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Abstract

Patient-reported Clinical Care Experiences while Navigating the Progression of Dysferlinopathy (Limb-Girdle Muscular Dystrophy 2B/R2)

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Dysferlinopathy is an ultra-rare, autosomal recessive form of limb-girdle muscular dystrophy (LGMD) with no existing treatments or disease-specific clinical care guidelines. Efforts have been made to prepare for future interventional trials of dysferlinopathy through preclinical research, natural history studies, outcome measure development, diagnostic standardization, and a disease-specific global patient registry known as the Dysferlin Registry. However, activities to de-risk drug development programs for the disease have neglected to explore the clinical experiences of individuals with the condition. Knowing what matters most to individuals with dysferlinopathy surrounding their clinical management can inform key opinion leaders as they develop the first standards of care guidelines for the condition. Here, we explore themes from interviews with eight participants through a qualitative, phenomenological framework with key findings suggestive of the need to educate the clinical communities, humanize clinical approaches, customize care, and utilize trauma-informed clinical communication with the dysferlinopathy patient community, facilitating productive clinical engagement.

Introduction

Dysferlinopathy, a form of limb girdle muscular dystrophy (LGMD), is an ultra-rare-orphan disease of autosomal recessive inheritance caused by mutations in the DYSF gene (Bushby, 1999). It was initially classified as LGMD2B, then renamed LGMDR2, and has also been named Miyoshi myopathy type 1 (Straub, et al. 2017, Liu, et al. 1998). The condition is associated with a lack of the dysferlin protein, which negatively impacts specific skeletal muscles, typically beginning in the teenage or early adult years after a healthy, active childhood. While not known to affect life expectancy, it slowly progresses to the point that an affected person needs assistance accomplishing fundamental activities of daily living such as walking, standing, rising from a chair, moving the legs, raising one's arms, full use of feet and hands, turning over in bed, using toilets, grooming, and feeding (Moore, et al. 2019).

Unfortunately, with no treatments available or any agreed international care standards for the disease, there is only minimal clinical guidance available to healthcare professionals or to patients navigating this devastating form of LGMD. Additionally, the condition qualifies as an ultra-rare-orphan disease, which is fewer than 20 patients in a population of one million (Saredella, et al. 2018). The exact prevalence has not been established. This has called for dedicated research and advocacy efforts to support dysferlinopathy preclinical research, patient identification, the development of diagnostic standards, the collection of natural history data, and the identification of disease-specific outcome measures in preparation for future clinical trials.

In 2005 the Jain (Family) Foundation was launched, with a mission to identify treatments for dysferlinopathy, as no treatment or disease-modifying clinical protocols were in place. In

addition to leading preclinical and clinical studies of dysferlinopathy, the Jain Foundation has developed a global disease-specific patient registry known as the Dysferlin Registry (DR) to support successful patient recruitment, community centralization, targeted communication, research, and the de-risking of drug development programs. Still, until recently, individuals with dysferlinopathy have not had many opportunities to directly contribute to working groups aiming to develop the first clinical care guidelines specifically for dysferlinopathy. In 2021, efforts were initiated by a clinical working group led by a core group of global key opinion leaders (KOLs) supported by the Jain Foundation and the European Neuromuscular Centre (ENMC). The KOLs began to develop standards of care guidelines specifically for dysferlinopathy (SOCD) and an important question arose: how can KOLs know what health concerns are most important to individuals with dysferlinopathy if their lived experiences are not well represented among exploratory clinical conversations?

