Routine treatment of insulin-dependent diabetic patients with ACE inhibitors to prevent renal failure: an economic evaluation

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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.

Health technology
Screening for microalbuminuria, hypertension and macroproteinuria and routine treatment of insulin-dependent diabetic patients (IDDM) with angiotensin-converting enzymes (ACEs). The treatment with ACE inhibition is equivalent to captopril 25 mg three times a day. If two of three tests were positive, patients were to be given > 20 mu/min or 30 mg albumin/g creatinine. The screening for hypertension and macroproteinuria required dipstick > 0.3 g/L or positive albistick confirmed with >300 mg/d or >200 mug/min proteinuria.

Type of intervention
Screening and treatment.

Economic study type
Cost-effectiveness analysis and cost-utility analysis.

Study population
A hypothetical cohort of male and female insulin-dependent diabetic patients. No further details were given.

Setting
Hospital. The economic study was carried out in Nova Scotia, Canada.

Dates to which data relate
The main effectiveness data were derived from previously published studies conducted between 1982-1996. Resource and cost data were obtained mainly from 1993-95 sources. The price year was 1995.

Source of effectiveness data
The estimates for probabilities and utilities for each treatment and health state were derived from a review of previously published studies. The estimates for risk of progression from normoalbuminuria to microalbuminuria were based on authors’ assumptions.

Modelling
A Markov model was used to compare three strategies to prevent the development of end-stage renal disease in insulin-dependent diabetic patients.

Strategy I consisted of screening for microalbuminuria in patients with more than 5 years of diabetes and treating incipient nephropathy with ACE inhibition.

Strategy II consisted of routinely treating all patients with an ACE inhibitor 5 years after diagnosis of diabetes.
Strategy III consisted of treating high risk patients routinely as in strategy II and screening low-risk patients for hypertension and macroproteinuria and treating those low-risk patients who later develop hypertension and/or macroproteinuria with an ACE inhibitor.

**Outcomes assessed in the review**
The outcomes assessed were probabilities and utilities associated with each treatment and health state.

**Study designs and other criteria for inclusion in the review**
No specific study designs were stipulated by the authors as inclusion criteria.

**Sources searched to identify primary studies**
Not stated.

**Criteria used to ensure the validity of primary studies**
Not stated.

**Methods used to judge relevance and validity, and for extracting data**
Not stated.

**Number of primary studies included**
16 primary studies were included in the review.

**Methods of combining primary studies**
Narrative method.

**Results of the review**
The transition probability from micro to macro was 0.055 per year. The transition probability in strategy III from micro to macro was 0.111 per year. The positive predictive value of screening for microalbuminuria and hypertension was 0.8. The fraction of patients with concomitant microalbuminuria and hypertension was 0.4. The transition probability from macro to end-stage renal failure was 0.067 per year. The transition probability from IDDM to death was 1.05 times age-adjusted US vital statistics for general population. The transition probability from micro and macro to death were twice and six times the transition probability from IDDM to death, respectively. The transition probability from end-stage renal failure to death was variable with age. These data formed part of the input parameters to the Markov model.

**Methods used to derive estimates of effectiveness**
Estimates of effectiveness were also based on authors’ assumptions.

**Estimates of effectiveness and key assumptions**
The transition probabilities in strategy I from IDDM-normoalbuminuria to microalbuminuria were 0.012 per year in the low risk case and 0.048 per year in the high risk case. The transition probabilities in strategy III from IDDM to hypertension were given by the product between the transition probability in strategy I and the fraction with
concomitant microalbuminuria and hypertension. The transition probability from IDDM to micro in strategy III was assumed to be the difference between the transition probability from IDDM to micro and the transition probability from IDDM to hypertension. The model assumed that in strategy III, a fraction of patients would develop hypertension at or about the onset of microalbuminuria. Therefore the model assumed that the start of ACE treatment in strategy III would occur at the onset of microalbuminuria in 40% of cases but be delayed to the onset of macroproteinuria.

**Measure of benefits used in the economic analysis**
The outcome measures were life expectancy and quality-adjusted life years (QALYs). Utilities were used to calculate QALYs (between 1 as perfect health and 0 as death).

**Direct costs**
Annual screening for microalbuminuria and macroproteinuria, ACE inhibition and treatment of end-stage renal failure costs were included in the analysis. Resources were reported separately from prices. Costs for the drug were reviewed from recent reports and discounted to 1995 values. Drug wholesale costs were increased by approximately 25% to account for dispensing fees, pharmacy overhead costs and drug monitoring. The 1992 costs were assumed to be unchanged for 1995. The quantity/cost boundaries adopted were the patient and provider (third party and government). A 3% discount rate was applied. The price year was 1995.

