Cost-effectiveness analysis of enoxaparin versus unfractionated heparin in patients with acute coronary syndrome in Poland

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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
Two treatments for acute coronary syndrome (ACS) were under study. The treatments to be compared were enoxaparin and unfractionated heparin (UFH). The treatment regimens were enoxaparin 1 mg/kg subcutaneously every 12 hours, and UFH intravenous bolus followed by continuous infusion with the dose adjusted to give an activated partial thromboplastin time of 55 to 85 seconds. The treatments were administered for between 2 and 8 days (median 6).

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients with ACS admitted to the Cardiological Intensive Therapy Unit. All patients with unstable angina and a mean time from symptom onset to hospital admission of 12 hours were included.

Setting
The setting was secondary care. The economic analysis was carried out in Poland.

Dates to which data relate
The effectiveness data were derived from a published, randomised controlled clinical trial that was carried out in 1997. The resource use data were collected from an observational study carried out in 2000. The price year was 2000.

Source of effectiveness data
The effectiveness evidence was derived from a single study.

Link between effectiveness and cost data
The costing exercise was based on an observational study of 163 patients, which was carried out in the authors’ setting. The patients included in the study approximately fulfilled the inclusion criteria of the ESSENCE study.

Study sample
Detailed information on the study sample in the clinical trial was not given, although details can be found in the parent clinical study (see Other Publications of Related Interest). The final sample comprised 1,067 patients randomised to enoxaparin and 1,564 to UFH.
Study design
The ESSENCE study was an international multi-centred, randomised controlled, prospective, double-blind study that compared the efficacy of enoxaparin and UFH in patients with ACS. The inclusion criteria included resting angina lasting at least 10 minutes in the 24 hours prior to randomisation, and evidence of underlying ischaemic heart disease.

Analysis of effectiveness
The primary health outcome was a triple composite endpoint of death (any cause), myocardial infarction (MI), or recurrent angina after 14 days. The secondary efficacy outcomes were a triple composite endpoint of death (any cause), MI, or recurrent angina after 2 or 30 days, and a double composite endpoint of death (any cause) or MI after 2, 14 or 30 days. The statistical level of significance was defined as a p-value of 0.048.

Effectiveness results
A total of 266 (16.6%) patients randomised to enoxaparin reached the primary composite score, compared with 309 (19.8%) patients randomised to UFH. The difference was statistically significant, (p=0.019).

The number of total revascularisations, (p=0.001), and percutaneous transluminal coronary angioplasties, (p=0.002), were significantly smaller in the enoxaparin group.

There were no statistically significant differences between the study groups in the occurrence of major haemorrhagic complications.

Clinical conclusions
The results of the trial suggested that enoxaparin appears to have been more effective than UFH.

Modelling
A decision tree model was employed to perform the economic analysis. The purpose of the model was to extrapolate the clinical results in the context of the Polish health system.

Measure of benefits used in the economic analysis
The measure of benefit used was the number of patients reaching a triple composite score of death, MI and recurrent angina at 30 days.

Direct costs
Only the direct health care costs associated with the management of ACS were included. These included the drugs used, laboratory tests, procedures, personnel salaries, and fixed costs of hospitalisation such as the number of days in hospital. The costs of complications were not considered. The unit cost of the drug was obtained from the wholesale price-list of CEFARM, while the costs of revascularisation were estimated from the Ministry of Health rates. Detailed information on resource use was not given. The costs were not discounted because of the 30-day time horizon chosen. The costs were expressed in 2000 prices.

Statistical analysis of costs
The costs were treated as point estimates (i.e. the data were deterministic). The costs for each arm of the decision tree were calculated using the expected value approach.

Indirect Costs
The indirect costs were not included.
Currency
Polish zloty (Zł).

Sensitivity analysis
One- and two-way sensitivity analyses were performed to test the robustness of the model results. The parameters varied were:

the probabilities of reaching the composite endpoint after 30 days in each arm of the trial;
the probabilities of recurrent angina in patients reaching the composite endpoint in each arm of the trial;
the probabilities of MI in patients reaching the composite endpoint in each arm of the trial;
the acquisition cost of enoxaparin and UFH;
the cost of UFH therapy monitoring; and
the composite endpoint cost in each arm of the trial.

Also determined were the threshold values for the probabilities of reaching the composite endpoint, the probabilities of recurrent angina and MI in patients reaching a composite endpoint, and the associated treatment cost.

Estimated benefits used in the economic analysis
A total of 19.8% (318 of 1,607) of the patients receiving enoxaparin versus 23.3% (364 of 1,564) of those receiving UFH reached a composite endpoint at 30 days. Therefore, to prevent one additional event of the composite endpoint, 29 patients should be treated with enoxaparin instead of UFH.

