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
Antihypertensive therapies were examined. These included diuretics, beta-blockers, calcium-channel blockers, angiotensin-converting enzyme (ACE) inhibitors, and various combinations of these.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients aged 20 to 69 years with hypertension (blood pressure of at least 160 over 95 mmHg, or taking antihypertensive drugs). Those with a diagnosis of bronchitis or diabetes were also considered.

Setting
The setting is likely to have been primary care. The economic study was conducted in the metropolitan area of Pelotas, Rio Grande do Sul, Brazil.

Dates to which data relate
The effectiveness and resource use data were gathered from December 1999 to April 2000. The price year was 2002.

Source of effectiveness data
The effectiveness evidence was derived from a single study.

Link between effectiveness and cost data
The costing was conducted prospectively on a sub-group of patients that were included in the effectiveness study.

Study sample
Power calculations were conducted in the preliminary phase of the study. These suggested that a sample of 1,800 individuals would be required to obtain a prevalence ratio of 1.6 with 80% power and a 5% alpha error for presentations ranging from 25 to 75%. An additional 10% of patients were enrolled to account for potential refusals, and a further 15% to ensure sufficient power for a multivariate analysis. A total of 1,257 families were identified, but 57 did not fulfil the age criterion and 4.5% could not be reached or refused to participate. Thus, the final sample comprised 1,145 families (95.4%) containing 2,177 persons, although only 1,968 (90.4%) were interviewed.
Study design
This was a prospective cross-sectional study, which was carried out in the area of Pelotas in Brazil. Thus, there was no explicit control group. The participants were randomly selected from 40 census sections using cluster sampling techniques. In each section, a starting point of one street block was selected at random and the first house was identified, followed by systematic sampling of the next 30 houses. The patients were not followed up. The patients were interviewed using a standardised pre-coded questionnaire and blood pressure was measured at home. All of the interviewers were trained and certified in the technique of interviewing and taking blood pressure measurements. The supervisors reviewed the questionnaire by repeating 10% of the interviews at random using a short version of the questionnaire.

Analysis of effectiveness
All of the patients included in the final sample were considered in the effectiveness study. The outcome measures were the rate of patients with hypertension, the proportion of patients using each antihypertensive therapy, and the percentage of patients with controlled hypertension.

Effectiveness results
The percentage of patients with hypertension was 23.5% (462 out of 1,968).

Diuretics were used in 27.4%, beta-blockers in 12%, calcium-channel blockers in 3%, ACE inhibitors in 9.7%, diuretics plus beta-blockers in 13.9%, diuretics plus calcium-channel blockers in 5%, diuretics plus ACE inhibitors in 11.6%, beta-blockers plus calcium-channel blockers in 2.3%, beta-blockers plus ACE inhibitors in 1.2%, and other combinations in 13.1%.

The mean percentage of patients with controlled hypertension was:

- 54.9% (95% confidence interval, CI: 43.3 - 66.5) for diuretics,
- 71% (95% CI: 55 - 86.9) for beta-blockers,
- 80% (95% CI: 55.2 - 104.7) for calcium-channel blockers,
- 52% (95% CI: 32.4 - 71.6) for ACE inhibitors;

- 55.6% (95% CI: 39.3 - 71.8) for diuretics plus beta-blockers,
- 61.5% (95% CI: 35.1 - 88) for diuretics plus calcium-channel blockers,
- 36.7% (95% CI: 19.4 - 53.9) for diuretics plus ACE inhibitors,
- 50% (95% CI: 10 - 90) for beta-blockers plus calcium-channel blockers,
- 66.7% (95% CI: 13.3 - 120) for beta-blockers plus ACE inhibitors;

- 47% (95% CI: 30.3 - 63.8) for other combinations.

Clinical conclusions
The effectiveness analysis showed that hypertension control was obtained more frequently with calcium-channel blockers and beta-blockers than with diuretics and ACE inhibitors.

Measure of benefits used in the economic analysis
The summary benefit measure used in the economic analysis was the percentage of patients with controlled hypertension. This was derived directly from the effectiveness study.

Direct costs
Discounting was not relevant because the costs were incurred during one year. The unit costs were not reported separately from the quantities of resources used. The health services included in the economic analysis were drugs, health insurance, medical consultations, laboratory tests, and transportation and meals. The cost/resource boundary adopted in the study was not explicitly stated, but it appears to have been that of the patient.

Resource use was estimated using data gathered through questionnaires alongside the effectiveness study from December 1999 to April 2000. A group of 259 patients who had a medical appointment within the month preceding the
interview was included in the analysis. The unit costs were based on the average official cost for each drug class, and on patient reports for the other cost components. The price year was 2002. Monthly mean costs were calculated to compare the costs of hypertension treatment with those associated with diabetes and bronchitis care. The annual therapy costs were calculated for each class of antihypertensive treatment.

Statistical analysis of costs
No statistical test of the costs was conducted, but the costs were presented as mean values with standard deviations.

