Systematic Review of Cost-Effectiveness Modelling Studies for Haemophilia

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Introduction

Haemophilia is a rare genetic disease that hinders blood clotting. Untreated haemophilia has severe consequences for patients. Medical improvements in recent decades have significantly changed the treatment of haemophilia, most recently extended half-life coagulation factors, emicizumab and gene therapies [1 - 3]. This systematic review aims to provide an overview of the key results, the main sources of input data and the quality of the included cost-effectiveness analyses (CEAs).

Methods

We conducted a systematic literature review of model-based CEAs of haemophilia treatments by searching Embase (OEMEZD) and MEDLINE (MEDALL), the Tufts Medical Center CEA registry, and grey literature. We summarized and qualitatively synthesized the studies' methods and results. We assessed their quality using the Consensus Health Economic Criteria (CHEC) list [4, 5]. We assessed the risk of bias via the source of funding. We extracted information on the sources of evidence of mortality, bleeding rates, and quality of life (QoL) used in the models.

Results

Study Identification

We initially retrieved 1,712 studies from the Embase and MEDLINE databases. After abstract and full-text screening, and combining with our grey literature search, we finally identified **32 eligible studies** that were performed in 12 countries and reported **53 pairwise comparisons (Table 1)**.

Quality and Risk of Bias

- The studies fulfilled **between 7 and 18 of the 20 CHEC points**, with a mean of 13.53.
- **19 of the 32** included studies received **industry funding**. Of these 19 studies, 15 found that the company's product was cost-effective.

Treatment Comparisons

- **Comparisons of prophylactic versus on-demand treatment** indicated that prophylaxis may not be cost-effective, but there was no clear consensus.
- **Emicizumab** was mostly found to be cost-effective compared with coagulation factor prophylaxis and bypassing agents.
- **Immune tolerance induction** following the Malmö protocol was found to be cost-effective compared to bypassing agents, while there was no consensus for the other protocols.
- **Gene therapies** as well as treatment with **extended half-life coagulation factors** were always found to be cost-effective versus their comparators.

Evidence informing the CEA Models

- Almost all studies (n = 30) incorporated evidence on **bleeding rates**, as most models included the annualized bleeding rate.
- 28 included studies incorporated evidence on **mortality**. Most included studies cited various types of real-world data on mortality. Only 11 studies considered bleeding-related mortality
- 21 studies incorporated evidence on the **QoL impacts via the treatment,** combining bleeding and adverse events.
- 18 included studies incorporated evidence for the direct impacts of **bleeding on QoL**.
- Evidence on the QoL impacts of **haemophilic arthropathy** (n = 15), **joint surgery** (n = 11), or **coagulation factor infusions** (n = 6) were incorporated less frequently.

Treatments		Comparators					
		Prophylaxis SHL	Prophylaxis EHL	On-demand SHL	On-demand EHL	Emicizumab	Bypassing agent
Interventions	Prophylaxis SHL	2	0	10	0	0	0
	Prophylaxis EHL	6	4	0	0	0	0
	Emicizumab	3	2	2	0	0	5
	Gene therapy	5	2	1	1	2	0
	ITI	0	0	0	0	0	6
	Bypassing agent	0	0	0	0	0	2

Table 1 An overview of all 53 treatment comparisons in the included studies, simplified into 8 categories of treatments. The numbers in each field indicate how many comparisons between the two treatment categories were identified in the included studies. If a field is coloured blue, it means that the intervention was cost-effective vs. the comparator. If a field is coloured yellow, it means that comparisons reached different conclusions regarding the cost-effectiveness of treatments. Green fields indicate a comparison within a treatment category.

SHL Standard half-life, *EHL* extended half-life, *ITI* Immune tolerance induction.

Discussion

Our CHEC quality assessment showed that the inclusion of relevant haemophilia-related clinical outcomes as model input parameters was of variable quality across studies. The heterogeneous results for some treatment comparisons may have been driven by the modelling approaches, clinical input data, and funding sources. Higher consistency across studies and good quality modeling approaches and input data will be needed to support reimbursement and pricing decisions on novel treatment approaches with potentially high benefits but also high costs.

References

1. Ar MC, Balkan C, Kavaklı K. Extended Half-Life Coagulation Factors: A New Era in the Management of Hemophilia Patients. Turk J Haematol. 2019;36:141–54. doi:10.4274/tjh.galenos.2019.2018.0393.
2. Meeks SL, Batsuli G. Hemophilia and inhibitors: current treatment options and potential new therapeutic approaches. Hematology Am Soc Hematol Educ Program. 2016;2016:657–62. doi:10.1182/asheducation-2016.1.657.
3. Shima M. Current progress and future direction in the treatment for hemophilia. Int J Hematol. 2020;111:16–9. doi:10.1007/s12185-019-02786-9.
4. Evers S, Goossens M, Vet H de, van Tulder M, Ament A. Criteria list for assessment of methodological quality of economic evaluations: Consensus on Health Economic Criteria. Int J Technol Assess Health Care. 2005;21:240–5.
5. Odnoletkova I. Cost-Effectiveness of Therapeutic Education to Prevent the Development and Progression of Type 2 Diabetes: Systematic Review: Appendix. J Diabetes Metab 2014. doi:10.4172/2155-6156.1000438.