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Treatment preferences in Fabry disease: a discrete choice experiment in Denmark and the UK

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INTRODUCTION

- Fabry disease, an inherited X-linked lysosomal storage disorder caused by deficiency of the enzyme α-galactosidase A, is a rare disease with a worldwide prevalence of approximately 1 in 40,000 to 1 in 117,000.[1,2]
- Before enzyme replacement therapy (ERT) was available, the mean age at death for male patients with Fabry disease was reduced by approximately 25 years when compared with patients without Fabry disease.[3]
- Patients with Fabry disease experience a wide range of symptoms that reduce quality of life, including pain (primarily in the hands and feet, but also in the legs, arms and abdomen), renal dysfunction, cardiac abnormalities, stroke and gastrointestinal symptoms.[4,5]
- Current treatment options for Fabry disease include ERT with agalsidase alpha or agalsidase beta, administered intravenously (IV), or migalastat, an orally administered pharmacological chaperone treatment suitable for patients with an amenable mutation; all treatments are required for life.
- Despite the availability of Fabry disease treatments with different attributes and modes of administration, there has been no assessment of which treatment characteristics are most important to patients with Fabry disease; this assessment is especially important given there is a choice between IV infusion and oral therapy modalities for certain eligible patients.
- This study was designed to develop and validate a two-phase cross-sectional discrete choice experiment (DCE) to elicit patients' views on the importance of outcomes in Fabry disease and modes of treatment administration.

METHODS

Survey development

- Qualitative interviews were performed to explore symptoms experienced and the impact of Fabry disease on patients' lives.
- Interviews also explored patients' views on the importance of different treatment features.
- The DCE was designed to present hypothetical treatment choices that vary in terms of discrete levels by defined treatment attributes.
- The attributes selected, based on in-depth qualitative work, included symptoms (pain, fatigue, gastrointestinal), possible waning of treatment effect, mode of administration and adverse events (risk of headaches and flu-like symptoms).
- An orthogonal design was used to combine attributes and levels into choice sets. An example choice question is shown in **Figure 1**.
- The draft survey was piloted with two Fabry patients to explore comprehension and general views on its merits.

Study design

- The study protocol was approved by an independent review board.
- Participants were recruited by the Society for Mucopolysaccharide Diseases (MPS Society) in the UK and the Fabry Patient Association in Denmark.
- All participants were adults currently receiving Fabry disease treatment.
- The survey was completed online in English or Danish.
- Choice data were analysed using conditional logit models.

Figure 1. Example choice question

Characteristic	Treatment A	Treatment B
Worst pain you experience PAIN SCORE 0–10 NUMERICAL RATING 0 No pain 1 2 3 4 5 Moderate pain 6 7 8 9 10 Worst possible pain	Your level of pain will **stay the same**	Your level of pain will **improve by 1 point** on the scale
Worst level of tiredness and fatigue you experience TIREDNESS SCORE 0–10 NUMERICAL RATING 0 No tiredness 1 2 3 4 5 Moderate tiredness 6 7 8 9 10 Worst possible tiredness	Your level of tiredness will **improve by 2 points** on the scale	Your level of tiredness will **stay the same**
Digestive problems	You **rarely or never** experience diarrhoea, stomach pains or constipation	You experience diarrhoea, stomach pains or constipation **several times a month**
Treatment waning Your treatment can start to wear off and symptoms will return until you receive another dose	Treatment **wears off completely** Pain & fatigue return before the next dose	Your treatment **wears off a little** and some pain and fatigue return before the next dose
How do I take the treatment?	Treatment is every 2 weeks at home **Self-administered** Delivered by an **intravenous infusion** in your arm	Treatment is every 2 weeks at home Administered by a **nurse** Delivered by an **intravenous infusion** in your arm
Side effects: headaches	You get no **headaches** from treatment	You get headaches from treatment **about 12 times a year** Can be treated with paracetamol
Treatment reactions Tingling feelings, chills, pain, tiredness, or general flu-like symptoms	You experience a reaction to your treatment about **6 times a year**	You **never experience** a reaction to your treatment
Which do you prefer? *Please tick A or B*	A ☐	B ☐

RESULTS

Sample demographics

- Patients in the ERT group were younger than those in the migalastat group and had been receiving treatment for longer; both groups contained a similar proportion of female participants (**Table 1**).

Summary of results

- DCE analyses showed that participants placed significant value on reducing their level of pain and tiredness (two-point improvement in pain: odds ratio [OR]=1.955, *P*<0.001; two-point improvement in tiredness: OR=1.419, *P*=0.001; **Table 2**).
- Participants also preferred to avoid digestive problems if they were affected several times a month, but once a month was not a significant driver of preference (several times a month: OR=0.545; *P*<0.001).
- Participants preferred to avoid treatments that were associated with a waning of effect (wears off completely: OR=0.652; P<0.001; wears off a little: OR=0.787; *P*<0.05).
- Participants preferred to avoid reactions to treatment (reactions 12 times a year: OR=0.538; *P*<0.001; reactions 6 times a year: OR: 0.726; *P*<0.01; compared with no treatment reactions).
- Participants preferred oral therapy over IV infusion regardless of whether it was self-administered or nurse-administered IV treatment (oral vs self-administered IV treatment: OR=0.301; *P*<0.001 or nurse-administered IV treatment: OR=0.361; *P*<0.001).
- Experiencing headaches 6 or 12 times a year was not a significant driver of preference in the data.

