Cost-utility analysis of prophylaxis versus treatment on demand in severe hemophilia A  
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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 primary prophylaxis, with clotting factor VIII concentrates, versus secondary prophylaxis, treatment on demand, or a combined strategy of primary prophylaxis in childhood and treatment on demand in adulthood, for severe haemophilia A. Prophylaxis, either primary or secondary, was more cost-effective than treatment on demand, and the combined strategy was not cost-effective. The analysis relied on a previous economic evaluation, applied to Italy, and some methodological limitations might affect the validity of the authors’ conclusions.

**Type of economic evaluation**
Cost-utility analysis

**Study objective**
This study examined the cost-effectiveness of primary prophylaxis with clotting factor VIII concentrates versus secondary prophylaxis, treatment on demand, or a combined strategy of primary prophylaxis in childhood with on-demand treatment in adulthood, for patients with severe haemophilia A.

**Interventions**
Primary and secondary prophylaxis consisted of 30 international units (IU) per kg of factor VIII, administered 2.5 times per week.

With primary prophylaxis, patients started treatment before the age of two years or before their first joint bleed.

With secondary prophylaxis, treatment was started after the age of two years or after more than one joint bleed.

With treatment on demand, patients of any age received a bolus dose of 40 IU per kg of factor VIII once or twice after each bleed.

With the combined strategy, patients received primary prophylaxis, until the age of 18 years, and then received treatment on demand.

**Location/setting**
Italy/secondary care and hospital.

**Methods**
**Analytical approach:**
The analysis was based on a published Markov model, with a hypothetical cohort of patients, from birth to the age of 70 years or death, if earlier. The authors stated that the analysis was carried out from the perspective of the Italian National Health System.

**Effectiveness data:**
Most of the clinical data were from a previous economic evaluation conducted in the UK (Miners, et al. 2002, see ‘Other Publications of Related Interest’ below for bibliographic details), which was the basis for this analysis. Some epidemiological inputs were changed to reflect the Italian setting. For example, the annual rate of major surgery was from the database of discharge records of an Italian hospital. Similarly, the probabilities of death for individuals treated
on demand or with primary prophylaxis were from Italian life tables.

Monetary benefit and utility valuations:
The utility values were from the previous economic evaluation and from a published study of utility assessment.

Measure of benefit:
Quality-adjusted life-years (QALYs) were the summary benefit measure.

Cost data:
The economic analysis included the costs of factor VIII concentrates and hospitalisations for bleeding, examinations, or major surgery. The cost of recombinant plasma- and albumin-free antihaemophilic factor (factor VIII) was from official prices. All other costs and resource quantities were from published Italian studies. All costs were in Euros (EUR) and a 6% annual discount rate was applied.

Analysis of uncertainty:
One-way sensitivity analyses were carried out on the discount rate, medication dose, and frequency of medication administration.

Results
In a hypothetical cohort of 100 patients who were followed-up for 70 years, the projected costs were EUR 87,426,642 with on demand treatment, EUR 129,600,063 with the combined strategy, EUR 166,168,643 with primary prophylaxis, and EUR 164,440,652 with secondary prophylaxis. The QALYs were 4,137 with on demand treatment, 4,491 with the combined strategy, 6,094 with primary prophylaxis, and 6,051 with secondary prophylaxis.

Compared with on demand treatment, the incremental cost per QALY gained was EUR 119,134 with the combined strategy, EUR 40,236 with primary prophylaxis, and EUR 40,229 with secondary prophylaxis. The main cost driver was the cost of factor VIII. The frequency of bleeding and the discount rate were influential parameters.

Authors’ conclusions
The authors concluded that prophylaxis, either primary or secondary, was more cost-effective than on demand treatment. The combined strategy was less effective and less cost-effective.

CRD commentary
Interventions:
The authors justified their selection of the comparators. Treatment on demand and secondary prophylaxis were the main comparators, the combined strategy was the usual care in Italy, and primary prophylaxis was implemented in Scandinavian countries, such as Sweden.

Effectiveness/benefits:
The clinical data were mainly from an economic evaluation conducted in the UK. The authors did not describe the methods of this published model, making it impossible to objectively assess the validity of the data. This UK analysis was adapted to Italy using appropriate epidemiological sources, but these were not fully described. The original economic evaluation was published almost 10 years earlier, and some clinical care patterns might have changed. QALYs were a valid benefit measure and they capture the impact of disease on both survival and quality of life, which are affected in these patients. The instruments used to elicit the preferences were not stated.

Costs:
The cost categories were appropriate for the perspective of the public health care system. The unit costs and resource quantities were reported only for the drugs; other costs were presented as category totals. The authors stated that most of the costs were from previous studies carried out in Italy, but their methods and the cost calculations were not reported. The price year was not given, which will hinder reflation exercises for other time periods. All costs appear to have been treated deterministically.

Analysis and results:
The results were extensively presented. An incremental analysis was used to synthesise the costs and benefits of the strategies. The uncertainty was investigated, using a deterministic approach, for selected model inputs. The results of these univariate sensitivity analyses were illustrated in diagrams. A more extensive analysis of uncertainty, including the cost categories, would have been more appropriate. A discount rate was applied to the costs, but it was unclear if it was also applied to the benefits. A rate of 6% was chosen, based on the previous UK analysis, but it was unclear whether this was appropriate for Italy. The results of the analysis might be transferred to settings with similar cost structures.

Concluding remarks:
The analysis relied on a previous economic evaluation that was applied to the Italian setting. Some methodological limitations might affect the validity of the authors’ conclusions.

Funding
Supported by Pfizer Italia Srl, Italy.

Bibliographic details

DOI
10.2147/CEOR.S16670

Original Paper URL

Other publications of related interest

Indexing Status
Subject indexing assigned by CRD

MeSH
Cost-Benefit Analysis; Factor VIII; Hemophilia A; Humans; Italy; Markov Chains; Quality-Adjusted Life Years

AccessionNumber
22011000710

Date bibliographic record published
06/07/2011

Date abstract record published
20/07/2011