Revisiting the cost-effectiveness of primary prophylaxis with clotting factor for the treatment of severe haemophilia A

Miners A

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 updated a previous economic evaluation, which examined the cost-effectiveness of primary preventive treatment with exogenous clotting factor in comparison with on-demand treatment for patients with severe haemophilia A. The author concluded that primary prophylaxis was a cost-effective alternative to on-demand treatment and was more cost-effective than was found in the previous analysis. The study was based on valid methodology, which makes the author’s conclusions more robust, despite some limited reporting of the data sources.

Type of economic evaluation
Cost-utility analysis

Study objective
The objective was to examine the cost-effectiveness of primary preventive treatment with exogenous clotting factor in comparison with on-demand treatment in patients with severe haemophilia A. This study updated a previous economic evaluation published by the author of the current study and other authors.

Interventions
A strategy of primary prophylaxis with exogenous clotting factor (factor VIII) was compared with on-demand treatment. On-demand treatment was a single infusion of 31 international units (IU) per kg of factor VIII, with two infusions in 10% of cases, while prophylaxis was 25 to 40 IU per kg of factor VIII three times per week over a person’s lifetime.

Location/setting
UK/out-patient.

Methods
Analytical approach:
The analysis was based on a published Markov model with a 70-year time horizon. The author stated that the analysis was carried out from the perspective of the UK National Health Service (NHS).

Effectiveness data:
The clinical data were taken from the previous analysis and no information on the design or other characteristics of the data sources was provided in this paper. The author reported some details for those estimates that were updated. The key clinical input was the rate of bleeding and this was obtained from age-adjusted data from a London-based treatment centre.

Monetary benefit and utility valuations:
The utility values were derived from a cross-sectional study of people who had mild, moderate, and severe haemophilia and had never received prophylaxis, and from a UK general population dataset.

Measure of benefit:
Quality-adjusted life-years (QALYs) were the summary benefit measure and a 3.5% annual discount rate was applied.

Cost data:
The author did not provide a breakdown of the cost items as these were taken from the previous economic analysis. Similarly, the cost categories and data sources were not reported. Some assumptions were made for the clotting factor doses. Some changes in the probability distributions for major surgery and the annual numbers of out-patient and day-patient visits were made. The costs were in UK pounds sterling (£) and were discounted at an annual rate of 3.5%. The price year was 2007.

**Analysis of uncertainty:**
A probabilistic sensitivity analysis was undertaken on the uncertain model inputs using pre-specified distributions and the details of these were clearly presented. Cost-effectiveness acceptability curves (CEACs) were generated and the expected value of perfect information (EVPI) and the expected value of partial perfect information (EVPPI) were calculated.

**Results**
Over 70 years, the expected costs were £644,000 with on-demand treatment and £858,000 with prophylaxis. The QALYs were 13.95 with on-demand treatment and 19.58 with prophylaxis. The incremental cost per QALY gained with prophylaxis over on-demand treatment was £38,000.

The CEACs indicated that the probability of prophylaxis being cost-effective at £30,000 per QALY was 13%, but this rose to over 90% at a willingness-to-pay threshold of £100,000. More favourable results were associated with reductions in three factors: the clotting factor price, the discount rate for QALYs, and the time between prophylactic infusions of factor VIII.

The results from the patient EVPI analysis showed that the value of further research was £44,000 at a willingness-to-pay of £30,000 per QALY and this increased to a maximum of £47,000 at a willingness-to-pay of £40,000 per QALY. The EVPPI analysis showed that the utility parameters associated with the health states had the highest value in terms of further research.

**Authors' conclusions**
The author concluded that primary prophylaxis was a cost-effective alternative to on-demand treatment and was more cost-effective than in the previous analysis.

**CRD commentary**

**Interventions:**
The selection of the comparators was appropriate as the two interventions were the available strategies for this patient population. The recommended dosages were reported.

**Effectiveness/benefits:**
The data sources were not described as most of the data were derived from the previous analysis. Further information should be available in the primary publication. The author updated some probability distributions for the clinical inputs using more recent evidence, but details of the new sources were not clearly reported. This limited reporting, although consistent with the study objective, limits the possibility making an objective assessment of the validity of the clinical estimates. Extensive sensitivity analyses were carried out on all the inputs, especially the utility values, the estimates of which were crucial to the calculation of the cost-effectiveness of the two treatments. QALYs are an appropriate benefit measure given the impact of the disease on both survival and quality of life. The recommended discounting was applied, but the sensitivity analysis highlighted the strong impact of the appropriate choice of discount rate on the cost-effectiveness of prophylaxis.

**Costs:**
No information on the cost categories and their data sources was provided and the author stated that the previous structure of the model remained unaltered except for some changes in the probabilistic distributions assigned to the key inputs. Only the price year, the use of discounting, and the price of clotting factors were reported. This means it is not possible to assess the quality of the economic analysis.

**Analysis and results:**
The costs and benefits were appropriately synthesised using an incremental approach, which identified the most efficient strategy. The issue of uncertainty was satisfactorily addressed and described. The study results were generally clearly presented and discussed, but limited information on the previous model was provided.

Concluding remarks:
The study was based on valid methodology, which makes the author’s conclusions more robust, despite some limited reporting of the data sources.

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