A cost-effectiveness analysis of a hypothetical catheter-based strategy for the detection and treatment of vulnerable coronary plaques with drug-eluting stents

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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 use of a catheter-based strategy for the detection and subsequent treatment of vulnerable coronary plaques in patients with coronary artery stenoses.

Type of intervention
Diagnosis and secondary prevention.

Economic study type
Cost-utility analysis.

Study population
The study population comprised a hypothetical cohort of 60-year-old male patients scheduled to be treated with percutaneous coronary intervention (PCI) for stenoses in coronary arteries.

Setting
The setting was a hospital. The economic study was carried out in the USA.

Dates to which data relate
Some effectiveness and resource use data were derived from studies published between 1989 and 2004. The price year was 2003.

Source of effectiveness data
The effectiveness evidence was derived from a synthesis of completed studies and authors' opinions.

Modelling
A Markov decision model was constructed to assess the costs and benefits of the hypothetical catheter-based strategy, compared with standard care, in a cohort of patients with coronary artery stenoses. All patients underwent coronary angiography, which could detect stenoses but could not assess vulnerability. The hypothetical new test could detect both stenoses and vulnerability. After the diagnostic test was performed, patients entered the Markov model. After a PCI was performed, the patient could enter an event-free state, have a stroke or myocardial infarction (MI), after which congestive heart failure and/or cardiac arrhythmia may occur, or could develop stable or unstable angina pectoris for which additional revascularisation was required. Short- and long-term complications could develop. The secondary procedures considered were medical treatment with statins, PCI and coronary artery bypass grafting (CABG). The patients were followed until death. The cycle length was one month.
Outcomes assessed in the review
The outcomes assessed were short- and long-term mortality, revascularisation rates, morbidity, and complication rates associated with standard care. Quality of life (QOL) reduction coefficients were also estimated from published sources.

Study designs and other criteria for inclusion in the review
An extensive evidence-based review of the literature was performed to derive clinical inputs for the comparator. Relevant references were also obtained from experts. Limited information on the design and other characteristics of primary studies was provided. Life expectancy came from US life tables.

Sources searched to identify primary studies
MEDLINE was searched for English-language literature.

Criteria used to ensure the validity of primary studies
Not stated.

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

Number of primary studies included
Thirty-five primary studies provided clinical evidence.

Methods of combining primary studies
A weighted average was calculated to combine the primary estimates. Otherwise, the estimate from the most recent study with the largest cohort of patients and the longest follow-up was chosen.

Investigation of differences between primary studies
Not stated.

Results of the review
Short-term outcomes (less than 1 month):
the rate of mortality was 0.001 (range: 0.00 - 0.01) for angiography, 0.01 (range: 0.00 - 0.03) for coronary stent placement, 0.01 (range: 0.00 - 0.03) for percutaneous transluminal coronary angioplasty (PTCA), and 0.04 (range: 0.01 - 0.06) for CABG;
the rate of minor complications was 0.04 (range: 0.01 - 0.07);
the rate of stroke was 0.002 (range: 0.00 - 0.05);
the rate of MI was 0.04 (range: 0.01 - 0.12); and
the rate of technical failure requiring revascularisation was 0.02 (range: 0.01 - 0.06) with PTCA and 0.02 (range: 0.01 - 0.06) with CABG.

Long-term outcomes (longer than 1 month):
the relative risk (RR) of mortality due to coronary artery disease was 2.14 (range: 1.5 - 3.0) in the first year and 1 (range: 1.0 - 3.0) per year in the follow-up period;
the RR of mortality due to MI was 5 (range: 4 - 6);
the RR of mortality due to stroke was 5 (range: 2 - 6) in the first year and 2 (range: 2 - 6) per year in the follow-up;
the RR of mortality due to congestive heart failure was 8 (range: 6 - 10);
the RR of mortality due to arrhythmia was 1 (range: 1 - 3);
the rate of MI was 0.02 (range: 0.01 - 0.09);
the rate of arrhythmia, given MI, was 0.041 (range: 0.03 - 0.30);
the rate of congestive heart failure, given MI, was 0.041 (range: 0.03 - 0.30);
the rate of repeated and additional revascularisation with PTCA was 0.11 (range: 0.07 - 0.20) in the first year and 0.024 (range: 0.01 - 0.03) per year in the follow-up;
the rate of repeated and additional CABG was 0.03 (range: 0.01 - 0.06) in the first year and 0.006 (range: 0.001 - 0.03) per year in the follow-up.

