The potential economic consequences of cognitive improvement with losartan
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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 losartan (50 mg once daily), an angiotensin-converting enzyme inhibitor, to improve cognitive function in hypertensive patients.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised elderly mild-to-moderate hypertensive patients (diastolic blood pressure 90 to 114 mmHg), with no diagnosis of dementia at baseline and with a Mini-Mental State Examination (MMSE) score above 18. The MMSE index ranged from 0 (worst) to 30 (best). Patients with recent myocardial infarction or stroke, renal failure, chronic severe liver disease, or congestive heart failure were excluded.

Setting
The setting of the study was not stated. The economic study was carried out in Sweden.

Dates to which data relate

Source of effectiveness data
The effectiveness evidence came from a single study, which was based on a published trial (see Other Publications of Related Interest).

Link between effectiveness and cost data
The costing was conducted on a different sample of patients to that used in the effectiveness study.

Study sample
Power calculations, if performed, were not reported. The method of sample selection was not reported in the present study. In addition, it was not stated whether any individuals refused to participate or were excluded for any reason from the initial study sample. The study sample included 69 patients, of which 42 were in the losartan group and 27 in the HCTZ group. The mean age of the patients in the losartan group was 55 (+/- 11) years (age range: 30 - 73) and 20 were women. The mean age of the patients in the HCTZ group was 54 (+/- 10) years (age range: 32 - 70) and 13 were
women.

**Study design**
This was a double-blind, randomised controlled trial. The study was conducted in Italy, but the sites where the study was carried out were not mentioned. The method of randomisation was not reported. The follow-up lasted for 26 months and no patient was lost to follow-up. Routine laboratory tests and outcome assessments were performed at baseline and after 26 months. The study investigators were blinded to the patients' allocation to the study groups and the treatment findings.

**Analysis of effectiveness**
All of the patients completed the study. The analysis of the effectiveness was conducted on an intention to treat basis. The primary health outcomes used in the analysis were quality of life and cognitive functions. The quality of life was evaluated using a questionnaire with 46 items and ranged from 0 (death) to 1 (perfect health). Cognitive functions were assessed using the MMSE and the Sandoz Clinical Assessment Geriatric (SCAG). A score of less than 24 on the MMSE and more than 40 on the SCAG indicated cognitive impairment. However, only the results obtained with the MMSE scale were relevant for the present study. At baseline, the two study groups were well balanced and comparable with respect to their demographic and clinical characteristics.

**Effectiveness results**
The health index used for the evaluation of quality of life changed from 0.90 (+/- 0.08) to 0.96 (+/- 0.06) in the losartan group, (p<0.01), and from 0.89 (+/- 0.07) to 0.94 (+/- 0.08) in the HCTZ group, (p<0.02).

The values of the SCAG changed from 45 (+/- 9.8) to 37 (+/- 8.4) in the losartan group, (p<0.01), and from 46 (+/- 7.2) to 43 (+/- 8.6) in the HCTZ group, (p>0.05).

The values of the MMSE changed from 23 (+/- 3) to 27 (+/- 3) in the losartan group, (p<0.01), and from 24 (+/- 3) to 25 (+/- 2.7) in the HCTZ group, (p>0.05).

Both drugs lowered the blood pressure.

**Clinical conclusions**
The effectiveness analysis showed that losartan was significantly more effective than HCTZ in improving cognitive function among elderly patients with hypertension. There was an observed 3-point improvement in the MMSE value when comparing losartan and HCTZ.

**Measure of benefits used in the economic analysis**
No summary benefit measure was used in the economic analysis. A cost-consequences study was therefore carried out. The health benefits are associated with the effectiveness results.

**Direct costs**
Discounting was not applied, although it appears to have been relevant since the costs were incurred over a 3-year period. The unit costs were not reported separately from the quantities of resources used. The health services included in the economic evaluation were hospitalisation, accommodation, home help, and drug consumption. Accommodation included ordinary living, service apartment, home for the elderly, group living and nursing home. The cost/resource boundary adopted appears to have been that of the health service payer.

The costing was performed on a subsample of 438 patients who participated in a population-based study of 1,810 individuals in Stockholm during 1987 to 1989. The patients were selected in order to match those included in the effectiveness study (see Other Publications of Related Interest). Resource use was evaluated for the year following the
baseline interview when the MMSE was administered and, for a subsample of 271 individuals, 3.4 years (range: 1.7 - 4.6) after the baseline interview. The cost data were obtained from diagnosis-related groups for hospital stay, from published data for home help and accommodation, and from official price lists for the drugs. It was assumed that patient accommodation and the use of home help would not change in the year following the baseline interview. The price year was 2000.

**Statistical analysis of costs**
Regression analyses were carried out to evaluate the impact of the MMSE score on resource utilisation. Also, to evaluate the relationship between the MMSE score and the total costs of care.

