Cost effectiveness of losartan in patients with hypertension and LVH: an economic evaluation for Sweden of the LIFE trial

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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 the antihypertensive drug losartan for the prevention of stroke.

Type of intervention
Prevention.

Economic study type
Cost-utility analysis.

Study population
The study population comprised patients aged between 55 and 80 years who had essential hypertension (defined as a sitting blood pressure of 160 - 200 mmHg/95 - 115 mmHg) and LVH ascertained by electrocardiogram (ECG).

Setting
The setting was the community. The economic study was carried out in Sweden.

Dates to which data relate
The effectiveness data referred to 2002, while the cost data referred to 2002 to 2004. The price year was 2003.

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

Link between effectiveness and cost data
The cost of the study medication was taken from the same patient sample as that used in the effectiveness study.

Study sample
The results of the trial on which the cost-effectiveness analysis was based have been published in another paper (Dahlof et al. 2005, see 'Other Publications of Related Interest' below for bibliographic details) which also reported the details of power calculations, randomization, loss to follow up etc. The trial recruited 9,193 patients, of which 4,605 were randomised to losartan and 4,588 to atenolol. Detail of refusals to participate and exclusions from the study were reported in Dahlof et al 2005.

Study design
The study was an international, double-blind, randomised controlled trial with centres in Sweden, Denmark, Finland,
Iceland and Norway. The method of randomisation was not reported. The average length of follow-up was 5.5 years (minimum 4 years). The authors did not report any loss to follow-up.

Analysis of effectiveness
The analysis of effectiveness was conducted on an intention to treat basis. The primary health outcome was the absolute risk reduction in stroke, defined as the difference between groups in the cumulative incidence of stroke after 5.5 years follow-up. The groups appeared comparable at baseline in terms of their age, gender, country, blood pressure, Framingham risk score, hypertension and diabetes. The baseline degree of LVH and Framingham risk score were used to adjust analyses.

Effectiveness results
The absolute risk reduction in stroke with losartan was estimated to be 0.016 (95% confidence interval, CI: 0.007 to 0.025; p<0.001) compared with atenolol after 5.5 years' follow-up.

Clinical conclusions
The authors concluded that losartan is effective in preventing stroke in patients with hypertension and LVH.

Measure of benefits used in the economic analysis
The measures of health benefits used were the life-years gained and the quality-adjusted life-years (QALYs) gained. Life expectancy with stroke was estimated with the Weibull model applied to the LIFE data, with baseline degree of LVH and Framingham risk score as covariates. The health-related quality of life was measured by visual analogue scale (VAS), which was included in the primary effectiveness study and completed by patients. The VAS score was collected every 6 months during the trial, and the scores adjusted for baseline quality of life, baseline degree of LVH, baseline Framingham risk score, month of follow-up, and a time-dependent variable for stroke status. In addition, the authors performed a sensitivity analysis in which they converted VAS scores to utilities using a power function (Torrance et al. 1976, see 'Other Publications of Related Interest' for bibliographic details). The health benefits were discounted at an annual rate of 3%.

Direct costs
The resource use quantities were not reported separately from the costs. (Note: since this abstract was published the authors have informed us that "calculations were done by multiplication of number of units of resources and unit cost. Unit costs are reported. The number of units of different resources is available from the corresponding author"). The study included direct costs to the health service. The total cost comprised study medication costs and stroke-related costs. The stroke-related costs were obtained from published studies and unpublished sources. The source of the price data for study medication was the official Swedish price for the drugs. Discounting was relevant and a rate of 3% per annum was applied. The study reported the average costs per patient.

Statistical analysis of costs
A 95% CI around the total costs was generated using a non-parametric bootstrap method.

Indirect Costs
The authors included the indirect costs in a sensitivity analysis. The study included the net costs of increased life expectancy for patients in terms of the difference between annual consumption and production by age. The estimates were based on a published study. The authors also included the cost of production lost to morbidity resulting from stroke, but reported no further details. The costs and the quantities were not reported separately. Discounting was relevant and a rate of 3% per annum was applied. The costs were reported in 2003 prices.
Currency
Euros (EUR). The authors also reported some costs in Swedish kroner (SEK).

Sensitivity analysis
The authors conducted one-way sensitivity analyses around the discount rate, the calculation of utilities, and excluding the baseline covariates used for adjustment. Therefore, the sensitivity analyses addressed analytical methods.

