Economic analysis of low-dose heparin vs the low-molecular weight heparin enoxaparin for prevention of venous thromboembolism after colorectal surgery

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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
Low molecular weight heparins (LMWH) and low dose heparin calcium for use in the prevention of venous thromboembolism in patients who have undergone colorectal surgery.

Type of intervention
Secondary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
Patients who have undergone colorectal surgery. The mean age of patients was assumed to be 51 years.

Setting
Hospital. The economic analysis was conducted in Toronto, Ontario, Canada.

Dates to which data relate
Effectiveness data were obtained from a 1996 study for which only an abstract has been published thus far and also from literature published between 1988 to 1997. Resource data were obtained from the 1996 unpublished study and also from 1993-1994 data from the Canadian Institute of Health Information on all patients who underwent colorectal surgery in Canada. Price years used in the analysis were not stated.

Source of effectiveness data
Effectiveness data were derived from a single study and a review of previously completed studies.

Link between effectiveness and cost data
Costing information was obtained retrospectively using different patient data to that used in the effectiveness analysis.

Study sample
1,349 patients were randomised to receive either low dose heparin (n=675) or LMWH enoxaparin (n=674) following colorectal surgery. It is not known whether power calculations were used to determine the sample size.

Study design
Multi-centre double blind randomised controlled trial.
Analysis of effectiveness
It was not stated whether the analysis of effectiveness was based on intention to treat or on treatment completers only. The primary health outcomes used in the analysis were the incidence of deep vein thrombosis and major bleeding.

Effectiveness results
Both treatment options were found to be equally efficacious: 9.4% of 468 patients in each group developed DVT with a relative risk of 1 (95% CI: 0.7 - 1.5). The relative risk of major bleeding using enoxaparin was 1.8 (95% CI: 0.8 - 3.9) compared with low dose heparin: 2.7% versus 1.5% of all patients in the two groups respectively.

Clinical conclusions
Not reported in the economic analysis.

Modelling
A decision analysis model was used to determine costs and benefits associated with the intervention and the comparator using efficacy information obtained from the Canadian trial and data in the literature.

Outcomes assessed in the review
Probabilities of developing deep vein thrombosis and having major bleeding following abdominal surgery were identified.

Study designs and other criteria for inclusion in the review
Trials comparing low dose heparin and LMWH enoxaparin in abdominal surgery were identified. Specific inclusion or exclusion criteria were not stated although all studies found were randomised trials with intention to treat based analyses. All studies had at least 90% patient follow up.

Sources searched to identify primary studies
A Medline search was conducted.

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

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

Number of primary studies included
6 studies were included. All of these were randomised controlled trials, and four were double blinded.

Methods of combining primary studies
Studies were not combined but probability values identified were used to determine parameter range for variables in sensitivity analysis.

Investigation of differences between primary studies
Not stated.
Results of the review
The incidence of DVT reported in primary trials and in meta-analyses for enoxaparin ranged from 14.7% to 0.5% and for heparin values ranged from 18.2% to 1.1%. The incidence of major bleeding for the LMWH and low dose heparin groups respectively, ranged from 5.2% to 1.5% and 6.1% to 1.5%.

Measure of benefits used in the economic analysis
Since the study used in the base case analysis demonstrated that the use of both the intervention and the comparator led to similar risks of developing DVT and pulmonary embolism, the economic analysis concentrated on the incidence of major bleeding in the two groups.