The odds ratio of drug-eluting stents versus bare-metal stents revascularisation was 0.26 (range: 0.14 - 0.45).

QOL reduction coefficients were as follows:
for coronary artery disease (before treatment), 0.74 (range: 0.64 - 0.84);
for MI, 0.91 (range: 0.81 - 0.98);
for major stroke, 0.61 (range: 0.51 - 0.71);
for arrhythmia, 1.00 (range: 0.89 - 1.0); and
for congestive heart failure, 0.88 (range: 0.78 - 0.98).

Methods used to derive estimates of effectiveness
The authors made some assumptions to derive clinical estimates for the new strategy, and to model some treatment patterns.

Estimates of effectiveness and key assumptions
Coronary angiography detected 70% of stenoses. Drug-eluting stents would be used in 50% of cases, while bare-metal stents would be used in the remaining 50%. The prevalence of vulnerable plaques was 0.50. The mean number of vulnerable plaques per patient was 1.5. The sensitivity and specificity of the hypothetical test were both 0.90.

In terms of the long-term outcomes of the new test (over 1 month):
the RR reduction in coronary artery disease mortality was 0.5 in the first year and 1.0 per year in the follow-up;
the RR reduction in MI was 0.2 in the first year and 0.5 per year in the follow-up; and
the RR reduction in repeated and additional revascularisation was 0.2 in the first year of follow-up and 0.5 in the subsequent years of follow-up.

Measure of benefits used in the economic analysis
The summary benefit measure used was the quality-adjusted life-years (QALYs). These were estimated using the
decision model. QOL and survival were combined to derive the QALYs. QOL was estimated from the literature and original time trade-off values were transformed to standard-gamble utilities. The QALYs were discounted at an annual rate of 3%.

**Direct costs**
The analysis of the direct costs appears to have been carried out from the perspective of the third-party payer. It included hospital and physician costs. The health services considered were stent acquisition and placement, PTCA, CABG, coronary angiography, annual treatment of coronary artery disease (services associated with nonfatal MI, cardiac arrhythmia and congestive heart failure), and the new test.

The unit costs were not presented separately from the quantities of resources used for all items, and some costs were reported as macro-categories. Some resource use data came from the literature or were based on authors’ opinions. The costs were mainly estimated from Medicare reimbursement rates, with additional cost data coming from the authors’ hospital accounting database. Some costs were also derived from published estimates. The authors set the costs associated with the new strategy. Discounting was relevant, owing to the long timeframe of the analysis, and an annual rate of 3% was applied. The costs were updated to 2003 values using the medical component of the Consumer Price Index.

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

**Indirect Costs**
The indirect costs associated with patient time were included in the analysis, which was appropriate given that a societal perspective was adopted. Resource use was estimated from published studies and was reported. The unit costs came from the daily wage rate but were not provided. As in the analysis of the direct costs, the price year was 2003 and discounting was applied at an annual rate of 3%.

**Currency**
US dollars ($).

**Sensitivity analysis**
One- and multi-way sensitivity analyses were performed to assess the robustness of the base-case results (cost and QALY estimates) to variations in the model inputs. Alternative scenarios (best and worst case of the new test) were considered. Threshold analyses were also carried out. Alternative ranges of values came from the literature or were set by the authors.

**Estimated benefits used in the economic analysis**
In a hypothetical cohort of 1,000 patients, the expected QALYs were 10.23 with the new strategy and 9.86 with standard care. The expected QALYs associated with the new strategy ranged from 9.90 (worst-case scenario: lowest prevalence of vulnerable plaque, lowest sensitivity and specificity) to 11.15 (best-case scenario: highest prevalence of vulnerable plaque, highest sensitivity and specificity).

