Antihypertensive treatment based on blood pressure measurement at home or in the physician's office: a randomized controlled trial

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 study examined blood pressure (BP) measurement at home or in the physician's office as guides to initiate and titrate antihypertensive drug treatment. The self-measured BP (at home) was the average of all readings collected during the 7 days prior to each follow-up visit. After 5 minutes of rest in the sitting position, patients performed three consecutive self-measurements of BP twice daily, in the morning between 6 and 10am and in the evening between 6 and 10pm. The office BP was the average of three consecutive BP readings taken by the physician during the day during usual practice hours, after patients had rested for 5 minutes in the sitting position. The target for both measurements was a diastolic BP of 80 to 89 mmHg.

Regardless of the type of BP measurement, patients began or switched to monotherapy with lisinopril, 10 mg/day (step 1). Treatment could then be intensified step by step, by doubling lisinopril to 20 mg/day (step 2), by combining lisinopril with hydrochlorothiazide 25 mg/day, or amlodipine 5 mg/day (step 3), and finally by adding amlodipine 5 mg/day (in patients taking the combination of lisinopril and hydrochlorothiazide or prazosin) or up to 6 mg/day in other patients (step 4). If the diastolic BP level guiding treatment was above the target (>89 mmHg), medical treatment was intensified by one step. If the diastolic BP level was within the target range (80 - 89 mmHg), medical treatment was left unchanged. If the diastolic BP level was below the target (<80 mmHg), medical treatment was reduced by one step. For patients receiving step 1 treatment this meant discontinuation of antihypertensive drug treatment.

Type of intervention
Primary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised adult patients with hypertension who were either untreated or treated with no more than two different antihypertensive agents. The exclusion criteria included heart failure, unstable angina pectoris, Stage 3 or 4 hypertensive retinopathy, and a history of myocardial infarction or stroke within 1 year of enrolment. Further exclusion criteria were severe noncardiovascular disease (e.g. cancer or liver cirrhosis), a serum creatinine concentration higher than 177 micromol/L (2.0 mg/dL), mental disorders and substance abuse.

Setting
The setting was primary care. The economic study was carried out in Belgium and Ireland.

Dates to which data relate
The effectiveness and resource use data were gathered from March 1997 to April 2002. 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 carried out prospectively on the same sample of patients as that used in the effectiveness analysis.

Study sample
Power calculations were performed in the preliminary phase of the study. These suggested that 200 patients in each treatment group would be required to detect differences of 5 mmHg in systolic BP, or 2 mmHg in diastolic BP, with 85% power at a 5% significance level. Of the 606 patients who were assessed for eligibility at the study institutions, 206 were excluded. Reasons for exclusion were office diastolic BP less than 95 mmHg (112), did not meet other inclusion criteria (17), consent not given (50), and unavailable for follow-up (27). This left a sample of 400 patients for allocation to the two study groups. One hundred and ninety-seven patients (51.8% women) were assigned to the office group and 203 (52.7% women) to the home group. The mean age of the patients was 52.6 (+/- 12.0) years in the office group and 54.2 (+/- 12.1) years in the home group, and the body mass index (BMI) was 27.7 (+/- 4.4) and 28.5 (+/- 4.7), respectively.

Study design
This was a prospective, blinded, randomised clinical trial that was carried out at 56 primary care practices and 3 hospital-based outpatient clinics in Belgium and 1 specialised hypertension clinic in Dublin, Ireland. The patients were stratified by centre and were then randomised to study groups using a computerised random-number function. The length of follow-up was 1 year. Follow-up visits were scheduled at 1 and 2 months and thereafter at 2-month intervals. The number of patients who withdrew from the study was 26 in the office group (10 missed at least 1 follow-up visit and 16 dropped out) and 27 in the home group (11 missed at least 1 follow-up visit, 14 dropped out, and 2 experienced adverse events). A physician at the coordinating centre, who was blinded to randomisation, made all treatment decisions on the basis of the BP measurements he received. The field investigators then implemented his treatment decisions.

Analysis of effectiveness
The analysis of the clinical study appears to have been conducted on an intention to treat basis since all patients included in the initial study sample were considered in the analysis of effectiveness. The outcome measures used were treatment intensity, BP control, patient compliance, symptoms, major adverse events and left ventricular mass. Symptoms were assessed using a score based on 33 questions. The study groups were comparable at baseline in terms of their demographics and BP values.

Effectiveness results
More home than office patients could stop antihypertensive drug treatment, as their diastolic BP was less than 80 mmHg and thereafter stabilised at or below the target range (25.6% versus 11.3%; 2.2 versus 1.0 patients per 100 followed up for 1 month; p<0.001). An opposite trend was observed for patients proceeding to multiple-drug treatment (38.7% versus 45.1%; 3.3 versus 3.8 patients per 100 followed up for 1 month; p=0.14). A further analysis showed that in the home BP group, a lower home diastolic BP at entry and the lack of previous treatment independently predicted permanent cessation of antihypertensive drug therapy. However, in the office BP group, only the lack of previous treatment predicted stoppage of antihypertensive treatment.

