Episodic versus prophylactic infusions for hemophilia A: a cost-effectiveness analysis

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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
Factor VIII supplementation.

Type of intervention
Primary prevention and treatment.

Economic study type
Cost-effectiveness analysis.

Study population
Boys with severe factor VIII deficiency (<2%) who were less than 18 years of age and attending one of the eleven participating haemophilia treatment centres for receipt of prophylactic or episodic care.

Setting
The setting was eleven US haemophilia treatment centres, located in four different regions of the country.

Dates to which data relate
Costs, resource and price data related to 1993.

Source of effectiveness data
Single study.

Link between effectiveness and cost data
Costing was undertaken retrospectively on the same patient sample as that used in the effectiveness study.

Study sample
A random sample of patients from each of the eleven haemophilia treatment centres receiving episodic care as well as all patients from these centres receiving prophylactic care were included in the study. The final sample size comprised 117 boys. Of these, 90 were treated episodically (control) and 27 prophylactically (intervention). No power calculations were undertaken to determine an appropriate sample size.

Study design
The study design was a case series. The median observation period was 26 months (range 6.5 to 72 months). No loss to follow-up was reported. There was no random allocation of subjects to intervention and control groups.
Analysis of effectiveness
It seems that the analysis was based on treatment completers only. The primary health outcome measured was bleeding event frequency.

Effectiveness results
The cohort receiving prophylactic treatment had fewer bleeding events per year (median, 3 versus 31). The p value was reported to be less than 0.005.

Clinical conclusions
Prophylactic care markedly reduced the number of bleeding events in boys with severe factor VIII deficiency and should prevent joint function impairment.

Modelling
A model was used to estimate both costs and benefits. The model comprised three hypothetical cohorts of patients (aged 3 to 50 years) who were receiving either episodic or one of two types of prophylactic treatment. In the first model of prophylaxis, treatment begins at the age of three (when regular bleeding usually begins) and continues until the age of 50. In the second model, prophylaxis is administered from the age of three to 20 years only (when the frequency of regular bleeding begins to decline).

Measure of benefits used in the economic analysis
Bleeding event frequency.

Direct costs
Some resources and costs were reported separately. Use of hospital and medical facilities, provider visits, units of factor consumed and diagnostic studies obtained during the observation period were included in the cost analysis. Units of service that generated charges were multiplied by the relevant institutional charge and totalled to yield a yearly cost per patient. Unit quantities and costs were reported separately. Medians rather than means were used for cost estimates due to the presence of outliers and marked skewness in the distributions of the data.

Statistical analysis of costs
Statistical analyses were performed to determine any differences in costs between the episodic and prophylactic care groups. Since medians were used, the tests were of the non-parametric type, although details of the actual tests employed were not stated in the report. P-values were reported.

Indirect Costs
Productivity losses as a result of disability were estimated by means of published data on men with polyarthritis as listed in the 1978 Social Security Survey of Disability and Work. This data indicated that the earnings differential between affected and unaffected men is approximately 38%. Expected future lifetime earnings were also calculated on the basis of published data. The loss of a school or work day was valued at $46 by using the 1990 average annual earnings converted to 1993 dollars and divided by 365. Costs were adjusted to 1993 dollars by using the annual per cent change in personal income. Future costs were discounted at a rate of 5 per cent.

Currency
US dollars ($).

Sensitivity analysis
Univariate sensitivity analyses were carried out with a zero discount rate assumed. Because concentrate accounted for most (93%) of the total cost of the prophylactic care strategies, sensitivity analysis of the direct and indirect costs was carried out only over the range of concentrate costs. Threshold analysis was employed to determine the price per unit of concentrate which would yield the same total cost for prophylactic therapy as for current episodic care.

**Estimated benefits used in the economic analysis**
The prophylactic use of factor VIII concentrate was associated with a tenfold reduction in the incidence of bleeding events, from 31.1% to 2.8% (p<0.005).

**Cost results**
The total direct medical costs to treat prophylactically were increased approximately threefold, from $23,435 to $75,574 (p<0.005).

**Synthesis of costs and benefits**
Estimated costs and benefits were combined in the form of cost per bleeding event prevented. An incremental analysis was performed. Compared with episodic infusion, prophylaxis from ages 3 to 20 years costs $1,100 (in 1993 US dollars) per bleeding event prevented, in comparison with $1,380 for prophylaxis from ages 3 to 50 years. Threshold analysis determined that the total costs of prophylactic care from ages 3 to 50 year would equal the current total costs of episodic care if the price of the concentrate was decreased by half.

**Authors’ conclusions**
Prophylactic care markedly reduced the number of bleeding events and should prevent joint function impairment, but at a substantial cost when based on current concentrate costs.

**CRD COMMENTARY - Selection of comparators**
The reason for choice of comparator is clear, and included the most widely used existing treatment versus some alternative approach.

**Validity of estimate of measure of benefit**
There is the potential for bias in the estimate of benefit (underestimate) due to the non-random allocation of patients to prophylactic and episodic care groups. Those receiving prophylactic care had a history of either frequent haemarthroses, intracranial haemorrhage or low titre inhibitors and thus were receiving factor VIII concentrate for the purposes of secondary prevention.

**Validity of estimate of costs**
Important costs were included in the analysis and resource quantities were reported separately from price although there is the potential for bias in the estimate of costs. For lifetime cost projections, it was assumed that the cost of primary prophylaxis would be the same as that for secondary prophylaxis, which may not hold true since those who were receiving secondary prophylaxis were more complicated cases.

**Other issues**
Based on the data collected for this study, the authors conclusions are justified. There is no comment in the discussion as to how representative the treatment centres involved in this study might be of US haemophilia treatment centres in general, although the authors do comment in the methods section that the patients attending the centres from which the data was collected represent both rural and metropolitan populations.

**Implications of the study**
A judgement concerning the relative economic value of prophylactic versus episodic care in boys with severe factor VIII deficiency requires a comparison with other health care programmes.
Source of funding
None stated.

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