Porcine factor VIII: pharmacoeconomics of inhibitor therapy
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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
Treatment modalities for acquired haemophilia were under examination. The three treatment strategies compared were treatment with porcine factor VIII (pFVIII), human factor VIII (hFVIII), or an activated prothrombin complex concentrate (APCC).

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients with acquired haemophilia.

Setting
The setting was secondary care. The economic analysis was carried out in Boston, USA.

Dates to which data relate
The dates to which the effectiveness and resource use data related were not reported. Year 2000 prices were used.

Source of effectiveness data
The effectiveness data were derived from published studies, patient chart reviews and a panel of experts.

Modelling
A decision analytic model was created to simulate the costs and the effectiveness assigned to each treatment strategy. The model presented three time points at which decisions could be made. More specifically, at presentation (choice of the treatment regimen), and at 6 and 24 hours (change or do not change the treatment regimen following clinical evaluation).

Base-case assumptions were made to develop the model, but they were not reported.

A base-case scenario was used in the model. A 53-year-old woman presenting with a retroperitoneal bleed and a history of systemic lupus erythematosus, who is given the presumptive diagnosis of a FVIII inhibitor, was considered. A panel of 5 experts was asked a number of questions as to what dosing regimen they would use with each of the treatment agents. In addition, the panel was asked to make a clinical evaluation at 6 and 24 hours. The panel was further restricted to using only two agents before the treatment was considered a failure. The panel could change the treatment regimen once following the clinical evaluation. At the end of the scenario, the panel was asked to assign specific probabilities
for success (clinical resolution without change the initial regimen), depending on how the scenario evolved.

The time horizon was not stated.

Outcomes assessed in the review
The outcomes assessed in the reviews and used as model inputs were the dose, duration and efficacy of each treatment agent. Efficacy was allowed to vary depending upon where in the treatment pathway the product was used (e.g. whether it was used as first- or second-line therapy).

Study designs and other criteria for inclusion in the review
The treatment efficacy of each product was obtained from medical literature. The specific source used to estimate the dose and duration of the treatment was not stated (it might have been the literature, patient chart reviews, or expert opinion).

Sources searched to identify primary studies
Not reported.

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

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

Number of primary studies included
Not reported.

Methods of combining primary studies
Not reported.

Investigation of differences between primary studies
Not reported.

Results of the review
Only data on treatment efficacy were reported.

The range of efficacy used in the model was 0.44 to 0.91 for pFVIII, 0.18 to 0.28 for hFVIII, and 0.49 to 0.80 for APCC.

Methods used to derive estimates of effectiveness
Expert opinions were used in the model to derive estimates of effectiveness.

Estimates of effectiveness and key assumptions
The estimates derived from expert opinions were not reported.
Measure of benefits used in the economic analysis
No summary benefit measure was used in the economic evaluation. This was, in effect, a cost-consequences analysis. The authors reported that they conducted a cost-minimisation analysis because they wanted to focus on comparing the costs. However, comparative effectiveness measures were included in the paper and the authors’ conclusions included comparative effectiveness statements.

Direct costs
The perspective adopted in the study was not reported. The direct costs included only the cost of treatment products. The authors did not provide any further details of the cost analysis. The unit costs and the quantities of resources used were not presented separately. The costs of each product were derived from the Average Wholesale Price for 2000. The source used to derive the resource use data was not clearly reported. In fact, it was unclear whether the resource use data were derived from guesswork, expert opinion, or published information from other studies. Discounting was not relevant, as all costs were incurred during less than one year, and was not reported.

Statistical analysis of costs
A statistical analysis of the costs was not carried out.

Indirect Costs
The indirect costs were not included.

Currency
US dollars ($).

Sensitivity analysis
One-way sensitivity analyses were performed on the efficacy of pFVIII (-10%) and on the cost of pFVIII (range: $1.50 - $2.50) and bypassing agent (range: $1.20 - $2.20). A two-way sensitivity analysis was performed on the efficacy of pFVIII (-10%) and APCC (+15%).

Estimated benefits used in the economic analysis
See the 'Effectiveness Results' section.