Minimal literature specific to the views of the dysferlinopathy patient community exists. The Jain Foundation funded a natural history study, called the Clinical Outcome Study for Dysferlinopathy (COS), which included patient questionnaires and an analysis comparing the results from multiple patient-reported outcome measures (PROMs). The COS study investigators recorded patient reporting instrument data such as the activity limitations for patients with upper and/or lower limb impairments (ACTIVLIM) and the Individualized Neuromuscular Quality of Life Questionnaire (INQoL) with the clinical assessments being explored in the study (Mayhew, et al. 2022). This work successfully articulated change over time that was synergistically captured through the ACTIVLIM PROM and the functional outcomes measured using the North Star Assessment for Dysferlinopathy (NSAD; now also referred to as the North Star Assessment

for limb-girdle like muscular dystrophies). These findings suggested that the NSAD assessments could be structured into a study in concert with the ACTIVLIM PROM, creating trial designs that utilize a disease-specific clinical assessment framework relevant to the activities of everyday life of individuals with dysferlinopathy. However, a deeper understanding of the essence of the clinical experiences of individuals living with the progressive muscle disease has not been documented. Could communicating the patient view to healthcare professionals improve rates of retention in future trials?

Additional literature explores examples of current structures for developing standards of care that were determined to be inappropriate for developing clinical guidelines for rare diseases (Pai, et al. 2015). Evidence-based methodologies are well documented and can be utilized when developing care guidelines for common diseases (Pai, et al. 2019). Rare diseases are notoriously understudied, and diagnostically non-linear. Clinical studies of rare diseases are often underpowered, with little structured data on the natural history of the disease. These factors create significant barriers to achieving the level of rigor needed to support clinical care recommendations for rare diseases.

Case studies for specific rare diseases have been compared to evaluate the role of patient perspectives in developing standards of care (van Breukelen, 2016). While these efforts are an important beginning, a significant limitation is that the patient/caregiver perspective was gathered and summarized by advocacy professionals, rather than coming directly from patients. Perspectives directly from patients can identify barriers, communication needs, and gaps in care. This can enable healthcare professionals to develop guidelines that support caring for patients in

ways that are meaningful to them. Various publications emphasize the need to scaffold the development of standards of care guidelines for rare diseases using methodologies specific to rare diseases (Pavan, et al. 2017, Kremp, et al. 2012, Sejersen, et al. 2014). However, patient voices are missing components within the proposed development strategies (Pai, 2015).

It has been observed that outcome measures used by rare disease drug developers do not always assess what matters most to the patients (Morel, et al. 2017). Surrogate biomarkers may be able to demonstrate efficacy in a clinical trial of a novel therapeutic, but will patients agree that this justifies the risks involved in taking the treatment? How can governmental regulatory boards make such determinations without knowledge of the experiences of individuals living with rare diseases like dysferlinopathy? Documenting and disseminating the perspectives of individuals with dysferlinopathy has the potential to inform future study design and support regulatory decision-making, in addition to supporting the development of standards of care.

Methods

The study was conducted using an observational, qualitative methodology following a phenomenological design framework, utilizing semi-structured, in-depth interviews, which were transcribed and analyzed following Interpretive Phenomenological Analysis, IPA (Groenewald, 2004, Braun/Clarke, 2006). IRB exempt status was approved with category 2 designation from the University of Washington, Human Subjects Division.

Eligibility criteria specified that participants must have genetically confirmed dysferlinopathy, be at least 18 years old, and reside in the United States. Participants were recruited directly from the following purposive sampling practices (Moser, et al. 2018). The DR is curated by the Jain

Foundation and is inclusive of individuals who have a genetic diagnosis of dysferlinopathy totaling 1,015 individuals worldwide as of June 7, 2022 (325 registry members live in the U.S.). The purposive sample strategy involved identifying registry members in the U.S. with diverse representations of gender, ancestry, and age, alongside a unifying genetic diagnosis of dysferlinopathy. A total of eight participants were recruited and individually interviewed in approximately one-hour-long interview sessions, using video recording. One participant chose to have their interview by phone which was recorded through the same video platform with audio being sourced by a phone.