**Cost results**
In a hypothetical cohort of 1,000 patients, the expected costs were $37,045 with the new strategy and $38,257 with standard care.

The expected costs associated with the new strategy ranged from $32,073 (worst-case scenario: lowest prevalence of vulnerable plaque, lowest sensitivity and specificity, lowest costs for the new test) to $41,451 (best-case scenario:...
highest prevalence of vulnerable plaque, highest sensitivity and specificity, highest costs for the new test).

**Synthesis of costs and benefits**
An incremental analysis was carried out to combine the costs and benefits of the two strategies. However, in the base-case, an incremental cost-utility ratio (cost per QALY) was not calculated since the new strategy was both less expensive and more effective than standard care (dominant). Fewer cases of MI, stroke, revascularisations, PTCA and CABG were observed with the new strategy over standard care.

The sensitivity analysis showed that when model inputs were set against the new intervention (i.e. test performance and effect of therapy were decreased and costs were increased), the incremental cost per additional QALY ranged from $58,591 to $87,105 (worst case scenario). In general, under plausible scenarios, the new strategy was either cost-effective (often below $10,000 per QALY) or cost-saving. Only in the worst-case scenario was the new strategy associated with a cost per QALY above the threshold of $75,000.

**Authors’ conclusions**
The use of a catheter-based strategy in combination with drug-eluting stents (DES) for the treatment of patients with coronary stenoses would be cost-saving from a societal perspective. Even under a moderate worst-case scenario, the new strategy was cost-effective in comparison with standard care.

**CRD COMMENTARY - Selection of comparators**
The selection of the comparator was appropriate as it reflected standard care. Usual treatment was clearly described. You should decide whether this is a valid comparator in your own setting.

**Validity of estimate of measure of effectiveness**
The effectiveness evidence came from a synthesis of published studies and authors’ opinions. Some information on the methods and conduct of the review was reported. For example, details of the search and pooling approach were given. However, issues pertaining to the validity and homogeneity of the primary studies were not addressed. Further, since the characteristics and designs of primary studies were not reported, it was not possible to assess the robustness of the clinical data. Given the lack of published data on the hypothetical new test, the authors were required to make assumptions. Extensive sensitivity analyses were carried out to assess the impact of changes in clinical estimates used in the decision model.

**Validity of estimate of measure of benefit**
The use of QALYs as the summary benefit measure was appropriate as they capture the effect of the interventions on QOL and survival, which represent two relevant dimensions of care for patients with coronary artery stenoses. Discounting was applied to life expectancy, in accordance with guidelines for economic evaluations. The impact of using alternative discount rates was not investigated. Some details of the method used to calculate utility coefficients were reported.

**Validity of estimate of costs**
The perspective adopted in the study was appropriate. It appears that all the relevant categories of costs have been included in the analysis. The direct costs were mainly derived from Medicare sources, and the authors stated that the use of reimbursement rates to derive costs makes the cost results generalisable to other US settings. However, the costs were presented as macro-categories for the majority of items, which limits the possibility of replicating the analysis in other settings. Further, there was limited information on resource consumption. The indirect costs were estimated using typical sources (daily wages). The costs were treated deterministically but extensive sensitivity analyses were carried out on economic items. The price year was reported, which will facilitate reflation exercises in other time periods.
Other issues
The authors did not make extensive comparisons of their findings with those from other studies (probably due to the lack of cost-effectiveness studies on the new hypothetical test), but stated that a well-known model had shown that secondary prevention interventions for coronary disease with a statin cost less than $50,000 per QALY. The issue of the generalisability of the study results to other settings was partially addressed in that the authors stated that the use of reimbursement rates to derive costs would favour the extrapolation of their findings to other US contexts. The authors noted that the use of modelling required simplifications and assumptions, which might limit the validity of the whole analysis. However, the sensitivity analyses showed that the base-case results were robust to variations in the model inputs.

Implications of the study
The study results supported the development of a catheter-based strategy for the diagnosis and subsequent conventional treatment (by DES) of patients with coronary artery stenoses. The authors recommended that the cost-effectiveness of alternative treatment options for vulnerable plaques should be evaluated in future studies.

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Other publications of related interest


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