A Systematic Review of Cost-Effectiveness Analyses of Gene Therapy Treatments for Hemophilia Type A and B

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Background:

In 2022-23, the US FDA approved two novel gene therapies (GTs) for hemophilia:

- Hemophilia A (Valoctocogene roxaparvovec-rvox (ValRox), Roctavian®).
- Hemophilia B (Etranacogene dezaparvovec (EtranaDez), Hemgenix®).
- Both gene therapies are a **one-time single-dose** intravenous infusion of an adeno-associated virus serotype 5 vector (AAV5) transgene. The two gene therapy treatments have been priced at a premium with list prices of about **2.9 million** and **3.5 million** US dollars for ValRox and EtranaDez, respectively.

Objective:

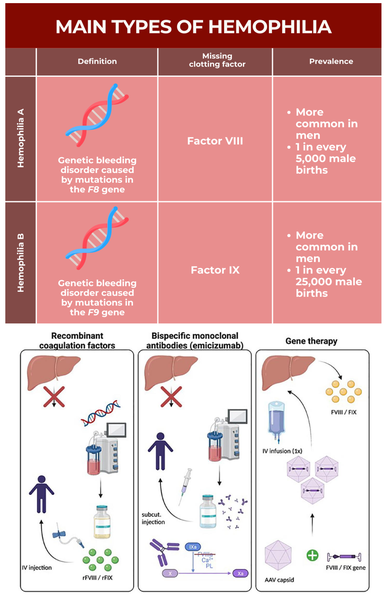
- To conduct a systematic review of cost-effectiveness studies (CEAs) for hemophilia A and B GTs to assess the validity and relevance of the **underlying data** and **assumptions** used in the identified cost-effectiveness models by using a structured approach and discuss how they relate to the challenges identified for CEAs of GTs.

Results:

Table 1. Summary of included studies characteristics and main results.

Study	Country & Perspective	Time horizon	Gene Therapy Assumed price	Intervention	Comparators	Health outcomes	Total cost		QALYs/LYs		QALYs/LYs gain	Base-case ICER
							Intervention	Comparator	Intervention	Comparator		
Hemophilia A (base case):												
Machin et al., 2018	US health system perspective	10 years	$850,000	ValRox	Factor 8 prophylaxis	• QALYs	$1,022,249	$1,693,630	8.33 QALYs	6.62 QALYs	1.71 QALYs	Dominant
Cook et al., 2020	US health system perspective	Lifetime horizon	$2,000,000	ValRox	Factor 8 prophylaxis	• QALYs • LYs	$16,656,470	$23,466,845	18.07 QALYs / 23.57 LYs	17.32 QALYs / 23.57 LYs	0.75 QALYs / 0 LYs	Dominant
ten Ham et al., 2022	Netherlands, Societal perspective	10 years	$2,251,905*	ValRox	C1: Factor 8 prophylaxis C2: Emicizumab	• QALYs • LYs	$3,009,563*	C1: $3,481,771* C2: $4,507,297*	7.03 QALYs / 9.29 LYs	C1: 6.38 QALYs / 9.28 LYs C2: 6.90 QALYs / 9.28 LYs	C1: 0.65 QALYs / 0.01 LYs C2: 0.13 QALYs / 0.01 LYs	Dominant
Hemophilia B (base case):												
Bolous et al., 2021	US health system perspective	Lifetime horizon	$2,000 ,000	EtranaDez	C1: On-demand factor 9 replacement C2: Factor 9 prophylaxis	• QALYs	$6,293,502	C1: $11,596,617 C2: $15,109,058	23.0 QALYs	C1: 11.81 QALYs C2: 20.95 QALYs	C1: 11.19 QALYs C2: 2.05 QALYs	Dominant

*Euros to US Dollars exchanging rate 1 Euro = 1.06 USD. Abbreviations: C, comparator; QALYs, quality-adjusted life-years; LYs, life years.



Method:

Study design:

- A systematic review of cost-effectiveness (utility) studies of novel hemophilia A and B gene therapy was conducted.

Search strategy and study selection:

- PubMed and Embase were searched for published studies from inception to January 12, 2024.

Quality of reporting assessment:

- Critical appraisal of the quality of reporting and the underlying modeling assumptions were conducted to assess the relevance and validity of the results.
- **The CHEERS checklist** was used to assess the quality of each economic evaluation completed for hemophilia.

Population	• Adults ≥ 18 years of age with hemophilia A or B without inhibitors
Interventions	• Valoctocogene roxaparvovec-rvox **OR** • Etranacogene dezaparvovec
Comparators	• F8 replacement therapy and emicizumab compared to ValRox **OR** • F9 replacement therapy compared to EtranaDez
Outcomes	• Incremental Cost-Effectiveness Ratio (ICER) in terms of cost per gained QALY, LY or evLYG

Discussion and conclusion:

- Based on base case ICERs, GTs had:
  - **Lower costs**
  - **Better health outcomes.**
- The GT interventions' total costs and QALYs/LYs varied among studies mainly due to the variation of:
  - **The assumed GTs price** (lower compared to the recently reported launch list prices)
  - **The study's time horizon** (10 years vs. lifetime).
- Moreover, the results were driven by the assumption that gene therapies will have:
  - **A durable effect of at least ten years**
  - **Offset the high cost** of the current standard of care and improve quality of life.
- The quality of reporting in the identified studies was **generally adherent to the CHEERs checklist** except:
  - Study context
  - The methods (study population, setting and location, perspective)
  - Details around the simulated patient cohorts.

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