Interviews were semi-structured, and flexible, with nearly 100% of the questions left open-ended, allowing deeper exploration into the topics that the participants focused on when describing their clinical experiences. Only the interviewee and the researcher were present (remotely, by video). Interviewees were offered the opportunity to have a support person present during the interview, which none elected to do (Noon, 2018). The interview methodology was structured by centering the conversations around the clinical experiences of the individuals and what they feel is important to be addressed prior to, during, and post muscular dystrophy-related exams. Participants were asked about their experiences in neurology clinics, their diagnostic journey, what tests were available, whether additional educational materials were offered and explained, whether their care team offered them access to genetic counseling, how prognosis and progression management was addressed, and whether advocacy materials were provided.

The interview process utilized a funneling technique, beginning with broad questions, and progressing to more specific questions related to the aims of the study (Smith, 2006). The interview guide is provided in Appendix A and the question template is shown in Table 1 below.

Table 1. Prepared interview questions

Access to care	Will you share your experience accessing supportive services related to dysferlinopathy?
Current clinical care	Do you currently have a care team?
Frequency of care	How often do you receive clinical care?
Prognosis	How have you accessed guidance about caring for yourself as the disease has progressed?
Education	What are your thoughts about being offered educational materials about dysferlinopathy at your clinic visits?
Barriers	Is there any care that you feel is not addressed in clinic visits?
Assistive Devices	What is your experience with using assistive devices?
Mental Health	Have you experienced stress and anxiety related to dysferlinopathy?
Genetic counseling	Will you describe the pattern of inheritance of dysferlinopathy and how you learned about it?
Advocacy	Have you connected with other people who have dysferlinopathy?
Physical therapy	Have you tried any physical therapy or occupational therapy?
Falls	Have you experienced any falls?
Injury	Do you experience any injuries related to dysferlinopathy?
Insights	Are there any other clinical experiences you would like to share?

The audio portion of the recordings was manually transcribed by the same researcher who conducted the interviews. Researcher notes were taken separately during the transcription process, and bracketing reflections were performed before and after interviews (Lowes, et al. 2001). After the interviews were transcribed, the transcriptions were read, and interview language was highlighted. The transcriptions were read again while notes were taken to the right of the transcription text in the margin. This process was repeated once (Alase, 2017). There were 165 pages of transcriptions produced which were re-read and annotated. Themes were identified in the descriptive summaries, itemized, categorized, subcategorized, and connected developing a table of themes following the order of the interview using page numbers and quotes (Pietkiewicz, et al. 2012). Main themes and sub-themes from the thematic framework were identified, named, and defined. Lastly, the superordinate themes were analyzed and explored using reflective notes

in a journal, and inferences were drawn through the researcher's interpretation (Noon, 2018). The phenomenological methods of interviews, transcriptions, recorded insights, thematic coding, and interpretive analysis, were intended to contextualize the participant's lived clinical experiences.

The intention of the interviews was to gather unique details and information about clinical care experiences specific to the circumstances and psychology of the participants while exploring any potentially universal themes. Themes that correlated to the prepared interview topics were recorded. Later, themes were explored beyond the structure of the interview topics to create subthemes based on the specific experiences shared beyond the structure of the prepared questions (Tables 2-5). Thematic mapping-flow illustrations were created for each interview and are shared in the discussion (Figures 1-2).

Results

Individuals represented multiple genders, non-Latino white and black, indigenous, and people of color (BIPOC) communities, and ages ranging from 22-67. All participants had genetically confirmed dysferlinopathy. The years since muscle weakness was first noticed by the participants (symptomatic onset) ranged from 3 to 27 years of living with disease manifestation. All but one of the participants regularly see a neurologist. The individual without a neurologist shared that participating in COS has provided surrogate neurological care.

Four of the participants could walk with and without assistance while the other four were using a powered wheelchair at the time of the study. Some of the participants had experienced disease progression beyond weakness in their hips and legs, with weakness moving into their shoulder girdle musculature, not allowing them the full use of their arms. Other participants were in earlier disease stages, experiencing changes to their gait, difficulty walking up stairs or getting up from a chair or the floor, difficulty navigating inclines or curbs, or standing for extended periods of time. All participants shared that over the years they have been learning how to safely navigate the progression of symptoms through trial and error.

