



A novel analysis of hemophilia treatment administration on patient utility: Combining a discrete choice experiment (DCE) with time trade-off (TTO) estimation

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Introduction

- Hemophilia A (HA) is a bleeding disorder characterized by factor VIII (FVIII) deficiency
- HA treatments differ in administration and outcomes
- This study aimed to elicit preferences of adult males (≥18 years) with HA and quantify the incremental impact of treatment attribute changes on health utility with DCE-TTO methodology
- This final study (n=119) updates earlier pilot study, (n=25) (Benton M 2023. 115 participants completed DCE-TTO, and 119 completed both DCE-TTO and EQ-5D)

Methods

- HA patients (aged ≥18y) were recruited from the Louisiana Center for Bleeding and Clotting Disorders at Tulane University and the National Hemophilia Foundation (NHF), the largest hemophilia patient advocacy organization in the USA, to participate in a web or in-clinic survey (**Table 5**)
- The DCE-TTO survey was developed based on the core outcome set for hemophilia gene therapy (coreHEM) (**Table 1**)
- Patients completed a DCE-TTO instrument with 20 randomly generated hypothetical choice sets to choose their preferred treatment (**Table 1**)
- Treatment characteristics were analyzed with TTO of 10, 15 and 20 years using conditional logistic models
- Socio-demographic data and clinical characteristics, were obtained from medical records or self-reports (**Table 2**)

Results

- The coreHEM attributes were all statistically significant, and are important for patients with HA, with treatment and mental health being the most important (**Figure 1**)
- 119 HA patients completed the survey (mean age 37y, range 18-70y; 50% with moderate hemophilia A). Heterogenous demographic and clinical characteristics are described in (**Table 2**)
- 56% reported their current treatment was moderately burdensome (**Table 3**) (40% treated once every 4 weeks)
- When a TTO component was added (**Table 4**):
 - Compared with a one-time IV treatment with 10-year or 5-year durability, treatment with multiple IV infusions weekly was associated with an annualized utility decrement (0.046 vs. 10-year durability and 0.044 vs. 5-year durability)
 - Treatment with multiple SQ injections monthly was also associated with an annualized utility decrement (0.037 vs. 10-year durability and 0.030 vs. 5-year durability)

