Barriers and facilitators to clinical trial participation:
improving accessibility, logistics, and awareness

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Background

- Fabry disease is a rare lysosomal disorder caused by mutations in the *GLA* gene, leading to a deficiency of the enzyme *α-galactosidase A*.[1] This enzyme deficiency results in multi-organ failure affecting the kidneys, heart, and nervous system.[2] Current treatments include Fabry-specific therapies such as enzyme replacement therapy and oral chaperone therapy alongside symptom management strategies.[3]
- For further advancements in Fabry treatment, active patient participation in clinical trials is required. Due to the low prevalence and dispersed nature of rare disease populations, clinical trial participation is challenging, as patients often face logistical hurdles like long-distance travel.[4] Although these challenges are not unique to rare diseases, they are intensified by the limited pool of eligible participants.

Objective

To gain insights on clinical trial awareness, perception and participation within the Fabry community.

Methods

Survey

- During the UK MPS Society's Fabry Matters Conference (March 1-3 2024) two 10-15 minute online surveys, comprising of multiple-choice questions, aimed to capture patient demographics and attitudes towards research activities and clinical trials.

Inclusion criteria

- Individuals with Fabry disease, including those awaiting confirmed diagnosis, who attended the conference.
- Caregiver or partner completing the survey on behalf of a person with Fabry.*
- Respondents aged ≥18 years who were able to give informed consent.

Analysis†

- Quantitative analysis: Descriptive statistics were used to analyze survey responses.
- Behavioral analysis: The Behavioral Change Wheel method[5] was used to analyze the barriers to trial participation.

Behaviour Change Analysis

- The Behavioral Change Wheel (BCW), developed by Susan Michie and colleagues[5] (Figure 1a), was utilized to guide the development of recommendations to improve participation rates. The process involved:

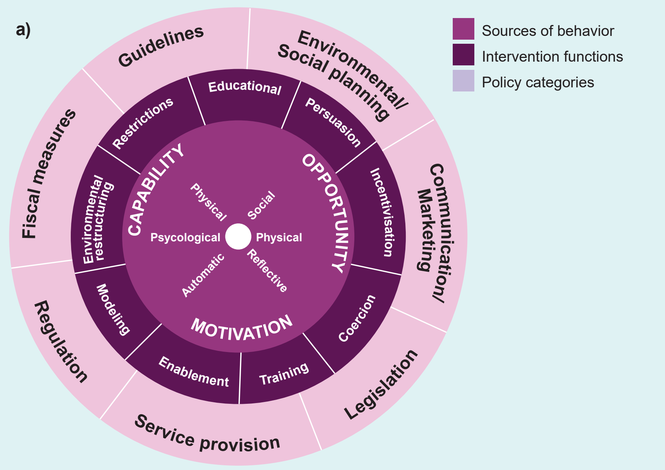
STEP 1 Identifying the source of behavior as either being a capability, motivation, or opportunity (Figure 1b).

STEP 2 Selecting the appropriate intervention strategies using the approaches developed by Susan Michie et al. (Figure 1c).

STEP 3 Choosing specific behavior change techniques to drive change within the selected interventions.[6]

STEP 4 Developing recommendations for overcoming barriers to trial participation for those conducting or supporting clinical trials and patient organizations, in the rare disease field based on the identified techniques.

a)



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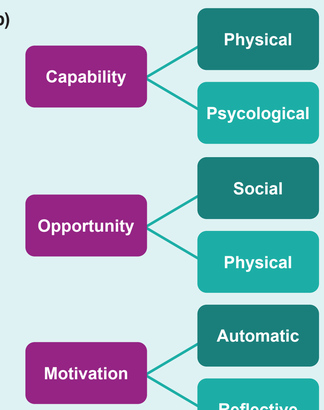

c)

Sources of behaviour:	Education	Persuasion	Incentivization	Coercion	Training	Restriction	Environmental restructuring	Modeling	Enablement
Physical capability					✓				✓
Psycological capability	✓				✓				✓
Reflective motivation	✓	✓	✓	✓					
Automatic motivation		✓	✓	✓			✓	✓	✓
Physical opportunity						✓	✓		✓
Social opportunity						✓	✓		✓

Figure 1: *Figure illustrating a) the behavior change wheel, b) the sources of behavior and c) a table showing the appropriate intervention strategies to use based on the source of behavior.*

Results

Patient demographics

Surveys for 51 patients were completed,‡ (36 females, 15 males). Thirteen were not receiving treatment, and the remaining 38 were either on enzyme replacement therapy or oral chaperone therapy.