Participants articulated that there are aspects to their experiences as individuals with dysferlinopathy that can produce feelings of confusion, isolation, fear, and anxiety. There were testimonies of a general deficit of support, lack of knowledge, and accessibility barriers related to interview questions about prognosis, progression, and available clinical care. Themes of trauma, anxiety, pain, mental health, barriers to accessing support and the need to self-educate were expressed multiple times in different contexts during the interviews. Tables 2-4 below visualize the themes identified through the interview transcriptions as they correlate with the subjects addressed in the interview questions (Table 1). These subjects included: access to care, current care, frequency of care, prognosis, education, barriers, assistive devices, mental health, genetic counseling, and advocacy.

Themes beyond those addressed through the prepared interview questions arose in the form of subcategories that included unmet needs of clinical care, psychological vulnerabilities,

connections, and navigating the progression of the condition. These subcategories and the themes that correlate with each of them are listed in Table 5 below.

Table 2. Themes correlated with prepared interview categories. Categories are listed in bold along the top row of the table. Themes that corresponded to the categories are listed vertically below the categories they are connected to, in no specific order.

Access to Care	**Current Care**	**Frequency of Care**	**Prognosis**	**Education**
Need Options	Dehumanizing	Annual	Confusion	Self-education
Look for connection	Pointless	Through studies	Frustration	Trial and Error
Long winding road	Re-traumatizing	Choosing alternative providers (not neurologists)	Anger	Personal Experiences
Revolving door of clinicians	Not worth it	PT provider critical	Shame	Patient to patient
Transportation	No answers	Depends on relationship	Pain	Rely on Advocacy
Cost	Focused on weakness	Do not attend clinic	Milestones	Personal effort
Need for self advocacy	Needs Customizing		No Details	Role reversal educating doctors
	Need relationship with clinicians		Trauma	
	Low expectations		Safety	

Table 3. Themes correlated with prepared interview categories. Categories are listed in bold along the top row of the table. Themes that corresponded to the categories are listed vertically below the categories they are connected to, in no specific order.

Barriers	**Assistive Devices**	**Mental Health**	**Genetic Counseling**	**Advocacy**
Mental health status	Trial and error	Fear	Not needed or relevant always	Transformative; Life-Changing

Depends on the stage of progression	Vital	Anxiety	Feel confident in understanding	Learning from other patients
Finding resources	Independence	Isolation	Accessible	Access to Resources
Anxiety	Self-identity	Protective	Not relevant	Support system
Low expectations	Barrier to accessibility	Overwhelming		Connection
Lack of specifics		Exhausting		Comradery
		Selective about social choices		Perspective

Table 4. Themes correlated with prepared interview categories. Categories are listed in bold along the top row of the table. Themes that corresponded to the categories are listed vertically below the categories they are connected to, in no specific order.

Physical Therapy/OT	**Falls**	**Injury**	**Insights**
Instrumental	Terrifying	Beginning of the end of ambulation	Goals are important
Essential	Hyper-vigilant	Anxiety	Reframe outlook
Too busy	Agony	Prevention	Constantly changing and learning
Not needed	Isolation	Isolation	Mental health is a process
Can be a strong advocate	Retreat from activities	Trauma	Need collaborative clinical relationships
Helps with troubleshooting	Constant concern	Hypervigilance	Clinical communication efforts needed
A burden to access PT	Mental paralysis		Clinics to offer access to assistive devices to try before purchasing
Customized	Vulnerable		Clinicians can facilitate patient empowerment
			Need different focus with conversations in the clinic

Table 5. Subcategorized themes beyond the prepared interview structure (partial list). Themes correlated with interview categories beyond the prepared interview structure. Categories are listed in bold along the top row with the themes that corresponded to the categories listed vertically below, in no specific order.