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

**Currency**
Swedish kroner (SEK). The costs were also reported in Euros. The conversion rate was Euro 1 = SEK 8.4.

**Sensitivity analysis**
Sensitivity analyses were not carried out.

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

**Cost results**
The statistical analyses showed that inpatient stay was significantly higher in patients with low MMSE score, after controlling for age, and that the MMSE score was also related to the number of hours of home help. In addition, patients with lower MMSE scores were significantly older, but there was no relationship between gender and MMSE score.

There was a clear association between the MMSE score and the total costs of care. A 1-point difference in MMSE score was associated with a difference in the annual cost of care of about SEK 5,700 (Euro 655). The 95% confidence interval (CI) of the cost difference per MMSE point was SEK 2,800 - 8,500 (Euro 322 - 977).

In the 271 patients whose follow-up data were available, the annual costs of care increased by SEK 21,400 (Euro 2,540). The costs increased significantly more among patients whose MMSE score decreased than among those with no change or increase in their MMSE score.

The regression analysis showed that each 1-point reduction in the MMSE was associated with an increase in the annual cost of care by about SEK 9,000 (Euro 1,034). The 95% CI was SEK 6,600 - 11,800 (Euro 759 - 1,356).

Assuming that the benefit in MMSE score was reached in 12 months, the cost-savings associated with losartan were SEK 38,000 (Euro 4,524). The savings ranged from SEK 10,800 (Euro 1,241) to SEK 65,200 (Euro 7,494) depending on the time required to reach the benefit.

The savings far exceeded the cost of losartan over the study period (SEK 5,700; approximately Euro 655). The cost-savings relative to HCTZ for a 3-point improvement were about SEK 28,500 (Euro 3,395).

**Synthesis of costs and benefits**
Not relevant because a cost-consequences analysis was carried out.
Authors' conclusions
The improvements in cognitive function obtained with losartan, compared with hydrochlorothiazide (HCTZ), led to economic benefits beyond those expected in terms of blood pressure control among patients with hypertension.

CRD COMMENTARY - Selection of comparators
The authors compared the study treatment with HCTZ, because this was the comparator in the primary trial used to provide the effectiveness evidence. However, the authors noted that alternative treatments for hypertension exist and may have different effects on cognitive status. You should decide whether HCTZ represents a valid comparator in your own setting.

Validity of estimate of measure of effectiveness
The analysis of the effectiveness was based on a single study, which had been published. The study was a randomised trial. A blinded assessment was performed and the length of follow-up was reported. No loss to follow-up was observed. The study design ensures the high internal validity of the analysis. However, some issues need highlighting. For instance, the methods of sample selection and randomisation were not reported. Also, power calculations were not carried out and the authors did not provide any evidence that the initial study sample was adequate for the study question. These aspects of the clinical study may have been reported in the associated publication (see Other Publications of Related Interest). The setting of the study was unclear.

Validity of estimate of measure of benefit
No summary benefit measure was used in the economic analysis. The analysis was therefore categorised as a cost-consequences study.

Validity of estimate of costs
The perspective adopted in the study was not explicitly stated, although it appears to have been that of the health service payer. It was unclear whether all of the relevant categories of costs were included in the analysis. The authors stated that the costs of informal care and indirect costs were not included in the analysis and that their impact on the estimated costs was not easy to predict. The unit costs and the quantities of resources used were not reported separately, thus limiting the reproducibility of the study results to other settings. Further, sensitivity analyses were not performed and the cost estimates were specific to the study setting. The authors noted that a limitation of the analysis could have been the fact that the costing was carried out on a sample of patients different from that used in the effectiveness study.

Other issues
The authors compared their findings with those from published studies evaluating the cognitive effects of blood pressure-lowering drugs. The details of the studies, such as the study sample, comparators and measure of cognitive function, were reported. The authors stated that the available evidence was quite inconclusive. The issue of the generalisability of the study results to other settings was not addressed and no sensitivity analyses were conducted. Thus, the external validity of the analysis may be low, bearing in mind that local estimates of the costs were used. The conclusions of the study appear to have been consistent with the aim of the analysis. The authors highlighted some limitations of their study. For example, the analysis did not distinguish between decline and improvement in cognitive function scores. Also, the improvement in MMSE score was based on data coming from Italy, which may not be fully transferable to the Swedish population. Further limitations noted by the authors have been reported in prior sections.

Implications of the study
The main implication of the study is that, compared with HCTZ, losartan produces improvements in cognitive function among hypertensive patients, which lead to cost-savings. However, caution is required when interpreting the results of
the study, due to the limitations of the analysis. The authors suggested that further studies should be carried out to confirm the results of their analysis, particularly among patients aged older than 75 years.

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**Other publications of related interest**

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