Direct costs
Direct costs were estimated from the perspective of both a Canadian and United States third party payer. In the Canadian analysis cost of prophylaxis was taken from 1995 inpatient cost data from a Toronto hospital. Costs due to thrombosis or major bleeding including bed days, laboratory fees, blood bank, operating room and other hospital costs were based on 1994 unit costs at the same hospital. Physician fees were taken from the 1995 Ontario Health Insurance Plan, 1995 drug costs were taken from the hospital pharmacy and 1995 to 1996 costs for blood transfusion products were obtained from the Canadian Red Cross. The volume of services used by patients with major bleeding or DVT was estimated based on data on patients with DVT within the Canadian trial, inpatients with DVT in the Toronto Hospital and from information from the database of the Canadian Institute for Health Information on all patients who underwent colorectal surgery in 1993-1994. In estimating costs from the perspective of a US third party payer, all costs were based on estimates in the literature published between 1990 and 1997, a 1995 and a 1996 study in the literature, as well as on information supplied by the drug manufacturer. Direct costs were not discounted as they occurred in a short time period, and the base price year used was not stated.

Indirect Costs
Lost productivity costs were estimated based on the time taken for physician visits, hospitalisation due to complications and incidence of premature deaths. The 1993 industrial aggregate of average yearly earnings published by Statistics Canada was used to value lost productivity. Indirect costs were discounted at a rate of 5% per annum. The base case price year used was not stated.

Currency
Canadian dollars (Can$) and US dollars (US$).

Sensitivity analysis
All clinical parameters including risk of thrombosis, pulmonary embolism and major bleeding were varied in sensitivity analysis. Cost estimates and the indirect cost discount rate were also varied in sensitivity analysis. A series of clinically relevant scenarios were considered in the sensitivity analysis.

Estimated benefits used in the economic analysis
In the baseline scenario, the decision analysis model estimated that there would be an additional 12 cases of major bleeding per 1000 patients in the enoxaparin group.

Cost results
The Canadian costs per 1000 patients with LMWH enoxaparin were Can$218,307 and with low dose heparin groups were Can$132,257. In the US analysis these costs were US$242,778 and US$97,111 respectively. Therefore the additional costs of using enoxaparin in the Canadian and US scenarios respectively were Can$86,050 and US$145,667.
Synthesis of costs and benefits
An incremental-cost effectiveness analysis was not conducted as the low dose heparin strategy was both more effective and less expensive than the LMWH enoxaparin strategy. In sensitivity analysis enoxaparin remained the more expensive strategy and only with optimal efficacy and safety estimates prevented 3 cases of major bleeding compared with low dose heparin.

Authors' conclusions
The authors concluded that the use of low dose heparin for the prevention of thrombosis, pulmonary embolism and major bleeding following colorectal surgery was a dominant strategy compared with the use of low molecular weight heparin enoxaparin, being both more effective and less costly.

CRD COMMENTARY - Selection of comparators
Justification was provided for the use of the comparator low dose heparin, on the basis that it was a well known standard protocol for the prevention of thrombosis following colorectal surgery.

Validity of estimate of measure of benefit
Case effectiveness data were taken from a large multicentre double blind randomised controlled trial in Canada comparing LMWH enoxaparin with low dose heparin, with an additional review of the literature being used to determine the range of variation of parameters to be used in sensitivity analysis. It would perhaps have been useful to have some more information on the protocol used in the Canadian trial as it is not clear whether the efficacy estimates for thrombosis were based on the intention to treat or on treatment completers only. More information on the study may also be useful given that only an abstract of the trial appears to be available in the literature. In identifying articles for the literature review, although an electronic search was conducted using Medline, it would have been helpful to provide some more information on the criteria used to identify literature and also on the methods used to assess the validity of articles identified. In particular, no articles not in the English language were identified, which may suggest that the review has been biased towards English language publications.

Validity of estimate of costs
Sufficient information was provided on the sources of costs used in the Canadian analysis. It appears to be unclear in the US cost analysis how indirect costs due to lost productivity were estimated. In addition the price year used in the base case analysis does not appear to be stated.

Other issues
Canadian cost estimates in the study may not be generalisable outside the Toronto hospital to other parts of Canada and in the US analysis the authors noted that literature did not clearly distinguish between costs and charges increasing uncertainty associated with these estimates. However, varying cost estimates in the sensitivity analysis did not change the base line conclusions of the study.

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