Unmet needs in clinical care	**Psychological vulnerabilities**	**Connections**	**Navigating progression**
Dehumanizing clinical engagement	Hypervigilance due to fear of falling	Can be life-changing and transformative	Information needed
Non-accessible facility furniture	Not having peers to learn from and support	The mentality of others/influencers is critical	Trial and error can be traumatic
Lack of educational structure	Carry the burden of symptoms, fear, and the unknown, alone	Support system needs are critical	Comparisons to others can cause internalized pain
Missed opportunities to facilitate advocacy connections	Self-identity	Need to feel connected for future trial recruitment	The resilience of the individual goes unrecognized
Lack of resources offered or shared	Grieving loss of abilities	Teamwork among care teams important	Reframe transitional ambulatory choices

Discussion

Connection and Engagement

Despite clinical examinations providing opportunities for connection and care, there are clinical difficulties facing both patients and clinicians involved with dysferlinopathy. The lack of widely available information and clinical guidance predisposes the clinical experience to be challenging. Without proper education and training for the medical staff, patients can experience counterproductive appointments where they leave the medical center feeling deflated and without support. Three of the participants in this study articulated that their neurology appointments feel *"pointless"*. Four participants shared that the inconsistency of clinicians' advice, the lack of specific guidance on prognosis and care, and the little understanding of disease mechanism, when combined with the toll that the appointments take on them,

outweighed the value they might receive from clinical examinations. This major finding must be prioritized; without individuals willing to be physically in the clinic, progress cannot fully reach the intended audience. It is common for advocacy leaders to learn that people with dysferlinopathy stop attending neurology appointments indefinitely. Nevertheless, the dysferlinopathy patient community has proven willing to partner in progress through studies related to understanding the disease pathology, developing disease-specific outcome measures, partnering with other LGMD advocacy organizations, sharing and re-sharing personal experiences, as well as mentally and physically showing up to support the furthering of progress for people who are impacted by dysferlinopathy.

Other findings iterated in variation across the interviews were the desire to receive disease-specific guidance to be offered reciprocal communication approaches, and to have their care needs to be addressed holistically (mental health, connecting with peers, multidisciplinary offerings, access to support, educational events). Despite the call for multidisciplinary care, all but one of the participants remained consistent in their desire to maintain a regular relationship with their neurologist.

Mental health support and clinical relationships

In 2009, Caroline Huyard (2009) published study findings that illustrated mental health implications for individuals with rare diseases. Of note was the finding that the mental health needs of an individual with a rare disease are unique and differ from those of people who do not have a rare disease. The study results suggested this was key, specifically surrounding clinical care tasks such as providing a diagnosis, education, and ongoing care.

One of the participants in this study shared the negative mental impacts following their clinical experiences due to the way their neurologist responded to their progression with surprise; and what the individual perceived as a shocked reaction by their neurologist during a routine visit. The individual had been seeing the same neurologist for 18 years at the time and yet, there was a significant disconnect between the clinician's understanding of the patient's individual pattern of progression, the personal process involved in their decision to transition using a wheelchair, and the fact that the examination table in the clinical exam room was no longer accessible for the individual. Rather than anticipate and accommodate the physical changes that are expected with the progression of dysferlinopathy, the reaction of the clinician was perceived as a surprise. This occurred when the patient shared that they had decided to begin using a wheelchair and that they could no longer climb up onto the exam table. The individual shared how this clinical experience occurred multiple times and was retraumatizing, ultimately contributing to internalized shame that their muscles had become weaker over time. The individual shared that there had already been years of personal experiences that led to their decision to use assistive devices and that the decision itself was one of the most significant decisions they have ever faced.

