Framing matters! Implications of loss aversion for communicating benefits to patients in preference studies (and beyond!)

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Background

- Discrete choice experiments (DCEs) are widely used in health economics to quantify patient and caregiver preferences, informing healthcare decision making.[1,2] DCEs assume rational, well-formed preferences. Traditional random utility models may miss systematic behavioral biases.[3,4]
- Prospect Theory suggests that choices are reference-dependent and subject to loss aversion.[5,6] Individuals perceive outcomes as gains or losses relative to these reference points and place greater weight on losses than on equivalent gains.[3,7,8]

Objectives

- **We investigate evidence of loss aversion in a DCE, using a case study of preference for hemophilia prophylaxis and discuss implications for interpreting preference data and communicating benefits to patients.**

Methods

- A web-based DCE was conducted among adults with hemophilia (n = 194) and caregivers of children with hemophilia (n = 169) in the US and UK.
- The primary efficacy attribute—the change in annual bleeds—was anchored to a reference point representing the average change from baseline in bleed rate for a patient on treatment. Attribute levels included both perceived gains (up to three fewer bleeds) and losses (up to two more bleeds) relative to this reference.
- The survey design and attributes were informed and selected based on an evidence review and input from clinical and patient advisors. The attribute levels were based on clinical literature review of the available and new prophylaxis treatment for hemophilia.
- The existence of loss aversion was tested for any difference between the effect of an increased number of bleeds vs. a decreased number of bleed
  $H_0: (|\hat{\beta}_{1\_more}| - |\hat{\beta}_{1\_less}|) = 0$; $H_1: (|\hat{\beta}_{1\_more}| - |\hat{\beta}_{1\_less}|) > 0$
- Hypothesis testing was conducted using a multinomial logit model. T-test and F-test were used to test the hypothesis. If the null hypothesis was rejected at the 5% significance level, it indicated the presence of loss aversion (effect for one more bleed > effect for one fewer bleed). Post hoc analysis was conducted to test $[H_0: |\hat{\beta}_{2\_more}| - |\hat{\beta}_{2\_less}| = 0; H_1: (|\hat{\beta}_{2\_more}| - |\hat{\beta}_{2\_less}|) > 0]$ (calculated using interpolation) as both $\hat{\beta}_{1\_more}$ and $\hat{\beta}_{1\_less}$ were not statistically significantly estimated.
- Mixed logit models specified using categorical and linear coding for the annual bleed attribute were used to explore the impact of accounting for loss aversion on minimum acceptable benefit.

Results

Sample characteristics

	Adults	Caregivers
	US (**n=150, 77%**)	US (**n=150, 88.8%**)
	UK (**n=44, 23%**)	UK (**n=19, 11.2%**)

Age (years)

	Adults	Caregivers	Children
Average	**38.5**	**43.3**	**12.6**
Range	**18–80**	**22–71**	**8–17**

Age of diagnosis (years)

	Adults	Children
Average age	**3.3**	**1.7**

	Adults	Children
Type of hemophilia	**84.5%** HA **15.5%** HB	**79.9%** HA **20.7%** HB
Severity of hemophilia	**90.0%** Severe **7.8%** Moderate **2.6%** Mild	**81.7%** Severe **12.4%** Moderate **5.9%** Mild

Inhibitor

	Adults	Children
Developed but not now	**13.4%**	**17.2%**
Currently have	**3.6%**	**6.5%**
Never developed	**81.4%**	**74.6%**
Don't know	**1.6%**	**1.8%**

The most bleeds experienced in a given year from past 5 years

	Adults	Children
None	**3.6%**	**10.1%**
1–3 times	**29.9%**	**50.3%**
3–5 times	**21.7%**	**21.3%**
6 or more	**29.9%**	**18.3%**

Table 1. Hypothesis testing of loss aversion

	Adults with hemophilia (n = 194)		Caregivers (n = 169)	
Preference estimates	**Estimates (SE)**		**Estimates (SE)**	
bleed.3less: 3 bleeds less	0.687 (0.128)***		0.353 (0.133)**	
bleed.1less: 1 bleed less	0.117 (0.133)		0.258 (0.141)	
Bleed.2less: 2 bleeds less (interpolated)	0.323[NR]		0.364[NR]	
bleed.1more: 1 bleed more	-0.127 (0.141)		-0.154 (0.15)	
bleed.2more: 2 bleeds more	-0.693 (0.121)***		-0.731 (0.129)***	
Hypothesis testing				
Test 1: Null hypothesis	T-statistic	Pr(>F)	T-statistic	Pr(>F)
H0: bleed.1less + bleed.1more = 0	-0.04	0.516	0.396	0.346
Test 2: Null hypothesis	T-statistic	Pr(>F)	T-statistic	Pr(>F)
H0: bleed.2less + bleed.2more = 0	41.539***	0***	45.091***	0***

