

# #ThinkRare – Harnessing the power of advocacy and community engagement for biomarker and clinical research

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## Introduction

Neurodevelopmental disorders (NDDs) can be rare and ultra-rare conditions characterised by severe intellectual and physical disabilities impacting the daily life of patients, their caregivers and their immediate families. Due to the rarity of some of these disorders, they have not received sufficient attention in terms of treatment and drug discovery, despite the fact that they usually have very clear genetic and molecular underpinnings; this is partly to ascribe to the difficulty of recruiting a sufficient number of participants and successfully reaching communities that are often geographically scattered in addition to living with a condition that increases burden on individuals.

Our #ThinkRare research currently focuses on the pathogenesis and treatment of the rare genetic NDDs **CDKL5 Deficiency Disorder (CDD)** and **Fragile X Syndrome (FXS)**, both of which are due to mutations of specific genes located on the X chromosome namely *Cdkl5* and *Fmr1*, respectively, and **Charcot-Marie-Tooth disease (CMT)**, which comprises a group of progressive genetic disorders affecting the peripheral nervous system. CDD is an ultra-rare and highly debilitating NDD associated with **early-onset seizures and severe global developmental delay**. FXS is also associated with **developmental delay** along with a psychological profile that includes **autism-like traits and anxiety**, while CMT is the most common inherited neuropathy and it causes **damage to the peripheral nerves** and often specifically nerves that control muscles, resulting in **progressive muscle weakness** (with a typical onset in adolescence or early adulthood).

#ThinkRare prioritises the concept of **patient-centricity** in order to better bridge the translational gaps between the day-to-day experience of the individual, the clinic and the preclinical research that underlies drug discovery efforts. Patients, caregivers and associations **actively participate in the design of our preclinical and clinical research** with the aim to improve the translational aspect of our projects. Understanding the patient needs and the community's specific profile allows for **greater integration of the patients into research**.



Figure 1. Families of the CDKL5 community engaged in a workshop activity.

## Engagement Strategies

The **Ulysses Neuroscience Clinical** team engages with patient communities by organizing focus groups and awareness events, and actively seeking feedback and collaboration on research protocols so as to improve accessibility. This can include changing the locations of collection centers or adding extra ones, as well as improving the wording of information leaflets and consent forms to ensure they align with the interests and needs of the community.

### Surveys

Surveys are a convenient method to gather information quickly and without the need for in person gatherings. If designed correctly, surveys can yield a **great deal of information** and a **deeper understanding** of the responders' needs and opinions. For example, Fig.2 shows the desired outcomes of an awareness event according to the Irish CMT population.



- Networking
- Information
- Specific information
- Cure
- Research

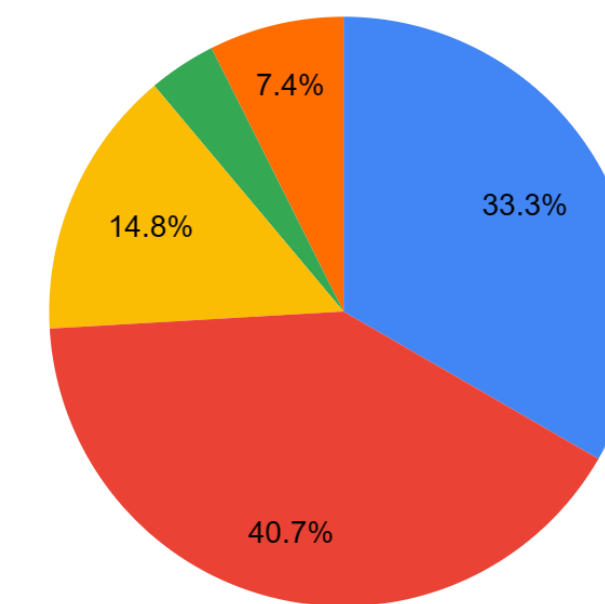


Figure 2. Common topic areas of answers to the question, 'What would you like to achieve from the day?' from a survey of CMT patients.

### Podcasts and Reels

Podcasts and reels are the tools with which we **directly ask** for patients to share their stories.

Reels are either recorded by team members who explain some aspects of our work, or they are sent to us by the families to share snippets of their life experience.

They have a strong **immediate impact** on the interaction with the patient communities, who engage with them in real time and spontaneously ask questions about our work and how to get involved or suggest improvements and projects. Podcasts, on the other hand, are initiated by the team who carries out some background research on the topic and then finds guests. While the podcasts do not provide as much of a platform for immediate interaction, they are **highly appreciated by the community** who is represented in a more thorough way, and they greatly help **promoting awareness**.

### Awareness Events and Family Days

These events are centered around the patients, facilitating them to include their usual social environment. Family days in particular are planned around the needs of the whole family, and they need to take into account the presence of other children in addition to the patient community - it is often a good idea to have a small brainstorming session either virtually or in person so that the event can be tailored to the people taking part in it. Awareness events include doctors, and the wider environment of caregivers, clinical workers, and research professionals. These events help build mutual trust between all stakeholders, promoting improved collaborations and heavily affecting recruitment efforts.