The clinician's response to the progression confused and angered the patient since the neurologist should be anticipating the weakening of muscles as there are no treatment options available. In contrast to the clinician's reaction, this individual shared how personally empowering it was when they decided to use a wheelchair and fully participate in life again. The impact of chronic disappointment during clinical exams, being repeated annually, and over decades, resulted in this individual dreading their annual exams. How could this individual's care

team have supported them through their transition from being ambulatory to using a wheelchair full time?

For decades there has been documentation that productive communication between patients and their clinicians can contribute to positive outcomes for the patient (Kaplan, 1984, Hall, 1988, Stewart, 1995, Oliveira, et al. 2015). And, that trauma-informed clinical care is essential in certain settings (Green, 2015). This example of disconnection is one of the multiple examples shared by this participant and others surrounding the theme of disconnection with clinicians. There have been missed opportunities to positively impact the patient's experience of navigating the disease progression. However, opportunities arise through insights offered by the participants such as connecting individuals with peers and helping to troubleshoot, prepare, and empower the individual to reframe how they plan to approach their life circumstances over time. All but one of the participants shared a variety of examples of clinical experiences that lead them to feel that their neurological exams were *"pointless", "disappointing", "frustrating"* and insensitive.

Insights from the individuals with dysferlinopathy

Insights shared by the participants included suggestions to treat the patients as whole people--not defined by the condition, to focus on solutions, strive to practice reciprocal clinical conversations, and partner with patients to help them navigate the disease progression. Care plans can be customized based on the unique, changing needs of the individual. Participants gave examples of experiences when it was important that their clinician actively listen to them and, ultimately work as a team with other providers to support successful access to physical and

mental therapy, occupational therapy, educational opportunities, and help patients connect with peers if desired.

A thematic summary map from one interview is shown below in Figure 1 (labeled interview number 4 of the 8 interviews). The pathway of themes followed the participant's interview story (transcriptions) to create a map that can illustrate the ways their experiences lead to dysfunctional clinical relationships. The thematic map from the fourth interview is shown below in Figure 1. Thematic maps for all the interviews can be found in Appendix B.

