Supplementary Material

Estimating the impact of hemophilia A treatment administration on patient health utility: Combining a discrete choice experiment with time trade-off method

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Utility Valuation

Separate models were fitted with and without Time Trade-Off (TTO) values as a treatment attribute. Fitting a model excluding TTO values allowed for the preferences of non-TTO attributes to be examined, without the influence of TTO values. The mixed logit estimating equation without TTO is below where V = β1 × Frequency/Mode of administration + β2 × Mental health + β3 × Pain + β4 × Annual bleeds.

Fitting an additional model including TTO values acts as a utility elicitation analysis to examine the extent to which TTO values influenced the preference weights of the core outcome set for hemophilia gene therapy (coreHEM) attributes. In the latter model, TTO values were included as a continuous variable. The conditional logit estimating equation with TTO is below where V = β1 × Frequency/Mode of administration × life-years + β2 × Mental health × life-years + β3 × Pain × life-years + β4 × Annual bleeds × life-years + β5 × TTO.

The objective here was to derive the mean utility value of state x*j* based on the Discrete Choice Experiment (DCE) that corresponds to a 20-year TTO value, which is t/20. The health state utility value estimate was implemented by assuming, as in TTO, that for each profile made up from living in state x*j* for 200 years, there is a number of years (t < 20) in full health which generates the same level of utility. Thus, the probability of choosing the profile describing living in full health (11111) for 20 years is equal to the probability of choosing a profile describing living in a particular health state x*j* for 20 years.

This can be solved so that this value is expressed as a function of the regression estimates: TTO-based health utility was computed using the results of the model with TTO life year values included. Time trade-off (with 95% CI) disutility was calculated for each treatment

attribute level that was significant in the model, by dividing the model coefficient (relative preference weight) of the attribute level by the negative model coefficient of the TTO life years.

In summary, the disutility was derived by dividing the coefficient for the treatment attribute level with the coefficient for the life-year attribute as below.

The disutility for treatment attribute i = β_i / β_5

The annualized disutility for 20 TTO years = $\beta_i / (\beta_5 \times 20$

Table S1: DCE treatment attributes without TTO, 5-year durability

Variable	*Coefficient*	*SE*	*p-value*	*95% CI*	
Treatment					
One-time IV infusion, 5 years	(reference)				
One-time IV infusion, 10 years	-0.341	0.088	<0.001	0.168	0.514
1-2 times SQ injection per month	-1.090	0.104	<0.001	-1.293	-0.886
2-3 times IV infusion per week	-1.647	0.101	<0.001	-1.845	-1.448
Mental health					
No concern about your hemophilia	(reference)				
Occasionally concerned about your hemophilia	-0.142	0.084	0.090	-0.307	0.022
Always concerned about your hemophilia	-1.368	0.082	<0.001	-1.530	-1.207
Chronic pain					
No	(reference)				
Yes	-0.355	0.058	<0.001	-0.468	-0.242
Bleeding					
None	(reference)				
1-4 times	-0.368	0.079	<0.001	-0.523	-0.214
5 or more	-0.725	0.075	<0.001	-0.872	-0.577

CI, confidence interval; DCE, discrete choice experiment; IV, intravenous; SE, standard error; SQ, subcutaneous; TTO, time trade off.

(Adapted from Benton, M., 2023)

Table S2: DCE treatment attributes without TTO, 10-year durability

Variable	*Coefficient*	*SE*	*p-value*	*95% CI*	
Treatment					
One-time IV infusion, 10 years	(reference)				
One-time IV infusion, 5 years	-0.341	0.088	<0.001	-0.514	-0.168
1-2 times SQ injection per month	-1.431	0.105	<0.001	-1.637	-1.225
2-3 times IV infusion per week	-1.988	0.101	<0.001	-2.186	-1.789
Mental health					
No concern about your hemophilia	(reference)				
Occasionally concerned about your hemophilia	-0.142	0.084	0.090	-0.307	0.022
Always concerned about your hemophilia	-1.368	0.082	<0.001	-1.530	-1.207
Chronic pain					
No	(reference)				
Yes	-0.355	0.058	<0.001	-0.468	-0.242
Bleeding					
None	(reference)				
1-4 times	-0.368	0.079	<0.001	-0.523	-0.214
5 or more	-0.725	0.075	<0.001	-0.872	-0.577

CI, confidence interval; DCE, discrete choice experiment; IV, intravenous; SE, standard error; SQ, subcutaneous; TTO, time trade off.

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Table S3: DCE treatment attributes with TTO, 10-year and 5-year durability

Variable	*Coefficient*	*SE*	*p-value*	*95% CI*		*Coefficient*	*SE*	*p-value*	*95% CI*	
Treatment	***10-year***					***5-year***				
One-time IV infusion, 10 years * years	(reference)					0.040	0.007	<0.001	0.026	0.054
One-time IV infusion, 5 years * years	-0.040	0.007	<0.001	-0.054	-0.026	(reference)				
1-2 times SQ injection per month * years	-0.084	0.008	<0.001	-0.099	-0.069	-0.044	0.007	<0.001	-0.057	-0.030
2-3 times IV infusion per week * years	-0.106	0.008	<0.001	-0.121	-0.091	-0.066	0.007	<0.001	-0.079	-0.052
Mental health										
No concern about your hemophilia * years	(reference)					(reference)				
Occasionally concerned about your hemophilia * years	0.011	0.006	<0.001	-0.001	0.023	0.011	0.006	0.081	-0.001	0.023
Always concerned about your hemophilia * years	-0.061	0.005	<0.001	-0.071	-0.050	-0.061	0.005	<0.001	-0.071	-0.050
Chronic pain										
No * years	(reference)					(reference)				
Yes * years	-0.002	0.004	0.660	-0.010	0.007	-0.002	0.004	0.660	-0.010	0.007
Bleeding										
None * years	(reference)					(reference)				
1-4 times * years	-0.033	0.006	<0.001	-0.044	-0.022	-0.033	0.006	<0.001	-0.044	-0.022
5 or more * years	-0.050	0.006	<0.001	-0.063	-0.038	-0.050	0.006	<0.001	-0.063	-0.038
Life duration	0.114	0.013	<0.001	0.089	0.139	0.074	0.013	<0.001	0.048	0.099

CI, confidence interval; DCE, discrete choice experiment; IV, intravenous; SE, standard error; SQ, subcutaneous; TTO, time trade off.

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