Cost-effectiveness of angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers in newly diagnosed type 2 diabetes in Germany

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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 examined the cost-effectiveness of different times for starting angiotensin-converting enzyme (ACE) inhibitors or angiotensin II receptor blockers (ARBs) for patients with type 2 diabetes, to prevent end-stage renal disease. The authors concluded that immediate treatment of newly diagnosed type 2 diabetes patients, using ACE inhibitors and switching to ARBs in the event of a cough, was the most cost-effective option. The methods were valid and this ensures that the authors’ conclusions are robust.

Type of economic evaluation
Cost-effectiveness analysis, cost-utility analysis

Study objective
This study examined the cost-effectiveness of different times for starting angiotensin-converting enzyme (ACE) inhibitors or angiotensin II receptor blockers (ARBs), in patients with type 2 diabetes, without hypertension and heart failure, to prevent end-stage renal disease.

Interventions
Three strategies were examined. The first strategy involved treating all patients at the time of diagnosis, which meant there was no screening and patients started on ACE inhibitors (ramipril 10mg daily) when diagnosed with type 2 diabetes. The second strategy involved screening for microalbuminuria, once a year, with treatment if the result was positive. The third strategy was screening for macroalbuminuria, once a year, with treatment if the result was positive. Patients were switched to ARBs (irbesartan 300mg daily) if they developed an ACE inhibitor-related cough. These strategies were compared with no screening and no treatment.

Location/setting
Germany/primary care.

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

Effectiveness data:
Various electronic databases were searched to identify relevant sources of evidence for the model. Some details on the search criteria and the design of the studies found in the literature were reported. Two meta-analyses providing evidence on the efficacy of ACE inhibitors in patients with type I and II diabetes were found in the Cochrane Database of Systematic Reviews and were used as the main source for efficacy data. The natural history of progression from diabetes to end-stage renal disease was based on several sources including the two meta-analyses already mentioned and other published clinical trials. Epidemiological data were based on German studies, when available.

Monetary benefit and utility valuations:
The utility values for diabetic patients were from a published cross-sectional study that included 292 patients interviewed using the time trade-off (TTO) method. The utility estimates for other health conditions were from a systematic review of empirical studies that used the TTO method.
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, monitoring, treatment of diabetes, management of end-stage renal disease (ESRD), and health care expenditure unrelated to diabetes. The costs of haemodialysis were also considered. The resource use data were from published studies and the costs of services were based on German official data and published reports. The annual costs for patients with ESRD were calculated as a weighted average of the costs of patients having different types of dialysis and a renal transplant. All costs were in Euros (EUR), the price year was 2006, and a 3% annual discount rate was applied.

Analysis of uncertainty:
A deterministic univariate sensitivity analysis was undertaken, using published confidence intervals for the clinical inputs and varying the costs by ±20%. A Monte Carlo simulation was carried out, using predefined probability distributions for the model inputs, to generate cost-effectiveness acceptability curves.

Results
In a typical 50-year-old patient, the expected costs were EUR 151,579 with no screening nor treatment, EUR 144,059 with screening for macroalbuminuria, EUR 137,406 with screening for microalbuminuria, and EUR 135,555 with treating all patients. The QALYs were 14.46 with no screening, 14.83 with macroalbuminuria screening, 15.14 with microalbuminuria screening, 15.21 with treatment for all patients. The strategy of immediate treatment was dominant as it was less expensive and more effective than the comparators.

The most influential inputs were the discount rate, the absolute risk of progression from normal albuminuria to microalbuminuria without ACE inhibitors, and the relative risk of progression from normal albuminuria to microalbuminuria with ACE inhibitors compared with without. The only case that drastically changed the results was the assumption of a low progression rate from microalbuminuria to macroalbuminuria without ACE inhibitors: in this case, screening for microalbuminuria dominated treatment for all patients.

The probability of immediate treatment being cost saving over screening for microalbuminuria was 89%.

Authors’ conclusions
The authors concluded that a strategy of treating all newly diagnosed type 2 diabetes patients with ACE inhibitors or ARBs was the most cost-effective option from the perspective of the German statutory health insurer.

CRD commentary
Interventions:
The comparators were appropriately chosen to reflect the possible management strategies in patients who were diagnosed with type 2 diabetes. Ramipril was selected as it was the most commonly used ACE inhibitor in the authors’ setting and the most effective dosage of irbesartan was considered.

Effectiveness/benefits:
The literature was appropriately reviewed, using a systematic approach, to identify the clinical inputs for the model. The sources appear to have been valid studies, given the methodological strengths of clinical trials and meta-analyses. Some key information on the methods and conduct of the review was reported. Where the data were pooled, the authors stated that the studies were homogeneous. These factors enhance the validity of the clinical analysis. QALYs were an appropriate benefit measure and they capture the impact of the disease on a patient's health in terms of both survival and quality of life. The utility weights were appropriately estimated from published studies.

Costs:
The cost categories were consistent with the perspective stated. It was noted that German statutory insurance covers approximately 90% of the German population. The data sources were not fully described, but most of the costs were from official sources. The unit costs were reported for some items, while others were presented as total categories.
Limited information on the resource quantities was given. The price year was reported, making reflation exercises for other time periods feasible.

Analysis and results:
The study used an appropriate approach to identify the best strategy. A synthesis of the costs and benefits was not required because treatment for all patients was dominant. The results were clearly reported. Deterministic and probabilistic approaches were used to investigate the uncertainty. The results of the sensitivity analyses were reported and discussed. Conventional discounting was applied to both the costs and benefits. The authors acknowledged some limitations of their analysis, which mainly related to some data sources, but these appear to have been overcome by the use of conservative assumptions and extensive sensitivity analysis.

Concluding remarks:
The methods were valid and this ensures that the authors’ conclusions are robust.

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