Estimated benefits used in the economic analysis
The authors reported that losartan resulted in a gain of 0.092 (0.141 undiscounted) life-years (95% CI: 0.038 to 0.146) and 0.069 QALYs (95% CI: 0.028 to 0.109) compared with atenolol. The time horizon for the analysis was lifetime and a discount rate of 3% per annum was applied.

Cost results
The total per patient direct costs were estimated to be EUR 5,097 for patients treated with losartan, compared with EUR 4,808 for treatment with atenolol, over a patient's lifetime and using a discount rate of 3% per annum. The difference was EUR 289.

Synthesis of costs and benefits
The costs and benefits were combined to calculate the cost per QALY gained.

The incremental direct cost per QALY gained with losartan compared with atenolol was EUR 4,188 (95% CI: -3,546 to 33,009).

When a societal perspective was adopted (indirect costs included), the incremental direct cost per QALY gained with losartan compared with atenolol was EUR 11,710.

In none of the sensitivity analyses did the cost per QALY gained exceed EUR 50,000, which the authors stated was the threshold used by the Swedish Pharmaceutical Benefits Board.

Authors' conclusions
Losartan is cost-effective in preventing stroke in hypertensive patients with left ventricular hypertrophy (LVH) from both the perspective of a national health care system and a societal perspective.

CRD COMMENTARY - Selection of comparators
The economic analysis was based on a single effectiveness study, which might have determined the choice of losartan and atenolol as the comparators. Atenolol is a widely used beta-blocking agent in hypertension and was also relevant in the clinical trial form which the effectiveness data were derived. You should consider whether atenolol and losartan are commonly used antihypertensive treatments in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness data were derived from a single study. The double-blind, randomised controlled design was appropriate for determining the efficacy of losartan in preventing stroke. The prevention of stroke was not the primary outcome of the study, which had a primary combined end point of stroke, myocardial infarction and cardiovascular death. The authors decided to use an outcome measure not calculated in the effectiveness study, as they believed it would be of more use in an economic evaluation. The authors stated that their assumption, that the treatment effects were limited to the 5.5 year follow-up period of the study, might be a limitation of the analysis since long-term effects might have been omitted. The study sample consisted of patients from many countries. The authors reported that a test of interaction found no differences among the countries in stroke incidence, so the pooled results should be applicable.
to an analysis from a Swedish perspective. The patient groups were shown to be comparable at analysis, but baseline covariates were still included in an adjusted analysis.

**Validity of estimate of measure of benefit**
The estimation of benefits was modelled by estimating the life-years gained by preventing stroke. The life-years were then weighted by health-related quality of life using VAS scores collected in the effectiveness study. The authors admitted that the utility values implied by the VAS scores were higher than those found in other studies. The authors also reported that the age- and gender-matched data from Swedish life tables used to estimate life-years gained were a good match for the 5-year survival of patients who did not experience stroke in the effectiveness study.

**Validity of estimate of costs**
All the cost categories relevant to the perspective adopted were included in the analysis. The authors included the indirect costs in a sensitivity analysis. The costs and the quantities were not reported separately. The small amount of descriptive data provided in the study may limit the generalisability of the study results. Many of the cost estimates were derived from published studies. The authors used a non-parametric bootstrap method to calculate 95% CIs for the cost data, which was an appropriate method to use. Discounting was appropriately carried out given the lifetime horizon. The price year was reported, which will aid any future refractions exercises.

**Other issues**
The authors made appropriate comparisons of their findings with those from other studies. The issue of generalisability to other settings was not directly addressed, although the authors reported that "the direct stroke costs were within the range of costs estimated for other countries, such as The Netherlands, Australia, the US, and the UK". The authors do not appear to have presented their results selectively. The authors' conclusions reflected the scope of the analysis. No further limitations of the study were reported.

**Implications of the study**
The authors made no explicit recommendations for changes in policy or practice, or for further research.

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None stated.

**Bibliographic details**

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**Other publications of related interest**

MeSH
Aged; Antihypertensive Agents /economics /therapeutic use; Atenolol /economics /therapeutic use; Clinical Trials as Topic; Cost-Benefit Analysis; Double-Blind Method; Electrocardiography; Female; Humans; Hypertension /complications /diagnosis /drug therapy /economics; Hypertrophy, Left Ventricular /complications /diagnosis /drug therapy /economics; Losartan /economics /therapeutic use; Male; Middle Aged; National Health Programs /economics; Quality of Life; Quality-Adjusted Life Years; Randomized Controlled Trials as Topic; Risk Factors; Stroke /prevention & control; Sweden; Treatment Outcome

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