Treatment subgroup analyses

- Subgroup analyses showed that participants in both ERT and migalastat treatment groups preferred oral treatment compared with IV treatment in the hypothetical DCE scenarios
  - Participants currently on ERT were 2.7 times more likely to choose an oral treatment than a self-administered IV treatment (OR=0.369; *P*<0.001)
  - Participants currently on migalastat were 5.7 times more likely to choose an oral treatment than a self-administered IV treatment (OR=0.176; *P*<0.001).

Limitations

- The study population is small and heterogeneous, which reflects recruitment for a rare disease where population numbers are limited.
- Participants in the study were not stratified or matched.
- Patients were only recruited from two countries, and the generalisability of the results would be improved if data collection was extended to other countries.

Table 1. Survey demographic characteristics (N=57)

Characteristic	ERT (n=37)	Migalastat (n=20)	Total (N=57)
Age, mean (SD)	43.8 (15.4)	53.2 (10.8)	47.0 (14.6)
Gender, N (%)			
Female	21 (57%)	13 (65%)	34 (60%)
Main activity, N (%)			
Paid employment	15 (41%)	12 (60%)	27 (47%)
Not working: health problems	11 (30%)	2 (10%)	13 (23%)
Other	11 (30%)	5 (25%)	14 (25%)
Missing	-	1 (5%)	1 (2%)
Career impacted by Fabry disease, n (%)			
Yes: stopped working	10 (27%)	4 (20%)	14 (25%)
Yes: reduced working hours	6 (16%)	4 (20%)	10 (18%)
Yes: changed jobs	1 (3%)	0 (0%)	1 (2%)
Yes: career progression affected	3 (8%)	0 (0%)	3 (5%)
No	13 (35%)	9 (45%)	22 (39%)
Age at diagnosis, mean (SD)	33.7 (14.4)	42.5 (14.9)	36.8 (15.1)
Time in years since starting current treatment, mean (SD)	7.1 (4.8)	2.7 (3.1)	5.6 (4.7)
Current treatment, n (%)			
Agalsidase beta	27 (73%)	–	27 (47%)
Agalsidase alfa	10 (27%)	–	10 (18%)
Migalastat	–	20 (100%)	20 (35%)
Previous treatment, n (%)			
ERT	11 (30%)	15 (75%)	26 (46%)
Migalastat	2 (5%)	–	2 (4%)

ERT, enzyme replacement therapy; SD, standard deviation.

Table 2. Results of clustered conditional logit model of patient preferences for Fabry disease treatment attributes (N=57)

Attributes and levels	Coefficients*	Standard error	*P* value	Odds ratios	95% CI	
Constant	0.328	0.078	<0.001	1.389	1.191	1.618
Pain						
Reference category: 'stay the same'						
Improved by 1 point	**0.338**	0.110	**0.002**	**1.403**	**1.130**	**1.741**
Improved by 2 points	**0.671**	0.113	**<0.001**	**1.955**	**1.566**	**2.441**
Tiredness						
Reference category: 'stay the same'						
Improved by 1 point	0.108	0.107	0.314	1.114	0.903	1.373
Improved by 2 points	**0.350**	0.105	**0.001**	**1.419**	**1.155**	**1.742**
Digestive problems						
Reference category: 'never diarrhoea, stomach pains or constipation'						
Once a month	–0.206	0.109	0.060	0.814	0.657	1.009
Several times a month	**–0.607**	0.106	**<0.001**	**0.545**	**0.443**	**0.671**
Treatment effect waning						
Reference category: 'same benefit all the time'						
Wears off a little	**–0.240**	0.112	**0.033**	**0.787**	**0.631**	**0.981**
Wears off completely	**–0.427**	0.104	**<0.001**	**0.652**	**0.533**	**0.799**
Mode of administration						
Reference category: 'oral treatment'						
Self-administered intravenous infusion	**–1.202**	0.114	**<0.001**	**0.301**	**0.240**	**0.376**
Nurse-administered intravenous infusion	**–1.020**	0.117	**<0.001**	**0.361**	**0.287**	**0.454**
Side effects: headaches						
Reference category: 'no headaches from treatment'						
6 times a year	–0.191	0.106	0.072	0.826	0.671	1.017
12 times a year	–0.184	0.121	0.129	0.832	0.656	1.055
Treatment reactions						
Reference category: 'never reaction to treatment'						
6 times a year	**–0.320**	0.108	**0.003**	**0.726**	**0.587**	**0.897**
12 times a year	**–0.621**	0.106	**<0.001**	**0.538**	**0.437**	**0.662**

Bold indicates *P*<0.05; model statistics: log likelihood=–568.075; prob >chi^2=0; number of respondents=57; number of choice sets per respondent=18. *The larger the coefficient value, the more likely the participant is to choose that treatment option (or not choose if negative). CI, confidence interval.

CONCLUSIONS

- This study is the first to explore treatment preferences for patients with Fabry disease using hypothetical DCE scenarios.
- Participants expressed a strong preference to reduce the burden of their disease, as demonstrated by the preference to reduce pain, fatigue and gastrointestinal symptoms.
- Participants also preferred oral therapy over IV therapy, irrespective of their current treatment regimen.

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References

1. Meikle PJ *et al. JAMA* 1999;281:249–54.
2. Scriver CR. Ed. *The metabolic & molecular bases of inherited disease.* 2001.
3. Schiffmann R *et al. Nephrol Dial Transplant* 2009;24:2102–11.
4. Burand J *et al. Pain* 2021;162:1305.
5. Mehta A *et al. QJM: Int J Med* 2010;103:641–59.

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