The pharmacoeconomic impact of amlodipine use on coronary artery disease
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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 study examined standard care supplemented by amlodipine besylate (AB) for patients with coronary artery disease (CAD).

Type of intervention
Secondary prevention.

Economic study type
Cost effectiveness analysis.

Study population
The study population was a hypothetical cohort of persons with angiographically documented CAD.

Setting
The setting was unclear. The economic study was carried out in Italy.

Dates to which data relate
The effectiveness and resource use data were derived from a prior study. The dates to which the data pertain were not specified. The price year was 2003.

Source of effectiveness data
The effectiveness data were derived from a single study (Pitt et al. 2000, see 'Other Publications of Related Interest' for bibliographic details).

Link between effectiveness and cost data
The costing was undertaken retrospectively on the same patient sample as that used in the effectiveness analysis.

Study sample
Limited details were reported in this paper. Overall, 825 individuals participated in the clinical trial. Details of any power calculations, method of sample selection, numbers in the intervention and control groups, and number of patients who refused to participate were not reported. Such details are likely to have been given in the paper reporting the clinical study (Pitt et al. 2000).

Study design
The study was a multi centre, randomised, placebo controlled, double blind clinical trial. The duration of follow-up was
3 years. The loss to follow up was not reported, nor was any method of blinding used in the assessment of the outcomes (see Pitt et al. 2000 for details).

**Analysis of effectiveness**
It was not stated whether the analysis of the clinical study was conducted on an intention to treat basis or on treatment completers only. All participants had angiographically documented CAD, which suggested that the groups were comparable at baseline (see Pitt et al. 2000 for details).

**Effectiveness results**
The results were reported on the basis of 1,000 individuals per group:

- the frequency of all cause mortality was 14.39 in the AB group compared with 19.6 for standard care;
- the frequency of fatal and nonfatal myocardial infarction was 45.56 in the AB group compared with 49.02 for standard care;
- the frequency of fatal and nonfatal stroke was 1,199 in the AB group compared with 1,225 for standard care;
- the frequency of other fatal events was 0 in the AB group compared with 9.80 for standard care;
- the frequency of congestive heart failure was 2.4 in the AB group compared with 12.25 for standard care;
- the frequency of unstable angina was 1,443.88 in the AB group compared with 208.33 for standard care;
- the need for coronary artery bypass grafting was 40.77 in the AB group compared with 71.08 for standard care;
- the need for angioplasty, stenting and arthrectomy was 95.92 in the AB group compared with 164.22 for standard care;
- the frequency of patients with any vascular event or procedure was 206.24 in the AB group compared with 284.31 for standard care.

**Clinical conclusions**
The patients randomised to AB exhibited a significantly slower progression of carotid atherosclerosis, as well as fewer hospitalisations for unstable angina or congestive heart failure and coronary revascularisation procedures, in comparison with placebo-randomised patients. No treatment differences were found in the rates of all cause mortality and major cardiovascular events.

**Measure of benefits used in the economic analysis**
The measure of benefits used was the reduction in the number of patients with any vascular event or procedure.

**Direct costs**
The quantities were derived using data from the literature. Direct medical costs referred to the combination of therapy and cardiovascular related hospitalisations. The unit costs were reported separately. The costs were calculated by multiplying the resources consumed by their corresponding unit costs. Discounting was carried out appropriately. The estimation of costs was based on the diagnostic-related groups’ tariffs and Italian market costs. The price year was 2003.

**Statistical analysis of costs**
The costs were treated deterministically.
Indirect Costs
The indirect costs were not included.

Currency
Euros (EUR).

Sensitivity analysis
A one way sensitivity analysis was performed on the key parameters. The costs of drugs, hospitalisation and clinical outcomes were varied, as were discount rates. The ranges selected were based on authors’ assumptions. A multi way analysis, simultaneously changing all clinical and economic parameters, was also performed. A threshold analysis was performed to obtain an AB price that would produce the same cost for the two treatment alternatives studied.