Indirect Costs
Indirect costs were included in the analysis. These were calculated from workdays lost due to disease, medical consultations, or performing tests. The unit cost was estimated from the proportional per-capita income earned during one working day in Brazil. However, the unit costs were not analysed separately from the quantities of resources used. Discounting was not relevant and was not carried out. Although not explicitly stated, it appears that 2002 prices have been used.

Currency
Brazilian reais (R$).

Sensitivity analysis
Sensitivity analyses were not carried out.

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

Cost results
The estimated annual costs were:

- R$63.84 with diuretics, R$162.24 with beta-blockers, R$609.60 with calcium-channel blockers, and R$316.44 with ACE inhibitors; and

- R$161.88 with diuretics plus beta-blockers, R$531.12 with diuretics plus calcium-channel blockers, R$459.60 with diuretics plus ACE inhibitors, R$522.72 with beta-blockers plus calcium-channel blockers, R$622.68 with beta-blockers plus ACE inhibitors, and R$654.24 with other combinations.

In the analysis of burden of disease, the estimated monthly per patient costs were R$89.90 (+/- 128.56) for hypertension, R$80.64 (+/- 245.22) for diabetes mellitus, and R$92.63 (+/- 254.22) for chronic bronchitis.

Synthesis of costs and benefits
An average cost-effectiveness ratio was calculated to combine the costs and benefits of the antihypertensive therapies.

The cost per patient with controlled hypertension was:

- R$116.3 with diuretics, R$228.5 with beta-blockers, R$762 with calcium-channel blockers, and R$608.5 with ACE inhibitors;

- R$291.2 with diuretics plus beta-blockers, R$863.6 with diuretics plus calcium-channel blockers, R$1,252.3 with diuretics plus ACE inhibitors, R$1,045.4 with beta-blockers plus calcium-channel blockers, and R$933.6 with beta-blockers plus ACE inhibitors;
A cost-effectiveness analysis, stratified by co-morbidities (diabetes or smoking), was also conducted. This showed that a less favourable cost-effectiveness relationship was observed for monotherapy with beta-blockers (R$321 versus R$215.28) and diuretics (R$127.98 versus R$109.88) or in association (R$388.06 versus R$299.15).

Patients without co-morbidities were associated with a less advantageous cost-effectiveness ratio for ACE inhibitors (R$869.73 versus R$487.73) and calcium-channel blockers (R$1,052.59 versus R$629.68).

Authors’ conclusions

Diuretics or beta-blockers were more cost-effective than angiotensin-converting enzyme (ACE) inhibitors and calcium-channel blockers for the treatment of hypertension. The burden of treating hypertension was comparable to that for treating chronic bronchitis and diabetes mellitus.

CRD COMMENTARY - Selection of comparators

The selection of the comparators under evaluation appears to have been appropriate, as all existing antihypertensive therapies were considered in the study. Both monotherapies and combined therapies were considered. In the burden of disease analysis, hypertension was compared with two common chronic diseases (diabetes and bronchitis), which appears to have been appropriate. You should decide whether they represent relevant comparators in your own setting.

Validity of estimate of measure of effectiveness

The effectiveness evidence came from a prospective cross-sectional population-based study, which was appropriate to obtain a picture of the actual situation of hypertension in the general population. The authors stated that this design had the advantage of including a representative sample of the entire population and it reflected the actual use of antihypertensive drugs. Further, power calculations were performed and a large sample was enrolled to take account of potential refusals. Overall, 90% of the individuals initially contacted were enrolled. The authors described the method of sample selection and sampling. However, this design was not the most appropriate for the study question, because there was no control group and exposure and disease were assessed simultaneously. The internal validity of the effectiveness analysis was low.

Validity of estimate of measure of benefit

The summary benefit measure was obtained from the effectiveness study and was specific to the study disease. Therefore, it would be difficult to compare the benefits of the therapies under evaluation with the benefits of other interventions.

Validity of estimate of costs

The perspective adopted in the study was not explicitly stated. Since it appears that the categories of costs included in the analysis were relevant to the patients, it can be suggested that this is the perspective from which the study was conducted. The indirect costs (productivity losses) were considered. The unit costs and the resources used were not analysed separately. The price year was provided, thus simplifying reflation exercises in other settings. The cost estimates were specific to the study setting and were estimated on the basis of patient reports. This may have introduced some error into the estimation of resource use. The issue of uncertainty in the estimates used in the analysis was not tested and sensitivity analyses were not conducted. The costs were presented as average values with standard deviations, but they were not compared statistically. However, the authors noted that the main cost driver (hospitalisation costs) was not considered. Thus, the costs may have been underestimated.

Other issues

The authors made several comparisons of their findings with those from studies conducted in other countries and settings. However, they did not address the issue of the generalisability of the study results to other settings. Sensitivity
analyses were not conducted and all the data used in the analysis were specific to the Brazilian setting. Thus, the overall external validity of the analysis was low. The authors noted some limitations of their analysis, such as the lack of hospital cost data.

**Implications of the study**
The authors stressed that the findings of their study may help health care planners to make a rationale allocation of resources between competing therapeutic options and priorities. However, the conclusions of the study should be interpreted with caution due to the limitations of the analysis.

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