Intermittent claudication: cost-effectiveness of revascularization versus exercise therapy


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
Revascularisation was compared with exercise therapy (ET) for the treatment of intermittent claudication (IC). Revascularisation included percutaneous transluminary angioplasty (PTA) and/or artery bypass graft (ABG). ET consisted of daily walks of between 2 and 6km, depending on the patient's ability.

Five different treatment strategies were considered:

ET alone;

ET followed by PTA if necessary;

ET followed by PTA or ABG if necessary;

PTA if feasible, if not then ET followed by PTA if necessary; and

PTA if feasible, if not then ABG if feasible, if not then ET followed by PTA or ABG if necessary.

Type of intervention
Treatment.

Economic study type
Cost-utility analysis.

Study population
The study population comprised patients who had experienced IC and who had received no previous treatment for the condition. For the baseline analysis, the study considered a 60-year-old man presenting with one-year history of intermittent claudication, and with no history of coronary artery disease.

Setting
The setting was community (for ET) and hospital (for PTA and ABG). The economic study was carried out in the USA.

Dates to which data relate
The effectiveness data were taken from sources published between 1960 and 1999, with the majority being published in the 1990s. All prices were converted to 1995 US dollars ($).

Source of effectiveness data
The effectiveness data were derived from a review of the literature in addition to three sources of original patient data.
Modelling
A Markov model was developed to predict the transition between five different states of health: asymptomatic or mild claudication; severe claudication; critical limb ischaemia; below-knee amputation; and above-knee amputation. First-order Monte Carlo analysis was performed 100,000 times for each treatment strategy, and average values recorded.

Outcomes assessed in the review
Estimates from existing literature and original patient data were used to determine the input probabilities and outcomes used in the model. These included probabilities of state transitions, probability of other complications and quality-adjusted life-year (QALY) estimates.

Study designs and other criteria for inclusion in the review
Effectiveness data were drawn from the literature as well as from original patient sources. Original patient data were taken from three sources, one based in Massachusetts, USA (722 patients), and two based in the Netherlands (Groningen and Rotterdam with 329 and 547 patients respectively). These studies made up a five-year consecutive series of patients between 1990 and 1995.

Sources searched to identify primary studies
Not stated.

Criteria used to ensure the validity of primary studies
The three sources of original patient data were drawn from studies whose protocols were approved by the relevant institutional review boards.

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

Number of primary studies included
Data were extracted from thirty-four published studies, and three sources of original patient data.

Methods of combining primary studies
Not stated.

Investigation of differences between primary studies
Not stated.

Results of the review
All parameters derived from both literature sources and original patient data were used as inputs into a Markov model. A total of sixty-two inputs are reported in the study. These included:

- the mortality rate ratio for peripheral arterial disease, 3.14 (95% CI: 2.74 - 3.54);
- probability of death following ABG for high-risk patients, 0.044 (range: 0.032 - 0.055) and low-risk patients, 0.007 (range: 0.005 to 0.009);
- probability of death following PTA for high-risk patients, 0.013 (range: 0.000 - 0.037) and low-risk patients, 0.001 (range: 0.000 - 0.029);
probability of death following amputation for under 75 years of age, 0.098 (range: 0.077 - 0.119) and over 75 years of age, 0.147 (range: 0.113 - 0.181);

probability of need for ABG, 0.083 (range: 0.063 - 0.102); and

probability of need for amputation, 0.380 (range: 0.377 - 0.383).

Utility weights were reported for the following health states:

above-knee amputation, 0.20 (range: 0.00 - 0.40);

below-knee amputation, 0.61 (range: 0.41 - 0.81);

critical ischaemia, 0.35 (range: 0.15 - 0.55);

severe claudication, 0.71 (range: 0.67 - 0.75);

no or mild claudication, 0.79 (range: 0.75 - 0.83);

systemic complication, 0.72 (range: 0.60 - 0.90); and

angina pectoris, 0.90 (range: 0.60 - 1.00).

**Measure of benefits used in the economic analysis**

The summary measure of benefit used in the study was the quality-adjusted life-year (QALY). Utility weights were reported for seven different health states, and these were applied in combination with the length of time spent in each state. Utility weights were estimated using time trade-off methods based on response to the EuroQol questionnaire. Discounting was performed on future health outcomes at a rate of 3%.

**Direct costs**

Direct costs were used as inputs to the model. These included the cost of angiography, amputation, long-term care for amputees, bypass procedures, angioplasty, other complications, professional services, short- and long-term care, follow-up visits and rehabilitation. Costs for procedures were estimated either from existing literature sources, or from the original patient data. Resource quantities were derived from the model. Unit costs were reported. All costs were adjusted to 1995 prices using the medical care consumer price index. Future costs were discounted at 3% per annum.

**Statistical analysis of costs**

No statistical analysis of costs was reported.

**Indirect Costs**

Indirect costs such as the patients' time were included in the study. This was particularly applicable to the ET strategy, since patients were required to undertake daily walks taking up to two or three hours. Costs were estimated using the average hourly wage. Indirect costs were reported at 1995 prices, and discounted at 3%.

**Currency**

US dollars ($).