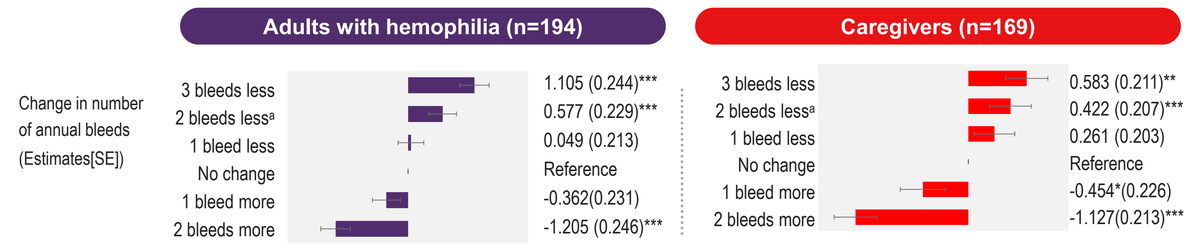
[a]As we do not have a 2-bleed-less attribute level in the DCE, the average preference estimates for 2-bleed-less were calculated using an interpolation approach based on the preference estimates for 1-bleed-less and 3-bleeds-less (midpoint estimate). Significance: ****P* value < 0.1%; ***P* value < 1%; **P* value < 5%.

Note: the loss aversion test was conducted using t-statistic and F test using a multinomial logit (MNL) model

- The analysis revealed statistically significant asymmetry between the desire to reduce two annual bleeds and the desire to avoid two additional annual bleeds (**Table 1**).
- Both adults and caregivers demonstrated statistically significant loss aversion. Among adults, the disutility of two additional bleeds was 2.09 times greater than the utility of two fewer bleeds. Among caregivers, the loss aversion ratio was even higher at 2.67 (**Figure 1**).

Results (cont.)

Figure 1. Adults and caregivers exhibited loss aversion



[a]As we do not have a 2-bleed-less attribute level in the DCE, the average preference estimates for 2-bleed-less were calculated using an interpolation approach based on the preference estimates for 1-bleed-less and 3-bleeds-less (midpoint estimate).
Significance: ****P* value < 0.1%; ***P* value < 1%; **P* value < 5%.

- Accounting for loss aversion did not significantly affect the relative attribute importance, suggesting that the overall ranking of treatment features remained stable regardless of whether loss aversion was accounted for in the model.
- Incorporating loss aversion into model estimation (i.e. categorical model) yielded lower estimates of the minimum acceptable benefit (MAB) compared with models assuming symmetric preferences (i.e. linear model) (**Table 2**). Conventional estimation of trade-off ratios typically presumes that the direction of change—gains versus losses—does not influence the estimation. However, in the presence of loss aversion, direction clearly matters.

Table 2. Implication of accounting for loss aversion: Minimum acceptable benefit

Adults (n = 194)	Categorical Model	Linear Model
	MAB (SE)	**MAB (SE)**
Administration and device type		
From IV to SC via prefilled pen	1.97 (0.31)	2.84 (0.52)
From IV to SC syringe	1.65 (0.28)	2.22 (0.48)
Refrigeration requirement		
From until use to no requirement	1.24 (0.34)	1.59 (0.54)
From until use to up to 7 days	1.15 (0.3)	1.31 (0.44)
From until use to up to 30 days	1.46 (0.29)	1.98 (0.46)
Dosing frequency		
From daily to twice weekly[a]	2.75 (0.42)	4.32 (0.59)
From daily to once a week[a]	3.67 (0.61)	6.35 (0.78)
From daily to every 2 to 4 weeks[a]	4.19 (0.75)	7.26 (0.88)
Second treatment for breakthrough bleeds		
From not required to required	0.6 (0.36)	-0.03 (0.39)
Risk of serious side effects		
Every 1% reduction	1.08 (0.26)	1.02 (0.15)
Risk of developing inhibitors		
Every 1% reduction	1.03 (0.27)	0.88 (0.11)

[a]MABs were greater than the upper bound included in the DCE. This should be noted when interpreting the results, as it is based on extrapolation. Thus, this extrapolation assumes that participants have the same trade-off behavior for the range beyond the attribute level range included in the experiment, which would need to be tested empirically

- **Future research**
- Investigate factors affecting the existence and magnitude of loss aversion, including heterogeneities across participant subgroups (by clinical and sociodemographic characteristics) and across different studies and contexts
- Integrate insights to inform the design of patient-centered communication strategies, decision aids, and policy frameworks that better reflect real-world behavior

Conclusions

- **These findings are consistent with Prospect Theory and provide evidence of reference-dependent preferences and loss aversion. Researchers should carefully consider whether to define treatment benefits as a loss or gain when designing a DCE.**
- **Accounting for behavioral patterns may enhance the interpretation of preference data and identify scenarios where the impact of benefits on treatment preference may be overestimated or underestimated, depending on an individual's reference baseline level.**
- **Describing benefits in terms of avoiding a loss may be more effective in communicating the benefits of treatment and could potentially enhance treatment adherence.**

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Disclosures

We would like to extend our heartfelt gratitude to the steering committee members (Dr. Chowdary, Dr. Dunn, and Mr. Woollard) for their invaluable contributions to the study design and results interpretation. Their expertise and guidance were instrumental in shaping the direction and outcomes of this research. We also wish to express our sincere thanks to all the participants (204 adults living with hemophilia and 179 caregivers in the US and UK). Their unique insights and input provided critical perspectives that enriched the study, which was essential to the success of this research.

HL, **AGV**, and **JW** are employees of PPD™ Evidera™ Patient-Centered Research, Thermo Fisher Scientific. This study was sponsored by Pfizer.

Acknowledgments

Editorial and graphic design support were provided by Caroline Cole and Richard Leason of Thermo Fisher Scientific.

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