location/setting
USA/primary care.

Methods
Analytical approach:
A Markov model was constructed to synthesise data from published observational and experimental studies and assumptions made by the authors. The analysis covered eight years and the authors stated that a health care payer’s perspective was taken.

Effectiveness data:
A literature review, using the MEDLINE and CINAHL databases, was undertaken. Studies up to 2006 were selected if they reported relevant disease transition rates or they compared ACE inhibitors with placebo. The clinical estimates included cardiovascular disease (CVD) events, dialysis, all-cause mortality, and a composite endpoint of these three measures. The transition probabilities for nephropathy progression came from randomised trials, that compared ACE inhibitors with placebo, and the evidence on CVD events was abstracted from two prospective cohort studies. The clinical inputs were fully reported and referenced.

Monetary benefit and utility valuations:
Not relevant.

Measure of benefit:
The measures of benefit were CVD events prevented, lives saved, and dialysis cases prevented.

Cost data:
The direct medical costs were those of the ACE inhibitors, CVD events including myocardial infarction, ischaemic stroke, angina, and microvascular or macrovascular complications. Average wholesale prices were used for the ACE inhibitors. The data on resources used and their values were abstracted from previous studies, one of which included 12,000 patients with diabetes and lasted for nine years (Brown, et al. 1999, see ‘Other Publications of Related Interest’ below for bibliographic details). The annual costs were presented and were clearly referenced. All costs were presented in 2005 US dollars ($) and adjusted using the medical component of the US Consumer Price Index.

Analysis of uncertainty:
The parameter uncertainty was addressed using one-way sensitivity analyses on the nephropathy progression rates, ACE inhibition rates, and costs, by varying them by ±25%. Two-way analyses on the progression rates and low- or high-cost ACE inhibitor combinations were also performed and the results were presented in a table.

Results
For the US health care payer, $1.1 billion over eight years was saved by those receiving ACE inhibitors. Compared with no ACE inhibitor, using ACE inhibitors would prevent 34,157 CVD events (2.54%), save 23,205 lives (1.72%), and prevent 24 dialysis cases (0.002%).

The incremental cost-effectiveness ratios were not reported because ACE inhibitors were dominant, with improved health benefits and cost savings, compared with no ACE inhibitor.

The sensitivity analyses showed that these base-case results were stable to 25% reduction in progression from micro- to macroalbuminuria and 25% reduction in CVD costs, but they were sensitive to drug costs. When high-cost ACE inhibitors were used, there were positive, but small incremental costs.

Authors’ conclusions
The authors concluded that using ACE inhibitors in the better stages of renal function led to cost savings and superior health benefits for patients with type 2 diabetes.

CRD commentary
Interventions:
The dosage for the ACE inhibitors was not stated and the comparator, no treatment, was not described well. Further detail on other treatments that were available in practice would have been useful.

Effectiveness/benefits:
The effectiveness data were derived from observational studies and randomised controlled trials. The authors appropriately conducted a review of the literature and the inclusion criteria were reported, but it was not clear how the studies were selected from those identified. No meta-analyses appear to have been performed. An assessment of the validity of the clinical endpoints is not possible without recourse to the source studies for their methods and analytical treatment.

Costs:
Direct medical costs were included and generally appear to have been appropriate to the perspective. It was unclear which types of resources were used and whether all of these were included, as only the general cost categories and annual costs were reported. The sources of costs were clearly presented and these should be consulted to assess whether patient-level data on costs were used and the statistical analyses undertaken.

Analysis and results:
The incremental cost per effect ratios were calculated and fully presented including all sensitivity and scenario analyses. A probabilistic sensitivity analysis was not undertaken and would have strengthened the study. The potential for generalising the results to other settings was acknowledged and comparisons with progression rates for other populations were discussed. Some limitations of the study were highlighted, such as that causality was tentative due to the use of observational studies, and the omission of treatment failure and adverse events. The impact of drug non-adherence in real-life may have led to overestimation in the findings.
Concluding remarks:
Despite some limitations with data transparency, the methods appear to have been appropriate. The authors’ conclusions appear to reflect the scope of the analysis.

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