An economic analysis of captopril in the treatment of 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.

Health technology
The use of captopril in diabetic patients with overt nephropathy (excreting a minimum of 500 mg/day of total urinary protein) versus blood pressure control alone without an ACE inhibitor (placebo).

Type of intervention

Economic study type
Cost-effectiveness study.

Study population
All patients in the USA with diabetes and overt nephropathy.

Setting
Outpatient and GP care for preventative care, inpatient and dialysis centre care for treatment of renal failure. The study was carried out in the USA.

Dates to which data relate
Clinical data relating to the first 4 years of therapy for IDDM patients and assumptions about the further progression of nephropathy and about NIDDM patients were based on a report published in 1993. Medical events after progression to ESRD were based on studies published between 1990 and 1993. Rates of cardiovascular events and other comorbidities were based on studies published between 1986 and 1993. Death rates from all causes at different ages were taken from statistics based on 1990 data. The model assumed captopril therapy was initiated in 1995 for 85% of all eligible patients. Resource dates were not specified. Costs were reported in nominal 1994 US dollars.

Source of effectiveness data
Clinical data relating to the first 4 years of therapy for IDDM patients were based on a single study. Progression from year 4 to death was based on the authors' opinions. Data relating to NIDDM patients, ESRD events, cardiovascular events and other comorbidities were based on a synthesis of several studies.

Link between effectiveness and cost data
Costing was not undertaken on the same patient sample as that used in the effectiveness study and was obtained retrospectively.

Study sample
There were 409 patients in the study: 207 patients in the captopril group and 202 in the placebo (blood pressure control...
alone) group. The entry criteria included having IDDM and excreting a minimum of 500mg/day of total urinary protein. The trial was randomised and double blinded. No power calculation was mentioned. Further details are given in a clinical report, (Lewis, 1993).

**Study design**
Randomised controlled trial. The trial was double blinded. The follow up was 4 years. No loss to follow-up was stated.

**Analysis of effectiveness**
It is not stated whether analysis was based on intention to treat. The primary health outcomes were life years saved and dialysis years saved.

**Effectiveness results**
Captopril treatment resulted in an approximately 50% reduction in the risk of both progressive renal insufficiency and the combined endpoint of death, dialysis and transplantation compared with blood pressure control alone. No confidence intervals or p values were stated.

**Clinical conclusions**
Captopril therapy reduced the rate of renal failure, ESRD and death in patients with IDDM and nephropathy.

**Modelling**
A multiple state, Markov-type decision analysis model was used to estimate final costs and benefits.

**Outcomes assessed in the review**
Data relating to NIDDM patients. Rates of progression to ESRD events and survival rates on dialysis and after transplants. Data relating to the risk of cardiovascular events and other comorbidities and survival rates associated with them.

**Study designs and other criteria for inclusion in the review**
Not stated.

**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**
Data relating to NIDDM patients were based on 5 studies of unspecified type. Data relating to cardiovascular events and other comorbidities were based on 11 studies.
Methods of combining primary studies
Not stated.

Investigation of differences between primary studies
Not discussed.

Results of the review
The same rate of progression of renal disease was used for NIDDM patients as for IDDM patients, but as patients in the US with NIDDM are older at onset of nephropathy than IDDM patients the mortality rates were adjusted. Rates of survival on dialysis and after transplant were used in the model but details were not given. Relative risks of cardiovascular events and other comorbidities were used in the model but no further details were given.

Methods used to derive estimates of effectiveness
The authors' assumptions were used to extend the model beyond the 4 years followed up in the single study.

Estimates of effectiveness and key assumptions
The progression of disease was assumed to be at the same rate as in years 2-4 of the clinical trial. This was stated to be a conservative estimate.

Measure of benefits used in the economic analysis
Life years saved and dialysis years saved.

Direct costs
All costs and resources were reported separately. Prices are in 1994 dollars. The cost boundary was that of the payer and included transportation costs to dialysis centres for treatment. Medical costs included: physicians’ fees, lab tests, medications, hospital fees, organ acquisition, transplant maintenance and transplant failure. Medical costs were estimated using Medicare reimbursement levels, average wholesale drug prices plus patients’ copayment levels and other out of pocket costs. No differences were reported between marginal and average costs. Costs were discounted at 5%.

