Modeling the cost-effectiveness of prothrombin complex concentrate compared with fresh frozen plasma in emergency warfarin reversal in the United Kingdom

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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.

CRD summary
This study examined the cost-effectiveness of using prothrombin complex concentrate, compared with fresh frozen plasma, for emergency warfarin reversal in patients with a life-threatening intracranial, gastrointestinal, or retroperitoneal haemorrhage. The authors concluded that prothrombin was a cost-effective alternative to plasma from the perspective of the UK NHS. The cost-effectiveness framework was valid and should ensure that the authors’ conclusions are robust, despite the poor quality of some clinical sources.

Type of economic evaluation
Cost-effectiveness analysis, cost-utility analysis

Study objective
This study examined the cost-effectiveness of using prothrombin complex concentrate compared with fresh frozen plasma for emergency warfarin reversal in patients with a life-threatening intracranial, gastrointestinal, or retroperitoneal haemorrhage.

Interventions
The two interventions were 30 units per kilogram of prothrombin complex concentrate plus 5mg of vitamin K compared with three units of fresh frozen plasma plus 10mg of vitamin K.

Location/setting
UK/hospital.

Methods
Analytical approach:
The analysis was based on a decision-tree model, with a lifetime horizon, for a hypothetical cohort of 65-year-old patients presenting with intracranial, gastrointestinal, or retroperitoneal haemorrhage. The authors stated that the analysis was carried out from the perspective of the UK NHS.

Effectiveness data:
A systematic literature search was undertaken to identify the relevant sources of evidence, in MEDLINE and the Cochrane Library, for articles from 1998 to 2008. The search criteria were reported. Clinical trials, retrospective cohort studies, and observational studies were selected. The mortality estimates were the key inputs for the model and they were from 16 studies for intracranial haemorrhage, three studies for gastrointestinal haemorrhage, and two studies for retroperitoneal haemorrhage. Average values were calculated without weighting by sample size, which some studies did not report.

Monetary benefit and utility valuations:
The utility values were from the literature.

Measure of benefit:
Life-years and quality-adjusted life-years (QALYs) were the summary benefit measures.

Cost data:
The economic analysis included the costs of hospital admission, drugs and other therapies, imaging studies and other diagnostic tests, ambulance transport, and stroke rehabilitation. The resource use was estimated by a panel of nine consultant physicians (six haematologists and three anaesthetists), with relevant clinical experience of warfarin reversal, plus the opinions of two of the authors. A structured questionnaire was used. The costs were estimated from official NHS prices. They were expressed in UK pounds sterling (£) at 2007 to 2008 prices.

Analysis of uncertainty:
A probabilistic sensitivity analysis was carried out, using Monte Carlo simulation. Conventional probability distributions were assigned to the model inputs and cost-effectiveness acceptability curves were generated. A deterministic sensitivity analysis was conducted to identify those inputs that affected the cost-effectiveness decision.

Results
For intracranial haemorrhage, the total costs per patient were £14,387.55 with prothrombin and £11,142.14 with plasma. Patients on prothrombin gained 4.2 life-years or 2.10 QALYs, yielding an incremental cost of £800 per life-year gained or £1,600 per QALY gained over plasma. The probability of prothrombin being cost-effective was 95% at a threshold of £10,000 per QALY.

For gastrointestinal haemorrhage, the costs were £8,225 with prothrombin and £7,823.52 with plasma. Prothrombin produced a gain of 0.2 life-years or 0.14 QALYs, and an incremental cost of £2,100 per life-year gained or £2,900 per QALY gained over plasma. The probability of prothrombin being cost-effective was 90% at the threshold of £10,000 per QALY.

For retroperitoneal haemorrhage, the costs were £8,264 with prothrombin and £7,730.14 with plasma. Prothrombin produced a gain of 1.0 life-year and 0.71 QALYs, and an incremental cost of £600 per life-year gained or £800 per QALY gained over plasma. The probability of prothrombin being cost-effective was 95% at the threshold of £10,000 per QALY.

The deterministic analysis showed that the probability of survival after a life-threatening haemorrhage and the initial dose of prothrombin or plasma were influential inputs, but prothrombin remained the more cost-effective strategy in all scenarios.

Authors' conclusions
The authors concluded that, from the perspective of the UK NHS, prothrombin complex concentrate was a cost-effective alternative to fresh frozen plasma for emergency warfarin reversal.

CRD commentary
Interventions:
The rationale for the selection of the comparators was clear as the two available first-line emergency warfarin reversal strategies were considered.

Effectiveness/benefits:
A valid approach was used to identify the relevant sources of evidence. Commonly used databases were searched and the keywords were reported. The authors stated that several study designs were selected and they had different levels of internal validity and risks of selection bias, but the data were pooled without weighting on the basis of their quality. The authors acknowledged that this was a limitation of their study, but it was representative of actual clinical practice. The sensitivity analyses investigated the impact of varying these inputs on the cost-effectiveness results. The derivation of the utility values (whose values, the instrument used, etc) was not given. Life-years and QALYs were both valid benefit measures that capture the impact of the interventions on both survival and quality of life. Both measures allow cross-disease comparisons to be made.

Costs:
The cost categories were consistent with the authors’ stated perspective. The unit costs and resource use were presented separately for some items, increasing the ability to replicate the analysis. The resource use was estimated by experts as no published evidence for the UK was found. These estimates are likely to have been a good proxy of the real resource usage.
use in the authors' setting. The unit costs came from typical and official sources. The costs were varied in the sensitivity analysis.

Analysis and results:
The projected costs and benefits were extensively presented and were appropriately synthesised in an incremental analysis. The sensitivity analyses satisfactorily investigated the uncertainty. The results of both the probabilistic simulations and the deterministic analyses were clearly presented and discussed. Discounting of the costs and benefits was not reported and would have been relevant for the lifetime horizon of the analysis. The analysis appears to have been UK-specific, but might be transferable to settings with similar cost structures.

Concluding remarks:
The cost-effectiveness framework was valid and should ensure that the authors’ conclusions are robust, despite the poor quality of some clinical sources.

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