References

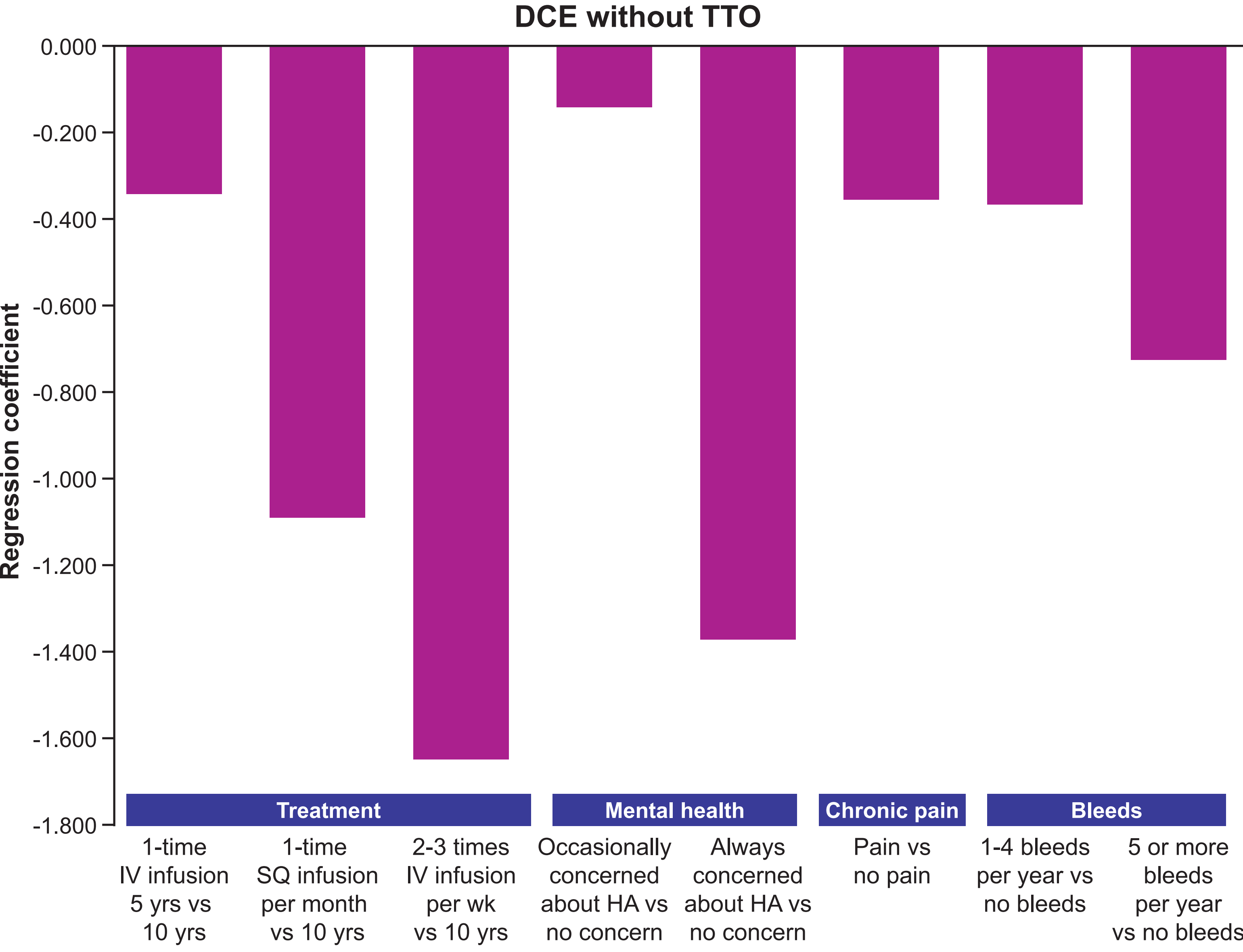
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Table 2: Demographic and clinical characteristics of respondents (n=119)

Characteristic	Adult patients* (n=119)
Age, years, Mean (SD)	37 (10.06)
Race, <u>Ethnicity</u> n (%)	
White	105 (88)
Black	9 (8)
Asian	3 (3)
Other, Prefer Not to Answer	2 (2)
<u>Hispanic or Latino/a</u>	<u>76 (64)</u>
<u>Non-Hispanic or Latino/a</u>	<u>40 (34)</u>
<u>Prefer Not to Answer</u>	<u>3 (3)</u>
Health insurance, n (%)	
Private [†]	33 (28)
Public [‡]	86 (72)
Employment status, n (%) [~]	
Full-time/Part-time	101 (85)
Long Term Sick/Disability, Unemployed, Retired	16 (13)
Full-Time/Part-time Student	6 (5)
Annual Income, n (%)	
<\$USD 25,000 ^a	18 (15)
>\$USD 25,000	101 (85)
Education level, n (%)	
High school or less ^a	15 (12)
>4y, 4y college or others [#]	104 (87)
Disease severity, n (%)	
Mild/moderate	80 (67)
Severe	39 (33)
ABR, n (%)	
No bleeds ^b	13 (11)
1 to 4 bleeds	82 (69)
> 5 bleeds	24 (20)
FVIII inhibitors in the past, n (%)	82 (69)
Current treatment (at time of consent), n (%)	
On-demand	46 (39)
Prophylaxis ^{††}	73 (61)
Type of treatment (at time of consent), n (%) ^{§§}	
Short-acting FVIII	2 (2)
Long-acting FVIII	18 (15)
Others ^{¶¶}	99 (83)
Frequency of Treatment, n (%)	28 (24)
≥ than once a week (2,3,4 times a week)	
Once every 2-4 weeks	79 (66)
< than 4 weeks (once every 5 or 6 weeks) ^c	12 (10)
Previous/current use of central device, n (%)	13 (11)
Previous/Current Joint Procedure	21 (18)
Previous/Current Joint Problems	67 (56)
History of HIV	8 (7)
History of Hepatitis C	17 (14)
General health over the past 4 weeks, n (%)	
Very good to Excellent	30 (25)
Fair to Good	88 (74)
Poor	1 (1)