## Engagement impact

Our experience with the different communities we work with can help get some insights on the impact that engagement has on the perception of pharma and clinical studies.

Reaching the CDKL5 families has been quite easy, with a clear point of contact in the Irish association and a tight knit global community which allowed us to create initiatives such as the multilingual podcast series.

In contrast, CMT is not represented locally, and during our initial pilot study recruitment was entirely handled in the clinic. Only through the help of related associations such as Muscular Dystrophy Ireland and CMT UK were we able to reach some patients directly, Fig. 3 shows the interest in clinical studies expressed at this point in time.

Would you be interested in participating in research?  
22 responses

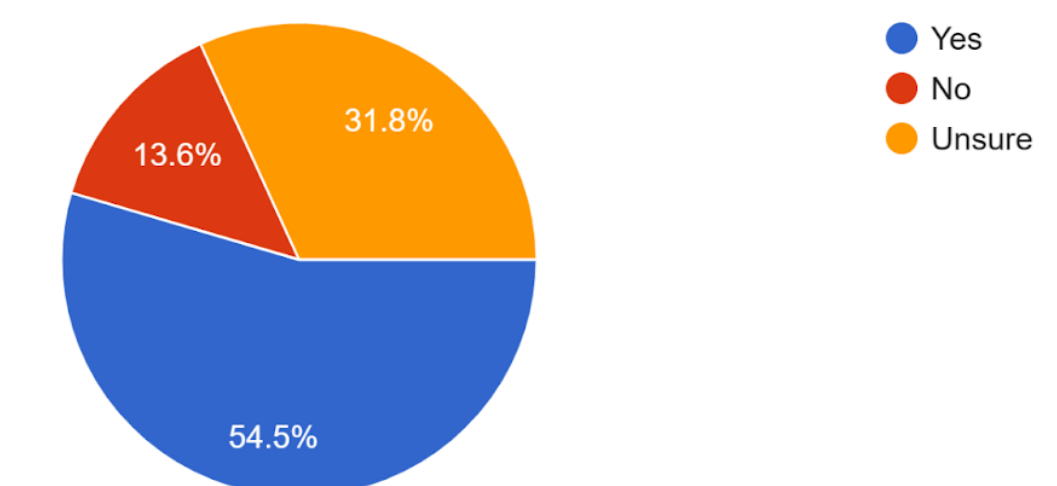


Figure 3. Answers to the question, 'Would you be interested in participating in research?' from a survey of CMT patients.

CDKL5 communities are very active and present around the globe, with regular forums that families often attend, and an overarching alliance that closely collaborates with doctors and researchers for a patient registry.

In addition to attending the Forums, we have organized the first family day in Ireland in 2019 and have, since then, held one at least every year barring the lockdown year; when it came to run a biomarker study on the clinical population the families were extremely eager to participate, and to bring age matched controls for the patients. After running a workshop activity that incorporated a survey, the parents manifested a strong interest in participating in more studies:

Are there any other types of studies you would be interested in enrolling your child/children in?  
5 responses

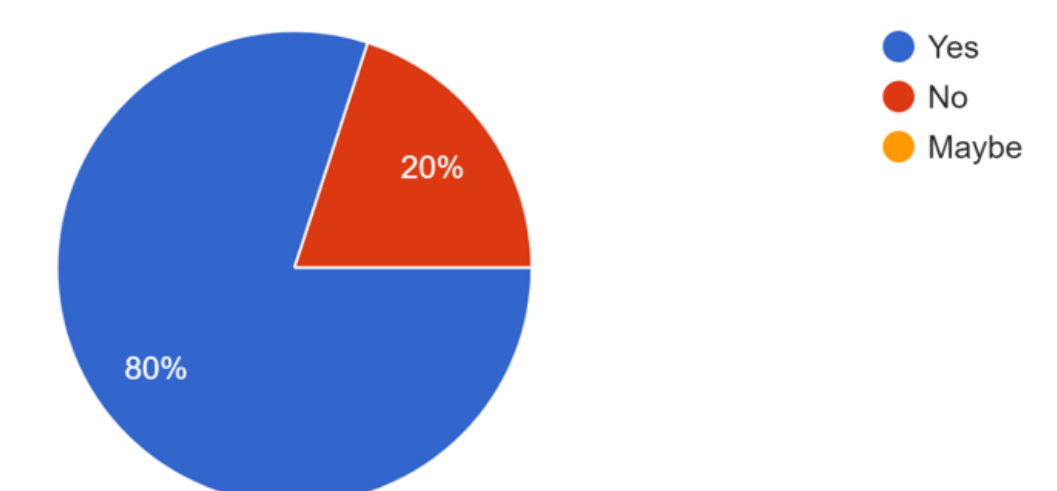


Figure 4. Answers to a question about participating in further studies, following an awareness day and an activity to structure feedback on our pilot study.

The data obtained through the surveys, as well as the experience with the community, suggest that when appropriately engaged, patients and caregivers are enthusiastic research participants and collaborators.