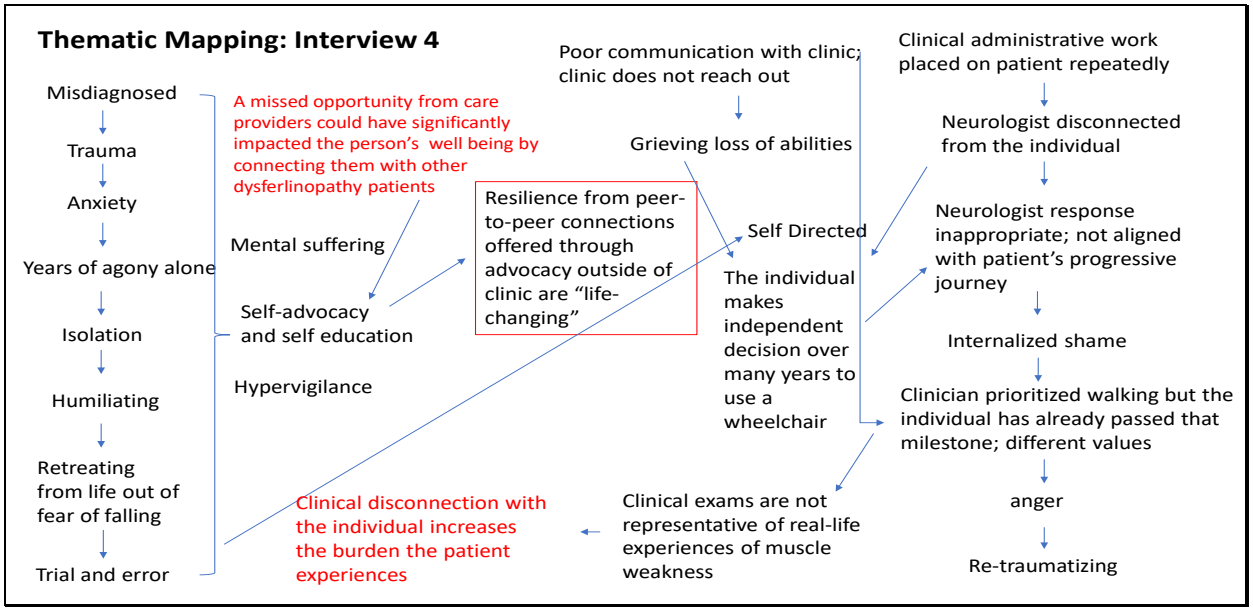


Fig.1 Thematic mapping from Interview #4. Coding from the interview is listed on the left with blue arrows indicating the order in which the codes followed the interview. The red text represents reflections made during the data analysis with arrows pointing to corresponding themes articulating how they developed. Codes and interview interpretations on the right have arrows pointing in the order of the experiences as they were described as well as arrows that reflect the evolution of the experience and takeaways from the interview. The text in the red box is representative of a positive experience and what influenced it.

Individual accounts of disappointment with clinical care were shared across all interviews and still, there was a universal expression of feelings of gratitude and acknowledgment among the

participants that it is challenging to give a set timeline of progression given the rarity of the condition. Opportunities for improved clinical care came up in conversation surrounding the focus of the conversation during examinations. Individuals shared that it feels counterproductive to have the provider tell them that they are getting weaker during a neurological exam when they already know firsthand how their muscles are changing. Another approach could be to focus on how individuals are coping, ways that they can care for their body, prescribing therapy sessions of mixed disciplines, and recording the progression of weakness in the chart without making it the focal point of the examination.

Additionallya , lack of consistency among providers can take a toll on individuals with dysferlinopathy. Participants shared that they feel the desire to help teach new providers about the disease but also feel like a *"lab rat"* or *"guinea pig"* and are not treated as a whole person. It can feel as though they are defined by the disease rather than the unique individual that they are when the providers speak about them as if they are not in the room as they work to describe the individual's phenotype during assessments. Teaching hospitals and clinics could take extra care to offer private examinations or work to balance privacy within the context of teaching.

One participant who sees a neurologist at the Veterans Affairs (VA), where there are clinical rotations, described their clinical examinations as dehumanizing. *"They're looking at me like a scientific study. They're not looking at me like a human being. They are like, oh yeah, this guy's got this weird thing. And, you know, I didn't get the sense that they were in tune with what this is like. It's my life. This is what I'm dealing with. I'm not on a hamster wheel. I'm a person. I am a human being."* Educating clinicians about this perspective could support the clinical staff in

making appropriate conversational choices during clinical examinations with and help them to modify the ways they conduct peer-to-peer discussions. The individual shared feelings of duty surrounding the need to study the condition and support clinical understanding. However, the experience was invasive and insensitive, furthering the individual's negative association with general neurological examinations.

Figure 2 below offers another visualization from a different interview and notes another pathway to understanding the essence of the individual's clinical experiences. This map includes quotes of the participant in red italics.

