Cost-utility analysis of immune tolerance induction therapy versus on-demand treatment with recombinant factor VII for hemophilia A with high titer inhibitors in Iran

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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
The study examined the cost-effectiveness of immune tolerance induction (ITI) therapy with plasma-derived factor VIII concentrates versus on-demand treatment with recombinant-activated FVIIa (rFVIIa) in haemophilia A with high titre inhibitors. The authors concluded that a low-dose ITI protocol was the most cost-effective option. The study relied on a previous cost-effectiveness model whose methodological characteristics were not reported. The authors’ conclusions appear dependent on the model assumptions.

Type of economic evaluation
Cost-utility analysis

Study objective
The study examined the cost-effectiveness of immune tolerance induction (ITI) therapy with plasma-derived factor VIII concentrates versus on-demand treatment with recombinant-activated FVIIa (rFVIIa) in haemophilia A patients with high titre inhibitors.

Interventions
Three ITI regimens for inhibitor eradication and one on-demand strategy were considered: high-dose Bonn protocol (FVIII at a dosage of 150 IU/kg twice daily); low-dose Van Creveld (Dutch) protocol (FVIII every other day at a dose of 25 IU/kg); dose decreased each time the absolute FVIII recovery exceeds 30%; these reductions are continued until a prophylactic FVIII dose of 10 to 15 IU/kg three times weekly is reached); Malmö protocol (extracorporeal immunoadsorption with protein A columns as needed to remove high-titre inhibitory antibodies); and an on-demand regimen with rFVIIa.

Location/setting
Iran/outpatient and in-patient.

Methods
Analytical approach:
The analysis was based on a published decision analytic model with a 10-year time horizon. The authors stated that the perspective was that of the Ministry of Health.

Effectiveness data:
Clinical inputs were based mainly on estimates already included in the published decision model (see Other Publications of Related Interest) so no information on these sources was provided. The success rate for each regimen was a key input of the model and was also taken from the published model. The authors stated that a few clinical parameters were changed to adapt the model to the Iranian context.

Monetary benefit and utility valuations:
Utility valuations were based on estimates already incorporated in the previous model. No Iranian data were available.

Measure of benefit:
Quality-adjusted life-years (QALYs) were used as the summary benefit measure.
Cost data:
The economic analysis was restricted to the costs of haemostatic agents because other costs associated with in-patient and outpatient health care services were not available. Unit costs and resource quantities were presented. Costs were based on official tariffs. Costs were in US dollars ($). The price year was 2011.

Analysis of uncertainty:
A one-way sensitivity analysis was carried out to investigate the impact of variations in the cost of clotting factor, drug dose and administration frequency.

Results
Expected costs of treatment and QALYs were: $5,528,649.60 and 33.0 with Bonn ITI; $2,243,649.60 and 29.1 with low-dose ITI; $4,306,629.60 and 28.1 with Malmö ITI; and $6,205,248.00 and 25.1 with on-demand treatment.

The incremental analysis showed that all ITI regimens were dominant over on-demand treatment, which was both less effective and more expensive. Among the ITI strategies, low-dose dominated Malmö; the incremental cost per QALY gained with the Bonn over Malmö regimens was $249,391.84 and the incremental cost per QALY gained with the Bonn regimen over low-dose was $842,307.69. Overall, low-dose ITI was the preferred strategy.

The authors stated that in the sensitivity analysis the cost of clotting factor and drug dose were influential inputs (results not shown).

Authors' conclusions
The authors concluded that a low-dose ITI protocol was the most cost-effective option versus both other ITI regimens and on-demand treatment with rFVIIa.

CRD commentary
Interventions:
The selection of the comparators was appropriate as the available treatment strategies for this patient population in the authors' setting were considered. Dosages and administration times were reported clearly.

Effectiveness/benefits:
No information was given on the design of the studies from which clinical parameters were taken (a previous decision model). The authors stated that these were based on a literature review which was likely to have identified relevant studies. No Iranian estimates were found and no sensitivity analysis was conducted, so it was not possible to judge the validity of the clinical side of the study. QALYs were a valid benefit measure for this patient population and enabled comparisons with economic evaluations conducted in other areas. Utility weights were based on the published model and no details were provided. No Iranian data were used.

Costs:
The economic analysis included only the costs of the treatments. The authors acknowledged that the analysis was carried out from a very restricted perspective but pointed out that the cost of clotting factor concentrates accounted for 98% of total costs. Thus, the adoption of a broader perspective and inclusion of other direct medical and indirect costs may not have substantially altered the results of the analysis. Unit costs and resource quantities were presented separately, which enhanced the transparency of the economic side of the analysis. The price year was reported. The cost of clotting factors was varied in the sensitivity analyses but the results were not reported.

Analysis and results:
The expected costs and benefits were reported for each regimen. An incremental approach was used to synthesise these outcomes, which enabled exclusion of inefficient (more expensive and less effective) strategies. Discounting was not reported and would have been relevant given the long-term horizon of the analysis. The issue of uncertainty was only partially investigated as only a few inputs were varied using a deterministic approach. The results of the sensitivity analyses were not illustrated. The authors acknowledged some limitations of their analysis related mainly to the need for assumptions and lack of Iranian data. The study results are likely to be relevant only to the Iranian setting.

Concluding remarks:
The study relied on a previous cost-effectiveness model, the methodological characteristics of which were not reported. In general, the authors' conclusions appear dependent on the model assumptions.

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