Cost-effectiveness of an invasive strategy in unstable coronary artery disease: results from the FRISC II invasive trial

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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 invasive treatment (IT) shortly after symptoms appeared (the target was 2 days after starting open-label dalteparin or standard heparin), or a non-invasive treatment (NIT) in patients with unstable coronary artery disease. The IT was percutaneous transluminal coronary angioplasty (PTCA) with and without stent and coronary bypass grafting (CABG), while NIT consisted of optimal anti-thrombotic medication.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
Patients with symptoms of ischaemia that were increasing or occurring at rest, or warranting suspicion of acute MI, were eligible for inclusion. The episode had to have occurred less than 48 hours before the first dose of dalteparin or standard heparin.

The exclusion criteria included increased risk of bleeding or anaemia, indications for thrombolysis or treatment for thrombolysis during the last 24 hours, angioplasty performed in the last 6 months, and being on the waiting list for a coronary revascularisation procedure. Also, other acute or severe cardiac disease, renal or hepatic insufficiency, known clinically-relevant osteoporosis, other severe illness, hypersensitivity to randomised drugs, and anticipated problems concerning co-operation or participation in a clinical trial. Patients with previous open-heart surgery, advanced age or conditions that made invasive procedures inappropriate, were also excluded.

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

Dates to which data relate
The effectiveness and resource evidence was collected from 1996 to 1999. The price year was 2000.

Source of effectiveness data
The effectiveness data were derived from a single study.

Link between effectiveness and cost data
The costing was carried out prospectively in 36 of the 58 participating centres. This comprised almost 80% of the patients in the trial.
Study sample
Power calculations were not reported in this paper, although full details of the study were reported in earlier papers (see Other Publications of Related Interest). All patients who met the eligibility criteria were included, there was no sample selection. Of the 2,457 patients initially included in the trial and randomised for treatment, 1,222 patients received IT and 1,234 received NIT (the authors did not state what happened to the missing person). A total of 591 patients were excluded from the trial because of prior open-heart surgery (256), advanced age (282) and other reasons (53).

Study design
This was a multi-centre (58 centres) randomised controlled trial with 12 months’ follow-up. Randomisation was carried out by an independent organisation (Clinical Data Care, Lund).

Analysis of effectiveness
The study was carried out on an intention to treat basis. The primary health outcomes used to evaluate the procedures were reduction in deaths and MIs. The two groups of patients had very similar health and demographic characteristics; the paper did not report statistical measures of similarity.

Effectiveness results
After 12 months, 27 of the 1,222 (2.2%) IT patients had died compared with 48 of the 1,234 (3.9%) NIT patients.

The number of patients who died and/or experienced MI was 127 (10.4% of 1,219) in the IT group and 174 (14.1% of 1,234) in the NIT group.

MI was experienced by 105 (8.6% of 1,219) IT patients and 143 (11.6% of 1,234) NIT patients.

The odds ratio for death and/or MI was 0.71 (95% confidence interval, CI: 0.56 - 0.90), (p=0.005).

The odds ratio for MI was 0.72 (95% CI: 0.55 - 0.94), (p=0.015).

The odds ratio for death was 0.56 (95% CI: 0.35 - 0.90), (p=0.016).

Clinical conclusions
When the interventions were evaluated 12 months after treatment had commenced, patients in the IT group had experienced lower rates of mortality and MI.

Measure of benefits used in the economic analysis
The benefit measures used were lives saved, and lives saved or MI avoided.

Direct costs
Discounting of the costs was irrelevant, as the costs were incurred over 12 months. The quantities and the costs were analysed separately and were derived from actual data. The quantities measured were days in hospital (broken down into type of hospital bed), investigations, invasive procedures, the amount of each kind of drug taken, and the amount of outpatient care. The recorded investigations were exercise test, echocardiogram and coronary catheterisation. The invasive procedures were PTCA without stent, PTCA with stent, and CABG. Outpatient care was broken down into physician, nurse, physiotherapist, physician home visit and nurse home visit. The costs of home-help and help from relatives were also calculated. The prices used were based on actual data. If necessary, an average price was calculated from the different prices faced by the different hospitals. The quantities of resources used were initially priced using prices applying in 1997. These were then reflated to 2000 prices, using the consumer price index.
**Statistical analysis of costs**
No statistical analysis of the costs was reported.

**Indirect Costs**
These were calculated as the loss of production resulting from patients being unable to work. Average daily labour costs stratified by gender were used as a measure. The quantities were based on actual data. The prices initially used were 1997 prices, which were adjusted to 2000 levels by the consumer price index. Discounting was not carried out as it was irrelevant, the costs being incurred over less than 1 year.

**Currency**
Swedish kroner (SEK).

**Sensitivity analysis**
The effect of using the maximum and minimum price was calculated, as the prices of resources used were averages from the different medical centres in the trial.

