Cost-effectiveness of enoxaparin compared with unfractionated heparin in ST elevation myocardial infarction patients undergoing pharmacological reperfusion: a Canadian analysis of the Enoxaparin and Thrombolysis Reperfusion for Acute Myocardial Infarction Treatment - Thrombolysis in Myocardial Infarction (ExTRACT-TIMI) 25 trial

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 enoxaparin compared with unfractionated heparin, plus fibrinolysis, in patients with ST-segment elevation myocardial infarction, using data from a clinical trial. The authors concluded that enoxaparin improved survival at a modest medication cost and was a cost-effective alternative to unfractionated heparin. The study appears to have been satisfactorily carried out and was well presented. The authors’ conclusions are robust, as shown by the sensitivity analyses.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
This study examined the cost-effectiveness of enoxaparin compared with unfractionated heparin, plus fibrinolysis, in patients with ST-segment elevation myocardial infarction, using data from a clinical trial.

Interventions
The two anticoagulation therapies were low-molecular weight heparin (enoxaparin) and unfractionated heparin. Enoxaparin was administered for the length of hospital stay and unfractionated heparin was administered for at least 48 hours; both were given with fibrinolysis. Unfractionated heparin was given as an intravenous injection of 60 units per kg followed by an infusion of 12 units per kg per hour. The enoxaparin dose depended on a patient’s age (younger than 75 years or 75 and older) and renal function.

Location/setting
Canada/secondary care.

Methods
Analytical approach:
The analysis was based on a decision analytic model, with a lifetime horizon. The authors stated that a societal perspective was adopted, but not all sources of costs could be included.

Effectiveness data:
The clinical evidence over 30 days came from the Enoxaparin and Thrombolysis Reperfusion for Acute Myocardial Infarction Treatment - Thrombolysis in Myocardial Infarction (ExTRACT-TIMI) 25 trial, which was a prospective, randomised, double-blind, double-dummy, parallel-group, multinational trial, involving 20,506 patients at 674 sites in 48 countries. The key endpoint was the composite of death from any cause and non-fatal recurrence of myocardial infarction, in the first 30 days after randomisation. Long-term data were estimated using published Framingham equations that were adapted to the ExTRACT-TIMI 25 trial patient characteristics and using Canadian life tables.

Monetary benefit and utility valuations:
Not considered.

Measure of benefit:
Life-years (LYs) were the summary benefit measure and they were discounted at an annual rate of 5%. The mean survival was calculated using data from the clinical trial and the Framingham Heart Study. The impact of baseline patient characteristics was accounted for by regression analysis.

Cost data:
The economic analysis included the costs of treatment (enoxaparin and unfractionated heparin), first hospitalisation, discharge to 30 days (major procedures, interventions, and management of severe adverse events), and long-term management costs. Drug costs were based on resource consumption observed in the clinical trial and Canadian unit prices. All the resources used over the first 30 days were based on the clinical trial. Hospitalisation costs and other costs incurred in the 30 days after discharge were from the clinical trial, US diagnosis-related group data, and the Ontario Case Costing Initiative. The long-term costs came from the Canadian literature. All medical costs, besides those in the 30-day trial and those associated with years of life lost, were assumed to be the same in the two arms of the trial. All costs were in Canadian dollars (CAD) and the price year was 2004. A 5% annual discount rate was applied.

Analysis of uncertainty:
Incremental cost-effectiveness ratios were analysed, using bootstrapping with 5,000 replications, and cost-effectiveness acceptability curves were generated. A deterministic analysis considered the variability in length of hospitalisation, using registry data, and years of life lost, using arbitrary estimates.

Results
The marginal time costs (the difference between in-trial costs and costs of LYs lost) were CAD 6,417.60 with enoxaparin and CAD 5,888.70 with unfractionated heparin. The additional LYs lost were 0.6984 with enoxaparin and 0.8057 with unfractionated heparin. The incremental cost per LY gained with enoxaparin over unfractionated heparin was CAD 4,930.4 and this ranged from CAD 1,176.2 to CAD 5,670.1 in the deterministic sensitivity analysis. The probabilistic analysis showed that there was a 99% probability of enoxaparin being cost-effective at a threshold of CAD 20,000 per LY gained.

Authors’ conclusions
The authors concluded that enoxaparin improved survival at a modest medication cost and was a cost-effective alternative to unfractionated heparin.

CRD commentary
Interventions:
The two therapies were appropriately selected as unfractionated heparin was the conventional treatment and enoxaparin was the proposed medication. The dosages and method of administration were clearly presented.

Effectiveness/benefits:
Data from randomised controlled trials are usually considered to be valid, given the strengths of the design and the rigour of outcome assessment. The randomisation procedure and the multinational nature of this trial should also have ensured the validity of the clinical data. Long-term clinical events were based on standard and appropriate equations, which are often used in cardiovascular disease studies. The benefit measure was appropriate as the expected survival was the relevant outcome for this patient population.

Costs:
The authors stated that the perspective was societal, but only the direct medical costs associated with treatment and related procedures were included. They reported that no data were available from the clinical trial to calculate the costs of concomitant medication and the indirect costs of lost productivity. The unit costs for some items were reported while total categories were presented for other costs, due to the accounting system used for diagnosis-related group data. The price year and discounting were reported and the economic analysis was generally presented in detail.

Analysis and results:
The analytic approach used to synthesise the costs and benefits of the two strategies was valid, as an incremental analysis was carried out. Both the total and marginal time cost estimates were reported. A probabilistic approach was appropriately used to analyse the uncertainty and the variability in key inputs was also investigated. Conventional discounting for both the costs and benefits was applied. The authors acknowledged some limitations of their analysis.
such as the need for some assumptions and the exclusion of some costs.

Concluding remarks:
The study appears to have been satisfactorily carried out and was well presented. The authors' conclusions are robust, as shown by the sensitivity analyses.

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