Indirect Costs
Resources and costs were reported separately. These were estimated using the human capital approach including the value of lost productive time. IDDM patients without nephropathy have a near normal labour force participation while ESRD patients, particularly those on dialysis, do not because of increased disability. Lost work time and lost household production time was computed based on estimated lost time due to those conditions. The indirect cost value of a death was computed in comparison with life expectancy of patients with diabetes and no ESRD. Costs were stated in 1994 dollars and were discounted at 5%.

Currency
US dollars ($)

Sensitivity analysis
One way sensitivity analyses were carried out on the discount rate, costs, cardiovascular event rate, rate of progression to ESRD or death, and risk reduction to test final cost savings.
Estimated benefits used in the economic analysis
Captopril treatment resulted in a reduction of approximately 50% in the risk of both progressive renal insufficiency and the combined endpoint of death, dialysis and transplantation compared with blood pressure control alone. The model estimate of the maximum lifespan in the IDDM group was 31 years. The estimate for the average increase in life years was 0.2 over a 5 year period and 2.15 over a 31 year period with the use of captopril therapy compared with the placebo. The savings in dialysis years were 0.18 over 5 years and 0.72 over 31 years. For the NIDDM group the model estimated a maximum lifespan of 12 years. The estimate for the average increase in life years over 12 years was 1.04 and 0.29 dialysis years. Benefits were discounted at 5%.

Cost results
Cost results were given per patient for 4 years, 12 years and for IDDM patients for 31 years for direct and indirect costs.

Direct costs.
IDDM patients with captopril for 4 years - $17,460;
IDDM patients with BP control only for 4 years - $22,310 (Saving $4,850);
IDDM patients with captopril for 12 years - $44,220;
IDDM patients with BP control only for 12 years - $74,320 (Saving $30,100);
IDDM patients with captopril for 31 years - $63,770;
IDDM patients with BP control only for 31 years - $96,320 (Saving $32,550);
NIDDM patients with captopril for 4 years - $19,900;
NIDDM patients with BP control only for 4 years - $22,690 (Saving $2,790);
NIDDM patients with captopril for 12 years - $35,560;
NIDDM patients with BP control only for 12 years - $45,460 (Saving $9,900)

Indirect costs.
IDDM patients with captopril for 4 years - $46,840;
IDDM patients with BP control only for 4 years - $72,490 (Saving $25,650);
IDDM patients with captopril for 12 years - $12,294;
IDDM patients with BP control only for 12 years - $223,860 (Saving $100,920);
IDDM patients with captopril for 31 years - $183,680;
IDDM patients with BP control only for 31 years - $268,070 (Saving $84,390);
NIDDM patients with captopril for 4 years - $119,310;
NIDDM patients with BP control only for 4 years - $160,580 (Saving $41,270);
NIDDM patients with captopril for 12 years - $239,580;
NIDDM patients with BP control only for 12 years - $285,310 (Saving $45,730).
Synthesis of costs and benefits
The intervention was the dominant strategy. Sensitivity analysis showed that the result was robust.

Authors' conclusions
Captopril therapy administered to diabetes patients with overt nephropathy provided savings in direct costs as well as an increase in life years and in dialysis free years. The indirect cost savings also reflected a significant overall societal benefit.

CRD COMMENTARY - Selection of comparators
The reason for the choice of comparator is clear.

Validity of estimate of measure of benefit
The estimate of the measure of benefit is likely to be internally valid. Although many assumptions had to be made, the authors gave valid reasons for making them.

Validity of estimate of costs
A full listing of items used in the model with base costs, conversion factors and total costs is contained in an appendix. Resource quantities used in the model were not given. The human capital method of estimating indirect costs is not reliable but indirect costs have been presented separately from direct costs. In the text the authors appeared to use indirect cost savings as a surrogate for measuring improvements in quality of life.

Other issues
As so many assumptions had to be made, particularly to apply the model to NIDDM patients and to cover a lifetime, the model must contain uncertainties. However the authors have justified their assumptions and made sufficient sensitivity tests to establish their conclusions. The authors' caveat, that payments for therapy in the early years would be borne by a different payer than would gain from savings in later years, would not apply in the UK, so that there would seem to be no reason why the conclusions of this study should not be applicable to the UK.

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Other publications of related interest

Indexing Status
Subject indexing assigned by NLM

MeSH
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