**Estimated benefits used in the economic analysis**
In the IT group, 1.7% of the patients (20.8) avoided death and 3.7% of the patients (45.1) avoided death or MI. The patients were assessed for 12 months after being assigned to treatment.

**Cost results**
The mean cost was SEK 201,622 for a patient in the IT group and SEK 177,746 for a patient in the NIT group, \( p<0.001; \) CI for the difference: -23,876 +/- 10,545. The costs were calculated for 12 months after treatment commenced and the costs of adverse effects were included.

**Synthesis of costs and benefits**
The incremental cost-effectiveness ratio (ICER) for choosing IT over NIT was SEK 1,404,000 per death avoided. The ICER of an avoided death or avoided MI was SEK 645,000.

When minimum and maximum prices were used, the cost of an avoided death came to between SEK 971,000 and SEK 1,735,000.

**Authors' conclusions**
When assessed after 12 months, the invasive treatment (IT) had resulted in fewer deaths and fewer myocardial infarctions (MIs), but was more expensive than the non-invasive treatment (NIT).

**CRD COMMENTARY - Selection of comparators**
The authors justified their choice of the comparator on the grounds that it is a widely used intervention in their setting. You should decide if these are valid techniques in your own setting.

**Validity of estimate of measure of effectiveness**
The source of the effectiveness data was a single randomised controlled trial, which was appropriate for the study question. There was no sample selection and all eligible patients were included. The patient groups appear to have been comparable, although no statistical measure was given in this paper. The effectiveness analysis was handled credibly, although the authors did not explain why they sometimes reported that there were 1,219 patients in the IT group and sometimes 1,222. Also, they did not explain why one patient in the original sample did not appear to have been
randomised to either group. The authors did not evaluate the treatments from the patients' perspectives, an omission that they acknowledged in the paper.

**Validity of estimate of measure of benefit**

Two measures of benefit were used, which were obtained directly from the effectiveness analysis. The authors justified their reasons for using the number of deaths avoided and MI avoided as end points. The authors acknowledge that a quality-adjusted life-year measure would have allowed better comparisons with other interventions. However, the 12-month follow-up made the use of such a measure impossible.

**Validity of estimate of costs**

All the relevant categories of costs were included in the analysis. They were presented in a clear and comprehensive fashion and all dates were clearly stated. The costs were reported separately from the quantities. Quantity use was obtained from the single study, while prices were largely taken from the authors' setting. All drug costs were obtained from published sources. The price of home help was estimated from published sources, as was the indirect cost due to loss of production. A statistical analysis of the prices was not carried out, but a sensitivity analysis of the minimum and maximum prices was.

**Other issues**

The authors made appropriate comparisons of their results with those from other studies. They did not, however, discuss the issue of generalisability. This is clearly very important for decision-makers in other countries, who would want to know whether they could duplicate the effectiveness results and whether the cost differences between the two treatments would be similar. In general, the authors' conclusions reflected very fairly the scope of the analysis, the only exception being the missing patients who were not fully accounted for. The main drawbacks of the analysis were that it only followed patients for 12 months (something that future papers will no doubt rectify), and that it did not evaluate the patients' experience of the 12 months with either kind of treatment. Only by evaluating the patients' experiences during the whole course of both treatments can a balanced evaluation be made. The study was supported and organised in collaboration with Pharmacia and Upjohn.

**Implications of the study**

The authors suggest that, in their setting, early IT for moderate and high-risk unstable coronary artery reduces deaths and MIs in comparison with a NIT strategy. The cost in their setting of an avoided death represented a 13% increase in per patient costs over a NIT. The authors will be publishing papers that take into account a longer follow-up, to see if these conclusions are modified in any way.

**Source of funding**

Supported by and organised in collaboration with the Pharmacia and Upjohn Company. The research group was also supported by the Health Research Council in the South-East of Sweden, and Stina and Birger Johansson Foundation, Linkoping Heart Center.

**Bibliographic details**


DOI
10.1053/euhj.2001.2695

**Other publications of related interest**


Indexing Status
Subject indexing assigned by NLM

MeSH
Aged; Ambulatory Care /economics; Coronary Artery Disease /complications /economics /mortality; Cost-Benefit Analysis /economics; Electrocardiography /economics; Endpoint Determination; Female; Fibrinolytic Agents /economics /therapeutic use; Follow-Up Studies; Health Care Costs; Hospitalization /economics; Humans; Male; Myocardial Infarction /complications /economics /mortality; Platelet Glycoprotein GPIIb-IIIa Complex /economics /therapeutic use; Prospective Studies; Scandinavian and Nordic Countries /epidemiology; Sensitivity and Specificity; Survival Analysis; Ventricular Function, Left /physiology

AccessionNumber
22002000241

Date bibliographic record published
31/07/2003

Date abstract record published
31/07/2003