Median age at diagnosis (n = 50)	Median age treatment started (n = 38)	Median age now (n = 51)
32.5 years **mean ± SD: 34.1±17.4** **range: 0.0–66.0**	41.4 years **mean ± SD: 40.6±17.1** **range: 8.5–68.8**	51.1 years **mean ± SD: 49.7±13.6** **range: 14.1–72.3**

Awareness and communication of clinical trials

Out of the 51 respondents, 65% (n=33) of patients were unaware when clinical trials were taking place.

- Among those who were unaware (n=33), the majority (88%, n=29) were unsure where to find information.
- For those who were aware (n=18), most reported obtaining information through their Fabry specialist (89%, n=16) and the MPS Society (50%, n=9) (Figure 2).

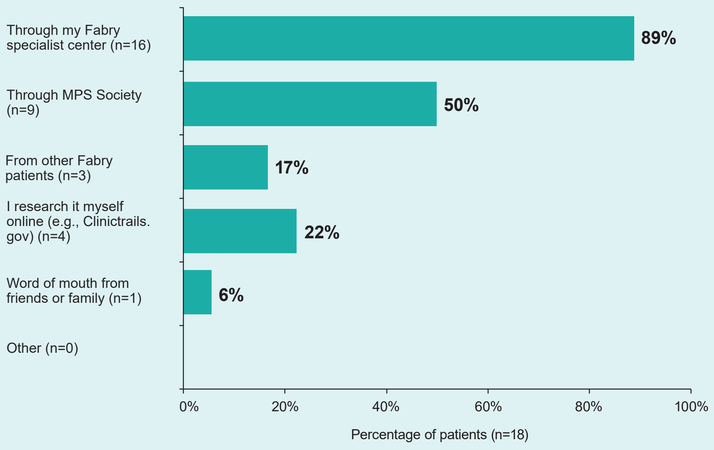

Figure 2: *Figures illustrating how respondents who were aware of ongoing clinical trials obtained their information.*

Respondents were also asked how they would prefer to be notified about clinical trials, and the majority indicated a preference for communication through MPS Society (80%, n=41), followed by their healthcare professional (73%, n=37) (Figure 3).

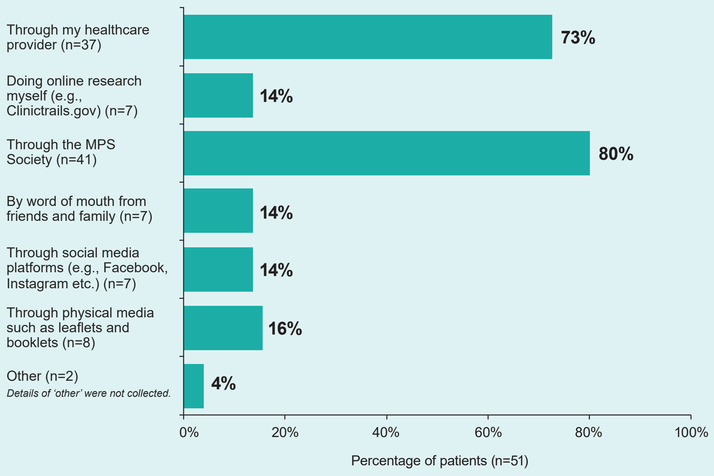

Figure 3: *Figure illustrating how respondents would like to be notified about current clinical trials.*

Perception of clinical trials

Among those who had participated in clinical trials (n=19), the key factors that would have improved their experience included regular trial updates (74%, n=14), flexible schedules (47%, n=9), and emotional or financial support (26%, n=5).

When asked to select and rank the statements that would discourage them from participating in clinical trials, the most common barriers for patients were concerns about side effects (84%, n=43) and having to relocate or travel long-distances (63%, n=32) (Figure 4).

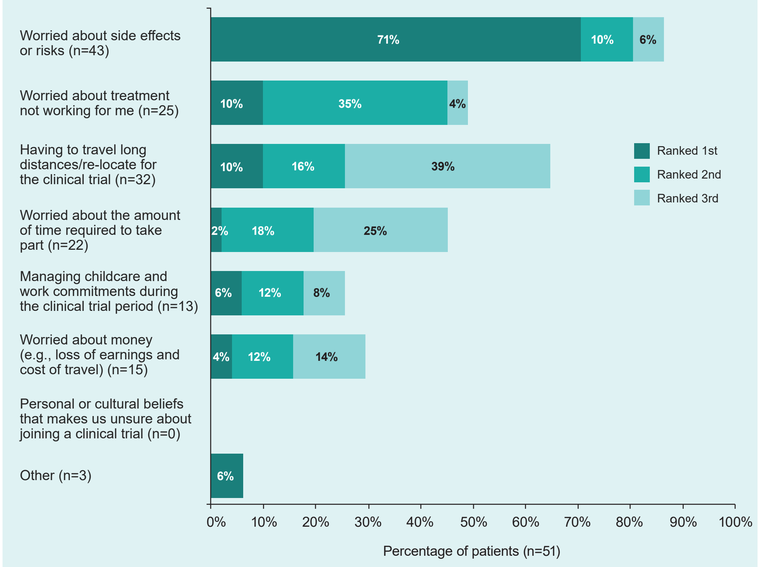

Figure 4: *Figure illustrating factors that encourage/discourage patient participation in clinical trials.*