Cost results
The treatment of the base-case patient was least expensive when one began the treatment with pFVIII ($331,000). Treatment with hFVIII was the most expensive ($378,000), followed by treatment with APCC ($347,000).

Synthesis of costs and benefits
A synthesis of the costs and effectiveness was not relevant since pFVIII was the dominant strategy (pFVIII was more effective and less costly than hFVIII and APCC).

When the cost of the bypassing agent was altered across a broad range of costs ($1.20 - $2.20), pFVIII remained the least costly strategy and thus the dominant strategy.

Similarly, when the cost of pFVIII was varied over a range from $1.50 to $2.50, pFVIII remained the dominant strategy.

If the efficacy of pFVIII was reduced by approximately 10%, initial therapy with APCC agent was more effective.
Similarly, if the efficacy of APCC was raised by approximately 15%, initial use of APCC was more effective.

**Authors' conclusions**

Treatment initiated with porcine factor VIII (pFVIII) would be less costly than treatment sequences initiated with a bypassing agent or human factor VIII (hFVIII). Many physicians believe pFVIII is the preferred strategy based on clinical considerations.

**CRD COMMENTARY - Selection of comparators**

The reason for the choice of the comparators would appear clear. However, the authors reported in the 'Introduction' section that four therapeutic products were available for acquired haemophilia, but only three were actually compared. No justification for the exclusion of the fourth product (recombinant factor VIIa) was provided. You should decide whether these technologies represent valid comparators in your own setting.

**Validity of estimate of measure of effectiveness**

The authors reported that published studies were used to estimate the effectiveness. However, they did not report whether a systematic review was conducted. Moreover, the sources searched to identify primary studies, the study designs and other criteria for inclusion in the review, and the validity of the studies were not reported. The authors acknowledged that the base-case scenario was not necessarily generalisable to all patients with an acquired inhibitor.

**Validity of estimate of measure of benefit**

No summary benefit measure was used in the analysis. In effect, a cost-consequences analysis was carried out. The reader is therefore referred to the comments in the 'Validity of estimate of measure of effectiveness' field (above).

**Validity of estimate of costs**

The perspective of the study was not stated, thus it is not possible to assess whether all the relevant categories of costs were included in the analysis. Discounting was not relevant and was not carried out. Details of the unit costs and price year were reported, which enhance the transferability of the economic analysis to other settings. However, it was unclear how the authors calculated the total costs from the unit cost of each product. It appears that other categories of cost have been used in the cost analysis (e.g. physician services, professional fees, or monitoring), but the authors did not report these. A potentially good feature of the cost analysis was that estimates were varied in the sensitivity analyses. However, the ranges over which costs were varied were not justified. Consequently, the internal and external validity of the cost analysis may be low.

**Other issues**

The generalisability of the results was hardly addressed. The authors did not compare their findings with those from other studies and did not report any further limitations of their study. The authors reported that a cost-minimisation analysis was conducted, although they reported a general conclusion with regard to both the effectiveness and cost results. The authors used the expression "is preferred", which has no sense in health economics (it was unclear if the strategy was dominant, cost-effective, more effective, less costly). In effect, a cost-consequences analysis was conducted. The authors should also note that an economic analysis of health interventions does not merely refer to monetary evaluations, but also to clinical outcomes.

**Implications of the study**

The authors suggested the need to focus on studies that better define the relative efficacy of each of the treatment modalities, rather than the issues of costs.

**Source of funding**

NHS Economic Evaluation Database (NHS EED)  
Produced by the Centre for Reviews and Dissemination  
Copyright © 2017 University of York
Supported by an unrestricted research grant from Ipsen Inc., Milford (MA), USA.

**Bibliographic details**

**PubMedID**
11882077

**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Algorithms; Animals; Autoantibodies /blood; Autoimmune Diseases /drug therapy; Blood Coagulation Factors /economics /therapeutic use; Cost-Benefit Analysis; Drug Costs; Economics, Pharmaceutical; Factor VIII /economics /immunology /therapeutic use; Hemophilia A /drug therapy /etiology /immunology; Humans; Swine; Therapeutic Equivalency

**AccessionNumber**
22002000721

**Date bibliographic record published**
30/06/2005

**Date abstract record published**
30/06/2005