**Statistical analysis of costs**
Not undertaken.

**Indirect Costs**
Not considered.

**Currency**
US dollars ($).

**Sensitivity analysis**
A one-way sensitivity analysis was carried out on drug costs, discount rate, rate of development of microalbuminuria and rate of development of macroalbuminuria.

**Estimated benefits used in the economic analysis**
The life expectancy was 42.9 years (strategy I), 44.2 years (strategy II) and 43.2 years (strategy III). The QALYs were estimated to be 19.15, 19.34 and 19.17 years for each strategy respectively. Utilities were 0.838, 0.826, 0.576 for IDDM, ACE inhibition and end-stage renal failure, respectively.

**Cost results**
Costs were estimated to be $29,350, $29,180 and $29,236 for strategy I, II and III, respectively.

**Synthesis of costs and benefits**
Costs and benefits were not combined. If the efficacy rate of treatment reduced the rate of development of microalbuminuria by 30%, strategy II produced more life-years (+1.6) and more QALYs (+0.35) at less cost (-$940) with respect to strategy I. A decrease in the drug cost (-$100) resulted in additional net cost savings for strategy II of $1,728 (an 18% reduction in the rate of progression to microalbuminuria was required to keep strategy II’s programme costs comparable to those of strategy I). With an increase in the drug cost (+ $150), a 37% reduction in the rate of progression to microalbuminuria was required to keep strategy II programme costs comparable to those of strategy I.
With a discount rate of 5%, a 31% reduction in the rate of progression to microalbuminuria would be required to produce more life-years and more QALYs.

A 20% reduction in the rate of progression to microalbuminuria in the high-risk strategy III patients produced more life-years (+0.3) and more QALYs (+0.02) for less cost (- $114) compared with strategy I. For a 30% reduction in the rate of progression to microalbuminuria, strategy III produced 0.12 more QALYs for $1,352 lower cost than that of strategy I. With a reduction (from 4:1 to 3:1) in the rate at which the high-risk group progressed over the low-risk group, the rate of progression to microalbuminuria had to be reduced by 24% for strategy III to be superior. For a 5% discount rate, a 23% reduction in the rate of progression to microalbuminuria was necessary to produce more life-years and more QALYs for less cost. A delay from 9 to 18 years (9 to 18 years was the baseline) in the rate of progression from microalbuminuria to macroalbuminuria for strategy I required a reduction in the rate of development of microalbuminuria by 28% for strategy III to produce more QALYS at lower cost than strategy I. A delay from 9 to 13 years in the rate of progression from microalbuminuria to macroalbuminuria for strategy I would require the rate of development of microalbuminuria to be reduced by 11% for strategy III to produce more QALYs at lower cost than strategy I.

**Authors' conclusions**

Screening for microalbuminuria may be unnecessary if ACE inhibitors truly can reduce the rate of development of early diabetic nephropathy. The lower the drug costs, the less the impact of the drug on quality of life. A small reduction in the rate of development of microalbuminuria could save money and produce more QALYs.

**CRD COMMENTARY - Selection of comparators**

The reason for the choice of the comparator is clear. ACE inhibitors have been shown to both delay the progression from microalbuminuria to macroalbuminuria and to delay the progressive loss of renal function in patients with overt diabetic nephropathy. As not all patients with insulin-dependent diabetes develop renal involvement, many patients will be treated at unnecessary cost with routine drug therapy and will derive little or no benefit. Ideally, treatment of only high risk patients could lead to health care savings and improvements in patient outcomes.

**Validity of estimate of measure of benefit**

The estimate of measure of benefit used in the economic analysis is likely to be internally valid. The data do not appear to have been used selectively. The modelled solutions were tested using sensitivity analysis in order to validate the robustness of the findings.

**Validity of estimate of costs**

Resource quantities were reported separately from the prices. Adequate details of methods of quantity/cost estimation were given. However, as noted by the authors, renal failure treatment costs for 1995 were unknown and therefore they were not included in the analysis. As the study was retrospective, the costs may need to be treated with a degree of caution.

**Other issues**

The authors’ conclusions are likely to be justified given the uncertainties in the data. The issue of generalisability to other settings or countries was not addressed. However, appropriate comparisons were made with other studies particularly in relation to efficacy rate for the reduction in the development of microalbuminuria, survival probabilities and overall life expectancy, cumulative incidence of macroalbuminuria and end-stage renal disease. Results do not appear to have been presented selectively.

**Implications of the study**

Further analysis is required within the context of a prospective trial.

**Source of funding**

None stated.
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