Key findings

- **A majority of respondents were unaware of when clinical trials were taking place, mainly due to difficulty accessing information.**
- **Those who were aware typically received details from their Fabry specialist and the MPS Society.**
- **To improve the patient experience, participants highlighted the need for regular updates, flexible schedules, and emotional or financial support.**
- **Side effects and travel demands were identified as major barriers to participation.**
- **To address concerns about side effects or risks, solutions include educational strategies such as providing guides on managing side effects, offering information on pharmacological support, and using expert-led videos to explain safety measures.**
- **To address travel-related concerns, recommendations include locating trial sites closer to patients, and providing comprehensive logistical support, such as assistance with transportation, accommodation, and emotional support to alleviate travel-related stress.**

Behavior change analysis

We focused on addressing the two main barriers to clinical trial participation:

1) Concerns about side effects

2) Traveling long distances or having to relocate (Figure 4)

1 Concerns about side effects or risks:

- **Step 1: Identifying sources of behavior** Concerns about side effects was identified as a form of **reflective motivation**, where patients carefully weigh the risks and benefits in their decision-making.
- **Step 2: Identifying intervention functions** To address this, we focused on *education* as the key intervention function. We excluded *persuasion* and *coercion* due to ethical concerns and decided against *incentivization*, as and decided against incentivization as there are strict regulatory guidelines for what can be provided to clinical trial participants that can vary from country to country.
- **Step 3: Behavior Change Techniques (BCT) and real-world recommendations**:

EDUCATIONAL RECOMMENDATIONS

BCTS:	RECOMMENDATIONS:
Pros and cons:	Develop educational materials such as expert-led videos to explain the positive impacts of trial participation and how risks are managed.
Instruction on how to perform a behavior:	Provide clear, step-by-step guidance on managing side effects and whom to contact for support during the trial.
Pharmacological support:	Provide information about the pharmacological support available to manage side effects.

2 Having to travel long distances/relocate:

- **Step 1: Identifying sources of behavior** We identified the need to travel as a **physical opportunity** barrier, where the external factor of traveling is preventing patients participating in clinical trials.
- **Step 2: Identifying intervention functions** To address this, we focused on *environmental restructuring* and *enablement* as intervention functions, while excluding *restriction* since it is not appropriate when trying to increase clinical trial participation.
- **Step 3: Behavior Change Techniques (BCT) and real-world recommendations**:

ENVIRONMENTAL RESTRUCTURING RECOMMENDATIONS

BCTS:	RECOMMENDATIONS:
Restructuring physical environment:	Offer trial locations closer to patients or provide virtual participation options.
Framing/reframing:	Reframe the need to travel as an investment in the patient's health rather than a burden.

ENABLEMENT RECOMMENDATIONS

BCTS:	RECOMMENDATIONS:
Problem solving:	Use clinical trial vendors to assist patients with specific logistical barriers, such as transportation and relocation.
Instruction on how to perform the behavior:	Use clinical trial vendors to provide clear guidance on arranging trial logistics, including travel and accommodation.
Social support:	Use clinical trial vendors to offer financial or logistical help to facilitate participation, as well as emotional support to ease travel-related stress.

Conclusion

This study highlights key barriers and motivators affecting clinical trial participation within the Fabry community. Increasing trial participation requires collaborative efforts from clinical trial sponsors, patient organizations, and clinical trial vendors to raise awareness through clear communication and targeted educational initiatives. By providing guidance, tools, and practical support, these stakeholders can help address patient concerns about side effects and reduce the burden of long-distance travel, ultimately enhancing a more positive perception of clinical trial involvement.

FOOTNOTE

*Included caregivers who completed the survey on behalf of patients who were not able to attend the conference. † This analysis only reports a subset of the data collected. ‡ One respondent was still awaiting a confirmed diagnosis, and one respondent was a caregiver completing the survey on behalf of a person with Fabry who did not attend the conference.

REFERENCES

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DECLARATION

This research was conducted in accordance with the British Healthcare Business Intelligence Association's Legal & Ethical Guidelines for Market Research. The survey study was non-interventional, and all participants signed a consent form.