**Sensitivity analysis**

A one-way sensitivity analysis was performed on a substantial number of the model’s parameters. These included the age of patients, the discount rate, direct and indirect costs, probabilities and outcome utility weights.
Four-way sensitivity analysis was reported for changes in age (40, 60 and 80 years), cost of revascularisation (50%, 100% and 150% of baseline costs), history of coronary artery disease (yes or no) and health utility weights (the difference between 'severe' and 'no or mild' claudication of 0.04, 0.08, 0.12 and 0.16 QALYs per year).

**Estimated benefits used in the economic analysis**
The average number of lifetime QALYs experienced by a 60 year old man, following each treatment strategy were estimated as follows: 'ET alone', 6.05; 'ET followed by PTA if necessary', 6.14; 'ET followed by PTA or ABG if necessary', 6.22; 'PTA or ET followed by PTA if necessary', 6.15; 'PTA, ABG or ET followed by PTA or ABG if necessary', 6.21.

Side effects related to the treatment strategy were included in the analysis, but other indirect side effects were ignored.

**Cost results**
For ET, the majority of the costs consisted of the patients' forgone leisure time due to time spent walking. The average US hourly wage of $11.35 was used as the basis for the monetary valuation of time. Revascularisation costs were significant, particularly bypass surgery (approximately $23,500). The long-term care required for amputees was also costly, estimated to be almost $32,000 per year.

The approximate total lifetime costs, following each treatment strategy were estimated as follows:

- 'ET alone', $17,400;
- 'ET followed by PTA if necessary', $21,400;
- 'ET followed by PTA or ABG if necessary', $43,000;
- 'PTA or ET followed by PTA if necessary', $21,200; and
- 'PTA, ABG or ET followed by PTA or ABG if necessary', $43,000.

**Synthesis of costs and benefits**
For a 60-year-old male, 'ET alone' was both the least effective and cheapest strategy. The next most effective strategy was 'ET followed by PTA'. However, 'PTA or ET followed by PTA if necessary' was both more effective and cheaper than 'ET followed by PTA', and so dominated this strategy. 'PTA or ET followed by PTA' offered 0.1 extra QALYs at an extra cost of around $21,800 (approximately $311,000 per QALY gained). The most effective (and most expensive) strategy was 'ET followed by PTA or ABG if necessary'. Compared with 'PTA or ET followed by PTA if necessary', this provided an additional 0.07 QALYs at an extra cost of $21,800 (around $311,000 per QALY).

Sensitivity analysis showed that changes to parameters either had very little effect, or affected all strategies equally. The model was most sensitive to changes in health utility weights (particularly for severe claudication versus mild or no claudication). Changes to the costs of revascularisation procedures affected the total cost of those strategies including PTA or ABG. For younger patients the incremental cost-effectiveness ratios become more attractive, whilst, for older patients, these become less attractive.

**Authors' conclusions**
The authors concluded that the additional health benefit from bypass surgery was not sufficiently large to justify the large costs associated with the intervention, except in exceptional circumstances. Angioplasty (when feasible) was more effective than exercise therapy alone, and incurred a relatively small additional cost.

**CRD COMMENTARY - Selection of comparators**
Five different strategies were included in the analysis, using various combinations of exercise therapy, bypass grafts.
and angioplasty. However, no "do nothing" option was included in the model. This was an important consideration, because leaving the condition untreated may not affect the outcome significantly. In order to gain a more meaningful understanding of the study's findings, the consequences of "doing nothing" should be addressed.

**Validity of estimate of measure of effectiveness**
Effectiveness measures were derived from published literature sources. No information was provided as to the inclusion/exclusion criteria applied in literature selection. It is possible that influences such as publication bias (i.e. studies that provide findings of significant effectiveness are more likely to be published) may result in the estimates not being truly reflective of the actual effectiveness. Many of the effectiveness data were drawn from original patient sources; however, since these were not randomised controlled trials, a significant number of biases may be present. Examples include the possibility that patients with greater severity of condition may be more likely to be selected for one particular treatment, creating the impression that it is less effective.

**Validity of estimate of measure of benefit**
The summary measure of benefit included in the study was the QALY. This allows both quantity and quality of life to be considered. Utility weights were derived using an appropriate technique (time trade-off), and were based on responses to the EuroQol, a well-established health utility elicitation tool.

**Validity of estimate of costs**
All appropriate costs were included in the analysis, including both direct treatment costs and indirect costs such as loss of productivity and leisure time due to time spent in hospital or exercising. Unit costs and the price year were reported, which helps with the generalisability of the results. Discounting was appropriately conducted.

**Other issues**
The authors acknowledge that other factors, such as quitting smoking, may have significant effects on the outcomes of intermittent claudication patients. Policy makers should consider all realistic options before drawing conclusions as to the cost-effectiveness of certain strategies, and so it is recommended that this alternative approach also be considered.

Due to the large degree of uncertainty associated with many of the model's parameters, an appropriate modelling tool may have been to use second-order Monte Carlo analysis. The authors acknowledged this, but suggested that it would have introduced unnecessary complexity into the study, thus making interpretation of the conclusions more difficult.

Although many of the model's parameters were taken from studies published in many areas of the world, this does not necessarily mean that the study's findings are applicable to all other settings. As a user of this database, you should carefully consider whether these findings could be generalised to other areas.

**Implications of the study**
The authors recommend that the most cost-effective strategy in the treatment of intermittent claudication is angioplasty, where feasible, otherwise exercise therapy. Furthermore, since new technology allows more patients to be suitable for angioplasty, it is likely that this strategy will become increasingly favoured.

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**Bibliographic details**