Estimated benefits used in the economic analysis
Compared with standard care, the use of AB resulted in 78.07 fewer patients with any vascular event or procedure in the hypothetical cohort of 1,000 patients. The duration of follow-up was 3 years. Side effects of treatment were not considered in the economic analysis.

Cost results
The total cost for vascular events per 1,000 individuals was EUR 531,426.33 in the AB group and EUR 746,764.88 in the standard care group.

The cost for procedures was EUR 1,105,514.27 in the AB group and EUR 1,909,612.50 in standard care group.

The cost of pharmacological therapy was EUR 1,158,485.91 in the AB group and EUR 0.00 in the standard care group.

The total direct costs were EUR 2,795,426.52 for the AB group and EUR 2,656,377.37 for standard care.

The discount rate was 5%.

Synthesis of costs and benefits
The incremental cost per patient free from any event (i.e. the incremental cost-effectiveness ratio) was EUR 1,776.53.

The results of the evaluation remained stable when the discount rate was varied in the sensitivity analysis. However, the results were sensitive to variations in the drug cost, hospital cost or clinical variables.

The incremental cost-effectiveness ratio ranged from EUR 296.42 (best scenario) to EUR 5,065.68 (worst scenario) per patient free from any event.

The threshold cost of therapy with AB was found to correspond to a 16% reduction in the 2003 Italian market price.

Authors’ conclusions
The patients randomised to amlodipine besylate (AB) in the study exhibited a significantly slower progression of carotid atherosclerosis, had fewer hospitalisations for unstable angina or congestive heart failure, and underwent fewer coronary revascularisation procedures in comparison with placebo-randomised patients. No treatment differences were found in terms of the rates of all cause mortality and major cardiovascular events. AB therapy can be a cost effective strategy for the treatment of coronary artery disease (CAD) in Italy. Vascular events and the need for revascularisation procedures were reduced, and these savings significantly offset the drug costs.

CRD COMMENTARY - Selection of comparators
The techniques used and the alternatives available were determined by the PREVENT trial used in the study. Although the comparators were explicitly stated (standard care and AB with standard care), 'standard care' was not defined.

**Validity of estimate of measure of effectiveness**
Only limited details of the methods were provided. The reader may need to consult the parent clinical trial for details that affect the validity of the present study. However, the analysis of effectiveness was based on a multi centre, randomised, placebo controlled, double-blind study. This was an appropriate study design and will have minimised the influence of bias and confounding. This suggests that the estimate of measure of effectiveness is likely to have high validity.

**Validity of estimate of measure of benefit**
The reduction in the number of patients with any vascular event or procedure was the measure of benefit used in the economic analysis. The estimation of benefits was obtained directly from the effectiveness analysis. The authors acknowledged that the issues concerning health related life quality were not addressed. The use of a cost utility analysis, such as the cost per quality adjusted life-year, would have enhanced the comparability of this study with other health care programmes.

**Validity of estimate of costs**
The perspective adopted in the study was explicitly reported. All the categories of cost relevant to the perspective adopted were included in the analysis. Some relevant costs were omitted from the analysis, for example, the authors acknowledged that the costs of non study drugs were not included. The cost of treating side effects and the indirect costs were also excluded from the analysis. A sensitivity analysis of the quantities was conducted using ranges that appear to have been appropriate. The unit costs and the price year were reported, which would assist in transferability and reflation exercises.

**Other issues**
The authors made appropriate comparisons of their findings with those from other studies. They acknowledged a number of further limitations to their study. In particular, the use of a study carried out in the USA which may not be generalisable and the lack of data on the indirect costs of treatment.

**Implications of the study**
The study suggests that AB can be cost effective when administered to patients affected by CAD and that this alternative should therefore be considered by decision-makers seeking to optimise the allocation of health care resources.

**Source of funding**
None stated.

**Bibliographic details**

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Other publications of related interest
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