BP control was better in the office group than in the home group. In particular, after adjusting for baseline BP, gender, age and BMI, the final differences between the two treatment groups ranged from 4.8 to 6.8 mmHg for systolic BP and from 2.9 to 3.5 mmHg for diastolic BP. For example, the difference between groups in the decrease in 24-hour systolic BP was 4.9 mmHg (95% confidence interval, CI: 2.5 - 7.4; p<0.001) in favour of the office group. Similarly, the difference between groups in the decrease in 24-hour diastolic BP was 2.9 mmHg (95% CI: 1.4 - 4.4; p<0.001), again in favour of the office group.
In terms of patient compliance, office patients and home patients with available pill counts (159 and 169, respectively) took similar percentages of the prescribed dosages of the study medications (89.3% versus 90.1%; p=0.90).

No statistically significant differences in symptoms, adverse events and left ventricular masses were observed between the groups. At the end of the trial, there was a marginal benefit only for the echocardiographic E:A ratio in the office group compared with the home group (change of 0.15 in the office group and change of -0.07 in the home group; p=0.02).

**Clinical conclusions**
The effectiveness analysis showed that BP control was better in office patients than in home patients, although more individuals in the latter group could stop antihypertensive treatment.

**Measure of benefits used in the economic analysis**
The health outcomes were left disaggregated and no summary benefit measure was used in the economic analysis. In effect, a cost-consequences analysis was carried out.

**Direct costs**
The analysis was carried out from the perspective of the Belgian health insurance system. It included physician fees, drug acquisition costs, and the depreciation rate of the home BP measurement device. The unit costs were reported, but information on quantities of resources used was not given for all items. Resource use was estimated using data derived from the sample of patients included in the clinical trial. The source of the costs was not explicitly stated, but the costs were likely to reflect monetary rates of the Belgian health insurance system. Assumptions about resource use were clearly reported. Discounting was not relevant since the costs per patient were incurred during a 1-year period. The price year was 2002.

**Statistical analysis of costs**
Standard statistical analyses were performed to test the statistical significance of cost-differences.

**Indirect Costs**
The indirect costs were not included.

**Currency**
Euros (EUR). The exchange rate from Euros into US dollars ($) on January 2004 was EUR 1 = $1.27.

**Sensitivity analysis**
Sensitivity analyses were not performed.

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

**Cost results**
The total costs per 100 patients for treatment for 1 month were EUR 3,875 (+/- 1,723) in the office BP group and EUR 3,522 (+/- 1,747) in the office BP group. The difference of EUR 353 (+/- 175) was statistically significant, (p=0.04).

In general, office BP was associated with higher physicians and drug costs that were not completely offset by the higher cost of monitoring associated with home BP.
Synthesis of costs and benefits
A synthesis of the costs and benefits was not relevant since a cost-consequences analysis was carried out.

Authors' conclusions
Home-based blood pressure (BP) measurement for patients with hypertension led to less intensive drug treatment and marginally lower costs in comparison with BP measurement in the physician's office, but also to less long-term BP control. General well-being and electrocardiographic or echocardiographic left ventricular mass were comparable between groups. Self-measurement allowed the identification of patients with white-coat hypertension.

CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparators was clear since the standard approach to BP measurement (i.e. at the physician's office) was compared with the proposed alternative approach (self-measurement). You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness evidence came from a clinical trial, which was appropriate for the study question. The randomised and prospective design should limit the potential impact of selection bias and confounding factors. The method of sample selection and details of the follow-up were reported. The use of intention to treat to deal with missing values and the baseline comparability of the study groups represent further strengths of the analysis. The size of the sample was justified on the basis of statistical calculations. Partial blinding was used, which should control for assessment bias. The patients were enrolled at several centres, thus the study sample should be representative of the patient population. The length of follow-up appears to have been appropriate. These issues tend to enhance the internal validity of the analysis.

Validity of estimate of measure of benefit
No summary benefit measure was used in the analysis because a cost-consequences analysis was conducted. Please refer to the comments in the 'Validity of estimate of measure of effectiveness' field (above).

Validity of estimate of costs
The analysis of the costs was consistent with the perspective adopted, thus only the direct medical costs were included. Since resource consumption was estimated from the sample of patients included in the effectiveness analysis, it is likely to reflect actual treatment patterns. The source of the costs was unclear. Data on the quantities of resources used were limited, which limits the possibility of replicating the cost analysis in other settings. However, the unit costs were provided for most items. Statistical analyses of the costs were performed. The cost estimates were specific to the study setting and sensitivity analyses were not carried out.

Other issues
The authors discussed the results from other published clinical trials and explained the possible reasons for differences among the results. A more extensive comparison with the results of a recent trial comparable to the current study was made. The issue of the generalisability of the study results to other settings was not explicitly addressed and sensitivity analyses were not performed, which limits the external validity of the study. The authors highlighted some limitations of the study, such as the short follow-up and the lack of information on what time of day the office BP was measured. The analysis referred to patients with hypertension and this was reflected in the authors' conclusions.

Implications of the study
The study results supported a stepwise strategy for the evaluation of BP in which self-measurement and ambulatory monitoring are complementary with conventional office measurement. However, prospective studies should be carried out to corroborate the current results. Self-measurement alone cannot be recommended as a unique type of BP control.
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