A cost-effectiveness evaluation of amlodipine usage in patients with coronary artery disease in Sweden


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 (10 mg/day), for the prevention of atherosclerosis in patients with coronary artery disease (CAD).

Type of intervention
Secondary prevention.

Economic study type
Cost-effectiveness study.

Study population
The study population comprised a hypothetical cohort of patients with CAD.

Setting
The setting was primary care. The economic study was carried out in Sweden.

Dates to which data relate
No dates for the effectiveness or resource use data were reported. Part of the effectiveness data were derived from a study published in 2000. The price year was unclear.

Source of effectiveness data
The effectiveness evidence was based on authors’ assumptions, which were partly derived from a published study, the Prospective Evaluation of the Vascular Effects of Norvasc Trial (PREVENT) (Pitt et al, see Other Publications of Related Interest).

Modelling
A Markov model was constructed to simulate event- and procedure-related health economic outcomes of CAD among 1,000 hypothetical patients on amlodipine treatment, in comparison with placebo. The model had a time horizon of 3 years (the length of follow-up in the PREVENT study). The health states involved were good health, angina, myocardial infarction (MI), congestive heart failure (CHF), percutaneous transluminal coronary angioplasty (PTCA), coronary artery bypass grafting (CABG), long-term care, and death. Each cycle lasted 6 months. Transition probabilities were derived from the authors’ assumptions, which were partly based on data from PREVENT, adjusted according to Swedish data.

Outcomes assessed in the review
The outcomes were derived from a single study and the authors’ assumptions. The outcomes included were hospitalisation for angina, hospitalisation for MI, hospitalisation for CHF, PTCA, CABG, death, and adverse cardiovascular clinical outcomes. No review of the literature was conducted.

**Study designs and other criteria for inclusion in the review**
No inclusion criteria were reported. However, the one study used was a randomised, double-blind placebo-controlled trial.

**Sources searched to identify primary studies**
Not reported.

**Criteria used to ensure the validity of primary studies**
Not reported.

**Methods used to judge relevance and validity, and for extracting data**
Not reported.

**Number of primary studies included**
Only one study was used.

**Methods of combining primary studies**
No combination was necessary since there was only one study.

**Investigation of differences between primary studies**
Only one study was used.

**Results of the review**
Not stated.

**Methods used to derive estimates of effectiveness**
The authors made some assumptions to derive the effectiveness evidence. Most of the assumptions were based on data derived from the PREVENT study and then adjusted to reflect Swedish epidemiological patterns. Thus, the original PREVENT data were not used directly in the decision model, but were matched with procedure rates reported in the European Society of Cardiology's European registries of cardiovascular diseases and patient management (see Other Publications of Related Interest). These assumptions were made on the basis of a modified Delphi panel study that involved Swedish experts.

**Estimates of effectiveness and key assumptions**
The authors assumed that patients in the treatment arm took a 10 mg/day dose of amlodipine throughout the simulation, or until death, in addition to other cardiovascular medications. They also assumed that the initial staging cohort was in good health. For the hypothetical cohort of 1,000 Swedish patients, the total number of hospitalisations due to angina was assumed to be 336 in the treatment group (t) and 406 in the control group (c). The corresponding values for the other outcomes 41(t) and 41(c) for MI, 10(t) and 42(c) for CHF, 61(t) and 119(c) for PTCA, and 22(t) and 40(c) for CABG. The overall number of estimated hospitalisations per 1,000 patients in the Swedish population over 3 years was 470 (47%) in the intervention group and 648 (64.8%) in the control group. Thus, the amlodipine treatment was
associated with an 18% reduction in the rate of hospitalisation, (p<0.001).

**Measure of benefits used in the economic analysis**
The benefit measure used in the economic study was the number of hospitalisation events. This was derived from the effectiveness study.

**Direct costs**
A 3% discount rate was used since the time horizon of the study was 3 years. The unit costs were not reported separately from the quantities of resources used. The costs of health services included in the economic evaluation were inpatient procedures, follow-up laboratory tests and physician visits, long-term care, and drug usage. These costs were evaluated for each cycle in the Markov model. The cost/resource boundary adopted in the study was that of the Swedish health care system. Resource use was estimated on the basis of assumptions made by a group of experts (modified Delphi panel), who evaluated Swedish treatment patterns such as the frequency of visits and laboratory tests. The costs were estimated using local data that came from University Hospitals, public reimbursement rates and wholesale prices. The price year appears to have been 2000.

**Statistical analysis of costs**
The costs were treated deterministically.

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

**Currency**
Swedish kroner (SEK).

**Sensitivity analysis**
Univariate and multivariate sensitivity analyses were conducted to evaluate the robustness of the estimated cost-effectiveness ratio to variations in the model inputs and study assumptions. In particular, the relative risk and the direct costs were varied by +/-15%, the discount rate was varied between 0 and 6%, and cardiovascular medical usage was excluded from the analysis (scenario analysis).

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

**Cost results**
The estimated costs per patient over the 3-year period were SEK 26,600 in the intervention group and SEK 27,400 in the control group. Thus, amlodipine was associated with cost-savings of SEK 800. These results were robust to all variations carried out in the sensitivity analyses.

**Synthesis of costs and benefits**
An incremental analysis was conducted to combine the costs and benefits. However, a cost-effectiveness ratio was not calculated because the treatment was dominant over placebo, that is, it was more effective and less costly.

**Authors' conclusions**
Treatment with amlodipine was effective in reducing hospitalisation events. It also resulted in cost-savings from the
CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparator was clear. Placebo was selected as the aim of the study was to evaluate the active value of the treatment. In addition, placebo was the basic comparator in the clinical trial from which most of the effectiveness evidence was drawn. You should evaluate whether it represents a valid comparator in your own setting.

Validity of estimate of measure of effectiveness
The analysis of the effectiveness was based on several assumptions, which were made by combining the clinical data coming from the PREVENT study and Swedish rates. A modified Delphi approach was used, but was not explicitly described in the paper. All the estimates used in the decision model were investigated in the sensitivity analyses.

Validity of estimate of measure of benefit
The benefit measure was derived from the effectiveness study.

Validity of estimate of costs
The perspective adopted in the study was reported, and it appears that all the relevant categories of costs have been included in the analysis. The authors stated that the indirect costs were not evaluated. However, their inclusion would have improved the estimated cost-effectiveness ratio of amlodipine, as the reduced rate of hospitalisation would have reduced the productivity losses. The analysis did not consider hospitalisations unrelated to cardiovascular disease, and the impact of including this item was unclear. The unit costs were not reported separately from the quantities of resources used. Resource consumption was estimated on the basis of experts’ assumptions, which were required to evaluate Swedish treatment patterns. The authors noted that hospitalisation costs used in the analysis were average estimates and great variation may exist due to the length of stay, type of treatment and type of hospital. The costs were treated deterministically in the base-case, but sensitivity analyses were conducted on the key economic variables.

Other issues
The authors made few comparisons of their findings with those from published studies. They did not address the issue of the generalisability of the study results to other settings. The overall external validity of the analysis was low because the authors focused on the Swedish setting. Sensitivity analyses were conducted, but were aimed at evaluating the robustness of the analysis. The study referred to a hypothetical population of patients with CAD and this was reflected in the conclusions of the analysis. The authors highlighted several limitations of their analysis, which have already been reported.

Implications of the study
The main implication is that amlodipine is a cost-effective treatment for patients with CAD. It proved to be an effective treatment that could represent a cost-saving alternative to more expensive treatments. Future studies should address quality-of-life issues to better evaluate the benefits of amlodipine.

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Bibliographic details
Other publications of related interest


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MeSH
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