The impact of different discounting rates on cost-effectiveness outcomes in chronic disease populations: Hemophilia A as an exemplary disease

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BACKGROUND

AAV-mediated gene therapy (AAVGT) is a novel treatment offering curative effects for several genetic diseases. The high upfront cost of AAVGT and the uncertainty around durability of its effectiveness are posing challenges for health economists. The ISPOR taskforce compiled a list of special considerations for gene therapies, including exploring different discounting rates.

OBJECTIVES

We examined the impact of different discounting rates when comparing AAVGT to alternative treatments: on-demand treatment (OD) and prophylaxis (pro), in persons with hemophilia A.

METHODS

We constructed a microsimulation Markov model with the following characteristics:

- **Time horizon:** Lifetime horizon.
- **Perspective:** Societal perspective in the United States.
- **Intervention and comparator:** Six treatment approaches were compared: three different strategies – on-demand treatment, prophylaxis, and gene therapy - first two were administered with either standard (SHL) or extended half-life (EHL) factor replacement. For gene therapy, each factor replacement regimen was used prophylactically before gene therapy infusion and after the gene therapy effect waned. Gene Therapy–SHL was selected as reference approach for comparison with all other alternatives.
- **Gene therapy price:** $2,000,000/patient
- **Gene therapy effectiveness:** 34 IU/dL post-infusion with 1 IU/dL decrement per year, switching back to prophylaxis at 3 IU/dL. Meaning, no bleeding episodes 0-9 years after infusion, incremental bleeding episodes 9-30 years, and switch back to prophylaxis at 31 years post-infusion.
- **Age at infusing gene therapy:** 18 years of age.
- **Model input parameters:** Utilities and transition probabilities were obtained from the literature, micro-costing exercise was conducted to estimate the costs associated with each arm.
- **Cost effectiveness threshold:** $150,000/Quality adjusted life year (QALY).
- **Discounting:** An annual discounting rate of 3% was applied in the base case.
- **Scenario analyses:** We conducted 6 scenario analyses varying the discounting rate: 1) 0% for both costs and QALYs, 2) 5% for both costs and QALYs, 3) 4% costs, 1.5% QALYs, 4) 4% costs, 2% QALYs, 5) 5% costs, 1.5% QALYs, and 6) 5% costs, 2% QALYs.

RESULTS

Base case results showed AAVGT–SHL not cost-effective compared to OD–SHL or OD–EHL with incremental cost-effectiveness ratio (ICER) of $1,060,000/QALY and $1,050,000/QALY, respectively and dominant compared to Pro–SHL and Pro–EHL. Varying discounting rate did not change the results with one exception, with 0% DR, AAVGT–SHL became cost-effective instead of dominant, compared to Pro–SHL with ICER of $140,000/QALY. AAVGT–SHL remained dominant compared to Pro in all other scenarios. Compared to OD, AAVGT–SHL was not cost-effective in any of the scenarios with ICER ranging between $460,000/QALY–$1,340,000/QALY.

Discounting Rate	Outcomes	On-demand		Prophylaxis		Gene Therapy	
		SHL	EHL	SHL	EHL	SHL	EHL
Base case 3%	Costs	$7,650,000	$8,210,000	$18,890,000	$23,420,000	$18,560,000	$22,550,000
	QALYs	13.78	14.13	22.89	23.48	24.04	24.49
0% both Costs and QALYs	Reference Gene Therapy ICER						
5% both Costs and QALYs							
4% Costs, 1.5% QALYs							
4% Costs, 2% QALYs							
5% Costs, 1.5% QALYs							
5% Costs, 2% QALYs							

	Reference intervention compared to all other alternatives.
	Dominant, reference is cheaper and more effective.
	Cost-effective, reference is more expensive yet more effective.
	Cost-effective, reference is less effective yet much cheaper.
	Not cost-effective, reference is more effective but much more expensive.

QALYs: Quality adjusted life years,
ICER: Incremental cost-effectiveness ratio .

CONCLUSIONS

Although the variation in the discounting rate changed the cost-effectiveness outcome in only one scenario, from dominant to cost-effective, the range of ICER varied widely depending on different discounting rates, indicating the significant influence of changing this input.