Asymptomatic peripheral arterial disease: is pharmacological prevention of cardiovascular risk cost-effective?

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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.

CRD summary
This study examined the cost-effectiveness of drug treatments for asymptomatic peripheral arterial disease, to reduce cardiovascular events, in those aged 65 years or older. The authors concluded that the drug treatments were cost-effective and angiotensin-converting enzyme inhibitors provided the greatest value-for-money. Contrary to recommendations aspirin was cheap, but had limited effectiveness. The methods were valid and the sources were robust, which should ensure the validity of the authors’ conclusions.

Type of economic evaluation
Cost-effectiveness analysis, cost-utility analysis

Study objective
This study examined the cost-effectiveness of drug treatments for asymptomatic peripheral arterial disease (APAD) to reduce cardiovascular events in those aged 65 years or older.

Interventions
Five treatment strategies were considered: low-dose aspirin, angiotensin-converting enzyme (ACE) inhibitors, non-aspirin anti-platelet therapy, statins for lipid lowering, and no active treatment.

Location/setting
Sweden/primary care.

Methods
Analytical approach:
The analysis was based on a Markov model that simulated the health and economic outcomes, over a lifetime. The authors stated that it was carried out from the perspective of the health care system.

Effectiveness data:
The clinical data were from a selection of relevant studies. The baseline risk for initial events was from epidemiological cohort studies carried out in the 1980s and early 1990s to ensure the inclusion of patients who rarely used preventive drugs, to represent event rates for the untreated group. The reductions in risk of cardiovascular events were the key inputs for the model and were from four clinical trials (one for each drug). Some assumptions were made, where clinical inputs were not available.

Monetary benefit and utility valuations:
The utility values were based on quality-adjustment weights from the literature.

Measure of benefit:
Quality-adjusted life-years (QALYs) were the summary benefit measure and were discounted at an annual rate of 3%. Life-years gained and the number of cardiovascular events, such as angina and stroke, were reported.

Cost data:
The economic analysis included the costs of medications and health care for the treatment of cardiovascular events. The event rates were from the four clinical trials, while their costs were from a large Swedish hospital-based registry.
Medication costs were based on the price list from Pharmaceutical Specialties in Sweden. Two scenarios for the estimation of drug costs were considered. In the first, patients were assumed to stay on medication for five years. In the second, patients were treated for a lifetime. All costs were in Euros (EUR) and the price year was 2009. A 3% annual discount rate was applied.

Analysis of uncertainty:
The overall uncertainty was investigated in a second-order Monte Carlo simulation, using predetermined probability distributions for the model inputs. Cost-effectiveness acceptability curves were created for different willingness-to-pay (WTP) thresholds. One-way deterministic sensitivity analyses were used to investigate the uncertainty in individual inputs and different starting ages (55 and 75 years).

Results
In men, the projected mean QALYs were 7.3674 with usual care, 7.4269 with statins, 7.3965 with aspirin, 7.4276 with non-aspirin anti-platelet therapy, and 7.4436 with ACE inhibitors. The costs were EUR 37,979 with usual care, EUR 37,776 with statins, EUR 37,904 with aspirin, EUR 39,808 with non-aspirin anti-platelet therapy, and EUR 37,688 with ACE inhibitors.

In women, the projected mean QALYs were 8.3809 with usual care, 8.4350 with statins, 8.4070 with aspirin, 8.4360 with non-aspirin anti-platelet therapy, and 8.4500 with ACE inhibitors. The costs were EUR 43,758 with usual care, EUR 43,521 with statins, EUR 43,667 with aspirin, EUR 45,566 with non-aspirin anti-platelet therapy, and EUR 43,425 with ACE inhibitors.

For both men and women, ACE inhibitors were the dominant strategy as they were more effective and less expensive than the other treatments.

The sensitivity analysis confirmed the superior clinical and economic profile of ACE inhibitors over the other strategies, regardless of the starting age. The probabilistic analysis showed that ACE inhibitors were the most cost-effective strategy at EUR 20,000 per QALY in 85% of simulations.

Authors' conclusions
The authors concluded that drugs to prevent cardiovascular events in APAD patients were cost-effective. ACE inhibitors provided the greatest value-for-money. In contrast to recommendations, aspirin was cheap, but not as effective as the other drugs.

CRD commentary
Interventions:
The rationale for the selection of the comparators was clear as the authors considered four available and commonly prescribed preventive treatments. The usual clinical practice, which was no active treatment, was included. The authors pointed out that the dosages reported in the main clinical trials were considered.

Effectiveness/benefits:
The most appropriate clinical data were selected by the authors and a literature review was not conducted. In general, appropriate sources were used. The epidemiological data were from old cohort studies to ensure the inclusion of patients who rarely used preventive drugs. Large clinical trials supplied the relative risk estimates, which was valid, but no head-to-head trials were used. It was unclear whether the patient populations in these trials were perfectly comparable. The authors undertook extensive sensitivity analysis to assess the uncertainty in the clinical parameters. Both QALYs and life-years gained were used as benefit measures, which was appropriate and allows comparisons with other disease areas. No details of the sources for the utility values were provided. The event rates were reported and might be of interest to clinicians.

Costs:
The categories of costs were consistent with the perspective. The unit costs and resource quantities were not presented separately, which reduces the transparency of the analysis. The authors pointed out the high quality of the cost data that were reported in Swedish registries. Other standard Swedish sources were used for the drug costs. The price year and
discounting were clearly reported.

Analysis and results:
The results were clearly reported. An appropriate incremental analysis was planned to identify the best treatment strategy, but a synthesis of the costs and benefits was not required as one treatment was dominant over the others. The uncertainty was investigated using valid approaches, and the methods were reported, including the types of probability distributions used in the Monte Carlo simulation. A clear diagram of the transition model was presented. The authors did not discuss the transferability of their results, but they appear to be applicable to other similar countries, such as other Scandinavian countries.

Concluding remarks:
The methods were valid and the sources were robust, which should ensure the validity of the authors’ conclusions.

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