SD, standard deviation; ABR, annualized bleed rate; Adult patients aged ≥18 years *All were male HA, †Includes employer/group sponsored or individual commercial insurance plans; †Includes Medicare, Medicaid or other federal insurance; & includes prefer not to answer, †Includes 2-year, vocational or technical degrees; ††Those reporting no treatment/don't know; †§Respondents could report more than one; none not shown, †¶Includes bypassing agents, non-factor products (e.g. emicizumab), or none, ~Three patients are full-time students and work part-time, two patients work full-time and are full-time students, one patient works part-time and is retired. †Includes don't know/prefer not to answer, †Includes don't know, †Includes don't know.

Figure 1. Regression Coefficient*-DCE on coreHEM attributes (n=115)



*Patient preferences based on the magnitude of the regression coefficient, is statistically significant when comparing at least one level of that attribute with the reference level. †Regression coefficient < 0 shows aversion to a treatment attribute.

Table 1: Treatment characteristics and their levels considered in the DCE-TTO survey

Treatment characteristic		Levels
Treatment	Frequency and mode of treatment	<ul style="list-style-type: none">▪ One-time IV infusion, works for 5yrs, followed by regular hemophilia treatment▪ One-time IV infusion, works for 10yrs, followed by regular hemophilia treatment▪ 2-3 times IV infusion per week▪ 1-2 times SQ injection per month
Mental health	Mental health status	<ul style="list-style-type: none">▪ Always concerned your hemophilia▪ Occasionally concerned about your hemophilia▪ No concern about your hemophilia
Chronic pain	Pain from a persistent cause	<ul style="list-style-type: none">▪ Yes▪ No
Bleeding	Number of bleeds per year	<ul style="list-style-type: none">▪ None▪ 1-4 times▪ 5 or more
Lifeduration	Remaining years of life	<ul style="list-style-type: none">▪ 10 years▪ 15 years▪ 20 years

*IV intravenous, **SQ Subcutaneous

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Table 3: Burden of hemophilia treatment

Characteristic	Adult patients (n=119) n (%)
No burden	13 (10.92%)
Slight burden	28 (23.53%)
Moderate burden	67 (56.30%)
Severe burden	11 (9.24%)

Table 4: DCE-TTO annualized utility decrement (n=115*)

Characteristic	n=115
10 yr Durability (multiple IV weekly infusions)	0.046
5 yr Durability (multiple IV weekly infusions)	0.044
10 yr Durability (multiple SQ monthly injections)	0.037
5 yr Durability (multiple SQ monthly injections)	0.030

*Note: 115 participants completed DCE-TTO, and 119 completed both DCE-TTO and EQ-5D.

Table 5: DCE-TTO survey example

Attribute	Treatment A	Treatment B
Treatment	2-3 IV infusions per week	1-2 times SQ injection Per Month
Mental health	Always concerned	Never concerned
Chronic Pain	Yes	No
Bleeding	None	1-4 times
Life Dduration	10 years	20 years

Discussion

- DCE attributes leveraged the coreHEM framework for gene therapy, which was developed by a multi-stakeholder patient-led task force
- This combined use of DCE and TTO provides a new approach to measuring health utility of hemophilia treatment administration. Future studies should compare this approach with other approaches such as standard health utility measures, vignette-based utility measures, and differences in patient preferences among subgroups (e.g., by severity, by treatment type)
- The study sample was recruited from a single Hemophilia Treatment Center in Louisiana and NHF. We cannot generalize the results to other study settings
- This updated final study confirms the results from the pilot DCE-TTO study presented at EAHAD

Conclusions

- A one-time IV treatment can improve the health utility over repeated prophylactic administration
- Durability of the one-time IV treatment impacts the incremental utility improvement; patients with hemophilia are willing to trade life years to reduce treatment burden
- Patients with hemophilia indicated that all coreHEM outcomes are important for treatment choices, but those of most importance are treatment characteristics and mental health