Cost results
The average costs were Zł 1,085 per patient receiving enoxaparin and Zł 1,097 per patient receiving UFH. For every 29 patients treated with enoxaparin, there was a saving of Zł 348.

Synthesis of costs and benefits
The costs and benefits were synthesised using the dominance criteria approach in economic evaluation. Enoxaparin was considered the dominant strategy because it was both more effective and less expensive than UFH therapy for ACS.

The sensitivity analysis suggested that the model was not robust to a number of parameters. More specifically, the probabilities of reaching the composite endpoint, recurrent angina, and myocardial infarction, and the cost of the composite endpoint in both groups, the enoxaparin treatment course, and monitoring UFH therapy.

The threshold analysis suggested that the dominance of enoxaparin would disappear if:

the costs of enoxaparin treatment were increased by 10%;
the cost of the composite endpoint in the enoxaparin group was increased to Zł 1,163;
the cost of monitoring UFH therapy was decreased by 12%;
the probability of the composite endpoint in the enoxaparin arm was increased to 0.22 or decreased to 0.21 in the UFH arm;
the probability of recurrent angina in patients reaching the composite endpoint in the enoxaparin arm was increased to 0.793 or decreased to 0.72 in the UFH arm; or
the probability of MI in patients reaching the composite endpoint in the enoxaparin arm was increased to 0.229 or decreased to 0.2 in the UFH arm.

Authors' conclusions
The model described in the study suggested savings and better outcomes for the enoxaparin alternative. Therefore, the use of enoxaparin dominates unfractionated heparin (UFH) in patients with acute coronary syndrome (ACS) in Poland.

CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparators was clear. Recent large clinical trials have shown enoxaparin to yield better outcomes than the current treatment, UFH. In addition, the cost-effectiveness of both treatments has been evaluated in different countries. The authors studied the impact of the alternatives in their own setting. The selection of the comparator appears to have represented current practice in the authors' setting. You should decide if this is widely used health technology in your own setting.

Validity of estimate of measure of effectiveness
The authors used a large, well-designed randomised controlled trial (RCT) to obtain the effectiveness data. Although detailed information was not given, the RCT is a well-known study in the public domain and it is likely that it was a good source of evidence from which to obtain the parameters used in the model. However, the authors did not mention whether a relevant systematic review was available, as this would have been a better source of evidence for the treatment effect parameters.

Validity of estimate of measure of benefit
The estimation of benefits was obtained directly from the effectiveness study. The authors did not state the reason for having chosen this outcome estimate. It seems that the authors conducted their study by replicating what was already published from other countries, which then allowed them to compare the results obtained.

Validity of estimate of costs
All the categories of cost relevant to the perspective adopted were included in the analysis. The authors made use of an observational study, conducted in a Warsaw hospital, to determine the costs of ACS, MI and recurrent angina. This was an appropriate source for their setting. However, detailed information on resource use was not given, which made it difficult to determine what categories were actually included. This may well influence the internal validity of the model, although it was well handled in the sensitivity analysis of the costs. It is unlikely that the omission of complications from the costing study would have influenced the final model results. The results from the RCT suggested that there were no significant differences between the arms of the study. Therefore, the incremental costs would not be affected. The unit costs were taken from published national sources and from the observational study. Both sources seem to have been fairly representative of the authors' setting, as Poland has limited data available. Discounting was not required as the costs were incurred during a 30-day period.

Other issues
The authors compared the effectiveness results of their study with published evidence. However, no comparison of the study with other economic evaluations was presented. It was recognised that the main limitation of the study was the availability of data to build the model in the Polish setting. Generalisability to other settings was not explicitly addressed, although the key parameters of the model, including some unit costs, were analysed in the sensitivity analysis. The results of the study do not appear to have been presented selectively. The authors suggested that it was unlikely that the indirect costs would have influenced their results, as the mean age of the participants was 67 years, but they did not consider other issues such as informal care.

Implications of the study
The authors stated that, based on the model results, UFH should be replaced by enoxaparin for the treatment of ACS in Polish patients.

**Source of funding**

None stated.

**Bibliographic details**


**PubMedID**

12828495

**Other publications of related interest**


**Indexing Status**

Subject indexing assigned by NLM

**MeSH**

Acute Disease /economics; Aged; Aged, 80 and over; Anticoagulants /economics /therapeutic use; Coronary Disease /drug therapy /economics; Cost-Benefit Analysis; Drug Costs /statistics & numerical data; Enoxaparin /economics /therapeutic use; Female; Heparin /economics /therapeutic use; Hospital Costs /statistics & numerical data; Humans; Male; Models, Statistical; Poland

**AccessionNumber**

22003008240

**Date bibliographic record published**

28/02/2005

**Date abstract record published**

28/02/2005