Losartan reduces the costs associated with diabetic end-stage renal disease: the RENAAL study economic evaluation


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 losartan combined with conventional antihypertensive therapy (CAHT). CAHT included diuretics, calcium-channel antagonists, alpha- or beta-blockers, centrally acting agents, or some combination of these, but excluded angiotensin-converting enzyme (ACE) inhibitors and angiotensin II receptor agonists (AIIAs).

Type of intervention
Primary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients with Type 2 diabetes and nephropathy, who had a urinary albumin-to-creatinine ratio of at least 300 mg/g on a first morning specimen and serum creatinine between 1.3 and 3.0 mg/dL.

Setting
The setting was primary and secondary care. The economic study was carried out in the USA.

Dates to which data relate

Source of effectiveness data
The effectiveness data were derived from a single study.

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

Study sample
The study sample comprised 1,513 patients, of which 751 were randomised to losartan-CAHT and 762 to placebo-CAHT. The study sample appears to have been appropriate for the clinical study question. The average age of the patients enrolled in the study was 60 years and 63% were male. Seventeen per cent of the patients were Asian, 15% were Black, 49% were Caucasian, 18% were Hispanic and the remaining 1% were other races. Ninety per cent of the participants had diabetes of more than 5 years' duration. Ninety-three per cent were using antihypertensive drugs, 18% were current smokers, 34% had lipid disorders, 9% angina pectoris, 11% had experienced a myocardial infarction, 0.1% had undergone a coronary revascularisation, 64% had retinopathy, 50% had neuropathy and 9% had had an
amputation (see Other Publications of Related Interest).

**Study design**
This was a multinational, double-blind, randomised controlled trial with a follow-up of up to 4 years.

**Analysis of effectiveness**
The analysis of effectiveness was conducted on an intention to treat basis and included all randomised patients. The primary health outcome was the time to the first event of doubling of serum creatinine, ESRD or death. The groups were shown to be comparable at baseline.

**Effectiveness results**
Over 3.6 years, treatment with losartan-CAHT reduced the number of days with ESRD by 33.6 (95% confidence interval, CI: 10.9 - 56.3), or 31% per patient, compared with placebo-CAHT treatment.

Twenty-four per cent of the patients in the placebo group and 19% of patients in the losartan group withdrew from the study therapy due to side effects. In terms of the incidence of adverse effects, no statistically significant difference between the groups was observed.

Treatment with losartan was associated with a relative risk reduction in the incidence of ESRD of 29%, (p=0.002), compared with placebo treatment. It was also associated with a reduction in risk of 25%, (p=0.006), for a doubling of serum creatinine concentration.

In terms of overall mortality, no statistically significant difference between the groups was observed.

**Clinical conclusions**
AIIAs, which include losartan, are associated with reductions in the number of days with ESRD and are recommended as first-line therapy for patients with nephropathy, hypertension and Type 2 diabetes.

**Measure of benefits used in the economic analysis**
No summary measure of health benefit was used in the economic analysis. Hence, a cost-consequences analysis was performed.

**Direct costs**
The resource use quantities and the costs were not reported separately. The study included those costs relevant to a health care payer, such as a managed care organisation. The costs of ESRD care and losartan therapy were derived from published data. The costs were discounted at a rate of 3% per annum. No explicit justification was provided for the choice of discount rate, but it was one commonly used in US-based economic evaluations. The costs were reported as year 2001 US dollars. The method of adjusting for inflation was not specified. Patients who withdrew from the study therapy were assumed not to incur further mediation costs. The costs of adverse events and other medications were assumed to be equal between the two groups. The costs of monitoring serum creatinine and potassium levels were omitted as patients with diabetes and renal disease would be routinely monitored (see Other Publications of Related Interest).

**Statistical analysis of costs**
The cost data were treated deterministically. This was appropriate for the simple within-trial analysis performed using an outside point estimate of cost. Compared with placebo, treatment with losartan was found to reduce the costs associated with ESRD by $5,144 per patient over 3.5 years, (p=0.003). If an analysis that calculated patient-level costs had been possible, the associated variance in the mean cost estimated for each group may have altered the outcome of a
test for a statistically significant reduction in the costs.

**Indirect Costs**
The indirect costs were not included in the analysis.

**Currency**
US dollars ($). 

**Sensitivity analysis**
The authors stated that several univariate sensitivity analyses were performed, but little detail was provided.

**Estimated benefits used in the economic analysis**
See the 'Effectiveness Results' section.

**Cost results**
The mean ESRD-related cost associated with losartan-CAHT treatment was $12,714 over 3.5 years, compared with $17,858 for placebo-CAHT treatment.

The difference in cost between the two groups was $5,144 (95% CI: 1,701 - 8,586; p=0.003).

The costs of adverse events were assumed to be equal between the two groups.

Treatment with losartan was still cost-saving if the cost of ESRD decreased by 68%, or if the cost of losartan increased three-fold.

**Synthesis of costs and benefits**
Not applicable.

**Authors’ conclusions**
Treatment with losartan combined with conventional antihypertensive therapy (CAHT) resulted in a reduced incidence of end-stage renal disease (ESRD) and substantial cost-savings over 3.5 years.

**CRD COMMENTARY - Selection of comparators**
The choice of the comparator was conventional antihypertensive therapy, excluding ACE inhibitors and AIIAs. You must decide whether this represents current practice in your own setting. If ACE inhibitors or alternative AIIAs are available, this study may be inadequate to inform on the cost-effectiveness of losartan.

**Validity of estimate of measure of effectiveness**
The basis of the study was an intention to treat analysis of a multinational, double-blind, randomised controlled trial, which was appropriate for the study question. The authors confined their conclusions to patients with similar characteristics to those in the primary study. The treatment and placebo groups were shown to be comparable at analysis. The analysis of effectiveness was handled credibly.

**Validity of estimate of measure of benefit**
The benefits (and cost-savings) were based on the number of days gained without ESRD, as estimated in the primary
study.

Validity of estimate of costs
Several categories of cost common to both groups were omitted from the analysis, but otherwise, the analysis appears to have included all costs relevant to the perspective adopted. The omission of some of the costs is unlikely to have affected the authors' conclusion that treatment with losartan is cost-saving, as this would be the case for any cost attached to the treatment of ESRD that was greater than the cost of medication. The costs were not reported separately from the resource quantities. They were derived from published data and were discounted at a rate of 3% per annum. The costs were reported in year 2001 US dollars.

Other issues
The authors made appropriate comparisons of their results with other studies in patients with diabetes. They suggested that the results of the study are generalisable to the Medicare programme in the USA and to other health care systems where care for ESRD is costly. The authors do not appear to have presented their results selectively and their conclusions reflected the scope of the analysis. The authors reported that their study was limited by a follow-up period of only 3.5 years, but concluded that the data over 3.5 years were still important to decision-makers.

Implications of the study
The authors recommended that losartan be added to the treatment regimens of patients with Type 2 diabetes, nephropathy and characteristics similar to the patients involved in the effectiveness study in the USA. They also recommended that research be conducted to ascertain whether the cost-savings observed in the study would be sustained over the long run.

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Other publications of related interest


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