Amlodipine treatment in patients undergoing PTCA in the UK: a cost-effectiveness analysis

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 amlodipine after percutaneous transluminal coronary angioplasty (PTCA), from 2 weeks prior to PTCA until 4 months after the intervention. The dose used was 5 mg during the first week and 10 mg thereafter.

Type of intervention
Secondary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients undergoing PTCA.

Setting
The setting seems to have been primary care and a hospital. The economic study was performed in the UK.

Dates to which data relate
The dates to which the effectiveness data and most of the cost data related, were not reported. Only the inpatient costs were reported to have been obtained in 1999. The price year was not reported.

Source of effectiveness data
The effectiveness data were derived from a single study, the results of which have been published elsewhere (Jorgensen et al., see Other Publications of Related Interest).

Link between effectiveness and cost data
The costing was not carried out on the same sample as that used for the effectiveness analysis.

Study sample
The authors did not report that sample calculations were performed in the planning phase of the single study to assure a certain power. In total, 635 patients were selected. Of the 585 (92.1%) who underwent PTCA, 291 were randomised to amlodipine and 294 to placebo. Patients with stents were excluded.

The method used to select the study sample was not reported. In addition, the authors did not provide any evidence that the study sample was representative of the study population.
Study design
The single study was a prospective, randomised, double-blind, multi centred trial (the authors reported that patients from different centres in Canada and Norway were considered in the effectiveness analysis). The period of follow-up considered at analysis was 4 months. The method of randomisation was not reported in this paper.

Analysis of effectiveness
The basis for the effectiveness analysis appears to have been intention to treat, although this was not explicitly stated. The health outcomes assessed in the effectiveness analysis for both groups (amlodipine and placebo) were mortality rates and the rates of having an MI, CABG, repeat PTCA, at least one adverse clinical event, or any adverse clinical event. The number of patients experiencing each event was also reported. The authors did not provide any evidence that the study groups were comparable at analysis.

Effectiveness results
The mortality rate was 0.3% (1 patient) in the amlodipine group and 0.3% (1 patient) in the placebo group, (p=0.99).

The rate of experiencing a MI after an initial PTCA was 1.7% (5 patients) in the amlodipine group, and 3.7% (11 patients) in the placebo group, (p=0.13).

The rate of having a CABG after an initial PTCA was 1.7% (5 patients) in the amlodipine group, and 4.4% (13 patients) in the placebo group, (p=0.058).

The rate of patients having a repeated PTCA was 3.1% (9 patients), and 7.8% (23 patients) in the placebo group, (p=0.011).

At least one clinical adverse event was experienced by 6.9% (20 patients) in the amlodipine group, and by 13.6% (40 patients) in the placebo group, (p=0.007).

Any adverse clinical event was experienced by 6.9% (20 patients) in the amlodipine group, and 16.3% (48 patients) in the placebo group.

These effectiveness results were included as input parameters in the decision tree model. It was assumed that the probabilities of the adverse events were mutually exclusive, that is, the authors considered only the independent rates of each one of the events in the model, and not the rates of having at least one or any adverse clinical events.

Clinical conclusions
The results of the single study showed that the use of amlodipine after PTCA significantly reduced the probability of having CABG, repeat PTCA, and, in general, the probability of experiencing at least one adverse clinical event and any adverse clinical event.

Modelling
A decision tree model was used to assess the impact of amlodipine on the risk of myocardial infarction (MI), repeat PTCA, coronary artery bypass grafting (CABG) and the subsequent total health care costs.

Measure of benefits used in the economic analysis
No summary measure of health benefit was used in the economic analysis. A cost-consequences analysis was therefore performed.

Direct costs
The resource quantities and the costs were not reported separately. The direct costs considered at analysis were those of
the health service. These included the inpatient (total and total urgent costs) and outpatient costs for PTCA, CABG and MI. The outpatient costs for each outcome were for laboratory tests, physician visits, drug costs and long-term care (not PTCA).

The costs were estimated using both actual data and expert opinion (since a Delphi panel approach was developed to obtain the outpatient costs). The inpatient costs were obtained from the 1999 National Schedule of Reference Costs of the NHS. The costs of physician visits, laboratory tests, treatment and rehabilitative care were obtained from 3 hospitals. The drug costs were taken from the British National Formulary (no. 37). The RITA trial (see Other Publications of Related Interest) was consulted to obtain the incremental costs associated with multiple revascularisation procedures within a single hospitalisation. The outpatient costs were obtained using a modified Delphi panel approach, in which 5 cardiology experts were asked for the relevant outcomes and the type and frequency of outpatient health care resources used during the treatment and follow-up for MI, PTCA and CABG.

The study reported the average costs. The price year was not given. Discounting was not performed, which was appropriate as the period of follow-up considered at analysis was 4 months.

