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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 most cost-effective time to start treatment to manage renal disease, for patients who were newly diagnosed with type 2 diabetes mellitus. Treatment with an angiotensin-converting enzyme inhibitor, for all patients, with a switch to an angiotensin II-receptor blocker for those who developed a dry cough, was cost-effective over screening, and reduced health care expenditure in the Netherlands. The cost-effectiveness analysis was well conducted and the authors’ conclusions appear to be robust.

Type of economic evaluation
Cost-utility analysis

Study objective
This study assessed the most cost-effective time to start treatment to manage renal disease, using an angiotensin-converting enzyme (ACE) inhibitor, for patients who were newly diagnosed with type 2 diabetes mellitus.

Interventions
The three strategies were to treat all patients at the time of their diagnosis of diabetes, to screen for microalbuminuria once a year and treat patients with positive results, and to screen for macroalbuminuria (proteinuria) once a year and treat patients with positive results. A background strategy of no screening and no treatment was considered.

Treatment was an ACE inhibitor, which was replaced by an angiotensin II-receptor blocker (ARB) if a dry cough occurred as a side-effect.

Location/setting
Netherlands/primary care.

Methods
Analytical approach:
The analysis was based on a published Markov model, with a lifetime horizon, and a hypothetical cohort of 50-year-old patients who were newly diagnosed with type 2 diabetes. The authors stated that the perspective of the health care system was adopted.

Effectiveness data:
Literature reviews were carried out to identify the relevant sources for the clinical inputs. Databases such as PubMed were searched. The efficacy of treatment was a key input and was pooled data from two published meta-analyses. Other transition probabilities were from clinical trials. Mortality was from Dutch national databases. The distribution of patients among health states was based on a Finnish study; other epidemiological data were generally from Dutch publications and databases.

Monetary benefit and utility valuations:
The utility values were from published sources, including a cross-sectional study of 292 patients and a systematic review of empirical studies. Both sources used the time trade-off questionnaire.

Measure of benefit:
Quality-adjusted life-years (QALYs) were the summary benefit measure and they were discounted at an annual rate of 1.5%. Undiscounted life-years were reported.

Cost data:
The economic analysis included the costs of the ACE inhibitors, ARBs, screening procedures, treatment for end-stage renal disease (ESRD), and general expenditure for diabetes and other health care. The most frequently prescribed ACE inhibitor (enalapril) and ARB (irbesartan) in the Netherlands were considered. The drug costs were based on official Dutch prices, including value-added tax (VAT) and pharmacists’ prescription fees. The costs of screening were based on recommended prices. The annual cost of ESRD was from a Dutch study. All costs were in Euros (EUR) and the price year was 2010. A 4% annual discount rate was applied.

Analysis of uncertainty:
One-way sensitivity analyses were carried out, using confidence intervals where available. A Monte Carlo simulation was performed, using conventional probability distributions for the model inputs. The net monetary benefit was calculated and cost-effectiveness acceptability curves were plotted.

Results
The expected lifetime costs were EUR 110,777 with screening for macroalbuminuria, EUR 101,140 with screening for microalbuminuria, and EUR 98,421 with treating all patients. The QALYs were 19.15 with screening for macroalbuminuria, 19.54 with screening for microalbuminuria, and 19.63 with treating all patients. The undiscounted life-years were also highest with treatment for all patients.

In the base case, both screening strategies were dominated by treating all patients, as this was more effective and less expensive.

The magnitude of the clinical and economic benefits depended mainly on variations in the rate of progression from microalbuminuria to macroalbuminuria without an ACE inhibitor and on the relative risk of progression from normal albuminuria to microalbuminuria without an ACE inhibitor, but treatment for all remained dominant in all the sensitivity analyses.

Treatment for all patients was cost saving in 70% of simulations in the probabilistic sensitivity analysis.

Authors' conclusions
The authors concluded that treatment with an ACE inhibitor for all patients diagnosed with type 2 diabetes, with a switch to an ARB for those who developed a dry cough, was cost-effective and reduced health care expenditure in the Netherlands.

CRD commentary
Interventions:
The rationale for the selection of the comparators was clear. Several possible strategies were considered and these are likely to have been relevant in other health care settings.

Effectiveness/benefits:
An appropriate approach was used to identify the relevant sources of data. Some details of the literature review were reported. The data from two published meta-analyses were pooled, as they were homogeneous, and this provided the treatment effect and most of the transition probabilities. Other estimates were generally from valid sources, including clinical trials and local epidemiology studies. Compliance with the drugs was from clinical trials and might be higher than in the real world. QALYs were an appropriate benefit measure, capturing the relevant dimensions of health for patients with diabetes, who were at risk of developing renal disease. They also allow comparisons to be made with the benefits of other health care interventions. The utility weights were obtained using a validated instrument.

Costs:
The cost categories were appropriate for the perspective adopted. The authors stated that the economic analysis followed official Dutch guidelines for pharmacoeconomic research. Dutch sources were used to derive the unit costs. The key resource quantities were reported. The calculation of the costs of ESRD was presented, with details in an
appendix. Conventional discounting was applied to the long-term costs. Reflation exercises will be possible as the price year was reported. Variations in the cost estimates were tested in the sensitivity analyses. The authors stated that several model assumptions were conservative and the cost savings might have been underestimated.

**Analysis and results:**
The expected costs and benefits of the various strategies were clearly reported. An incremental analysis was conducted to identify the optimal strategy. The uncertainty was satisfactorily investigated in deterministic and probabilistic analyses, and the methods and results were clearly described. The key details of the decision model were reported. The authors stated that the impact of ACE inhibitors on cardiovascular disease was not considered and the benefits of treatment for all patients might have been underestimated. Other assumptions might have underestimated the benefits, and the results were conservative. The findings were specific to the Dutch context, but other published economic evaluations had found similar results.

**Concluding remarks:**
The study was based on a well-conducted cost-effectiveness analysis and the authors’ conclusions appear to be robust.

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