**Statistical analysis of costs**
No statistical analysis of the costs was reported.

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

**Currency**
UK pounds sterling (€).

**Sensitivity analysis**
The authors reported that both one-way and multi-way sensitivity analyses were carried out to evaluate the robustness of the results when key parameters were changed. The area of uncertainty investigated was variability in the data. In the one-way sensitivity analyses, the authors considered a 20% increase and decrease of the inpatient medical costs, and changes in the rates of adverse clinical outcomes of amlodipine after PTCA. In the multi-way sensitivity analyses, the probabilities of adverse clinical events were varied across the 95% confidence interval, and the costs were increased and decreased by a 10%. In addition, a secondary analysis was performed that considered the possibility that the events were not mutually exclusive, that is, the authors assumed that patients experiencing more than one event would incur only the cost of one event.

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

**Cost results**
The total expected cost was 3,832.82 for a patient receiving amlodipine after PTCA, and 4,036.91 for a patient receiving placebo after PTCA. Therefore, compared with placebo after PTCA, amlodipine after PTCA saved 204.09 per patient over 4 months.

When the secondary analysis was performed, the total expected cost for a patient receiving amlodipine after PTCA was the same, while this cost was reduced to 3,953 for a patient-receiving placebo after PTCA. Therefore, the cost-saving obtained with amlodipine was reduced to 121 per patient over 4 months.

The results from the other one-way and two-way sensitivity analyses showed that the results of the model were fairly robust. However, the model was sensitive to changes in the rates of events such that a 6.7% increase in the rate of
adverse clinical outcomes of PTCA with amlodipine resulted in a break-even of the total expected costs between the two cohorts.

**Synthesis of costs and benefits**
Not applicable due to the cost-consequences approach adopted.

**Authors' conclusions**
The use of amlodipine after percutaneous transluminal coronary angioplasty (PTCA) decreased the incidence of adverse clinical events. It therefore led to a reduction in the four-month total expected cost for patients using amlodipine, compared with those who received placebo. These cost-savings were mainly due to the fewer participants in the amlodipine group who had to undergo revascularisation procedures.

**CRD COMMENTARY - Selection of comparators**
The authors chose placebo as a comparator for the intervention drug. This allowed the active value of the treatment to be evaluated. You should decide if this is a valid comparator in your own setting.

**Validity of estimate of measure of effectiveness**
The analysis used prospective randomised double-blind trial, which was appropriate for the study question. The study sample was not shown to be representative of the study population, and the authors did not provide any evidence that the patient groups were comparable at analysis. However, the fact that the patients were randomised to one of the two groups may have increased the probability of the groups being comparable. No statistical analysis was reported to take account of potential biases or confounding factors. This introduces uncertainty into the reliability of the conclusions. The authors highlighted the fact that patients with stents were not considered for the effectiveness analysis, which was unfortunate since the practice of coronary stenting with PTCA is one currently used because it improves thrombosis and restenosis rates.

**Validity of estimate of measure of benefit**
The authors did not derive a summary measure of health benefit. The analysis was therefore categorised as a cost-consequences analysis. The authors reported one limitation, namely the fact that quality of life, which is an important outcome measure in this kind of intervention, was not considered in the analysis.

**Validity of estimate of costs**
All the categories of costs relevant to the perspective adopted appear to have been included in the analysis. The costing was not performed using the same sample as that in the effectiveness analysis, which may have biased the results obtained. The resource quantities and the costs were not reported separately. Further, a Delphi panel approach was used to estimate the outpatient resource use and costs, which may have introduced uncertainty into the reliability of the conclusions. The fact that the sensitivity analyses showed fairly robust results for the model (regarding the costs considered at analysis), helps to overcome this uncertainty. The dates to which the costs related were not given, and neither was the price year. These factors may hinder reflation exercises to other settings.

The authors reported that only the direct costs were considered at analysis, and the indirect costs derived from the loss of productivity were not included. If a wider perspective were to be adopted (that is, a societal one), these costs should be included in the economic analysis. Moreover, as the authors stated, the time horizon considered in the model was quite short, although they justified their choice arguing that it was uncertain whether the health benefits observed in the four-month clinical trial would have persisted for a longer period.

**Other issues**
The authors did not make appropriate comparisons of their findings with those from other studies. The issue of the
generalisability of the results to other settings was addressed. The authors reported that, since the effectiveness analysis considered patients from Canada and Norway, the results of the trial might not have been generalisable to the UK population, which limits the value of the economic results obtained. The authors do not appear to have presented the results selectively. The conclusions of the study reflect the scope of the analysis.

**Implications of the study**
The results of the study show favourable outcomes for the use of amlodipine after PTCA, in terms of lower rates of adverse clinical events and, therefore, fewer repeat procedures needed. The use of amlodipine after PTCA was shown to be cost-saving. The authors recommend that further research should be performed to quantify the benefits, in terms of quality of life, that amlodipine generates because of the lower revascularisation rates among patients receiving it.

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**Bibliographic details**

**Other publications of related interest**


**Indexing Status**
Subject indexing assigned by CRD

**MeSH**
Amlodipine /economics /therapeutic use; Angioplasty, Transluminal, Percutaneous Coronary /adverse effects /economics; Calcium Channel Blockers /economics /therapeutic use; Comparative Study; Coronary Artery Bypass; Cost-Benefit Analysis; Decision Trees; Drug Costs /statistics & numerical data; Graft Occlusion, Vascular /surgery; Great Britain; Humans; Mortality; Myocardial Infarction; Outcome Assessment (Health Care) /economics

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