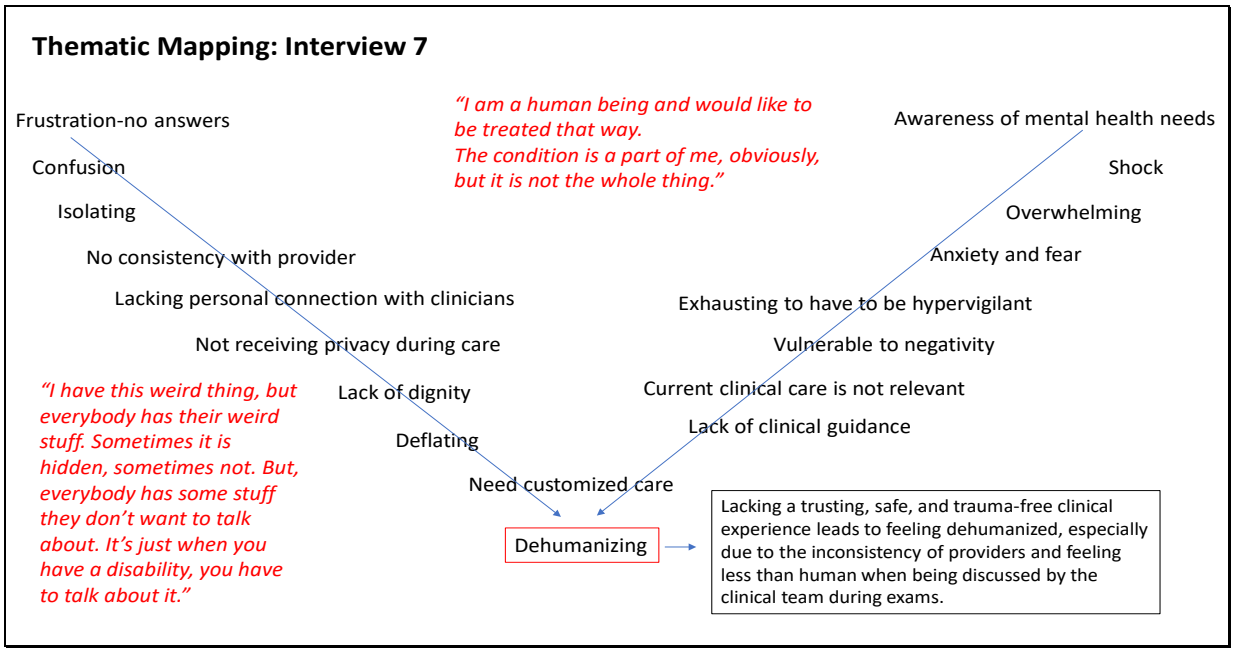


Fig. 2 Thematic map from interview #7. Codes generated from the interview follow two lines with the left line representing early on experiences and the right line representing the resulting themes and additional codes. Both lines point to the overarching theme of "dehumanizing" labeled with a red box to show significance. The box to the right of the red box is the distillation of the experiences shared by the participant. The red text in italics are quotes from the participant.

Mental health themes of vulnerability, intimacy, fear, privacy, anxiety, anger, and desperation arose during moments in the interviews for all participants. Some participants shared that they must use caution about their mental health and the people they have in their life. There is a sensitivity to negativity as if it could knock the individual from a healthy mental state and impact their ability to cope and stay healthy.

A participant who is within the first five years of symptomatic onset shared that it is important to contextualize clinical conversations to the specifics of that patient. For example, being asked questions about their symptoms, especially those symptoms that are not manifested yet, can be terrifying and overwhelming. This individual gave an example of being asked by advocacy staff if they were experiencing any falls during an interview screening call for study recruitment. The individual later shared that they were not ready to think about that at the time, and it was unsettling. Having reciprocal communication can shine a light on areas of communication practices needing to be refined or evolved. This participant showed incredible strength in composure. But, when asked specifically what it was like to get the genetic confirmation that they have dysferlinopathy, they responded with, *"It was devastating. I mean, it was obviously horrible, and, I mean it has been since. It's been like a nightmare that you can't wake up from." There was "zero guidance,"* and they were just told to *"keep an eye on it."* A family member connected the individual with advocacy, dysferlinopathy studies, and a neurologist they work well with while living independently and finishing college. What will the experience be for individuals who do not have family members willing or able to advocate and support the individual through the disease progression?

Asking questions about how participants felt at different timepoints opened a different perspective of that individual's experience. A person can appear perfectly composed but be suffering, nevertheless. Having a baseline of respect, trust, and sincerity was integral to having an open dialogue during the interviews. Seven of the participants did not offer to elaborate on how they felt about their clinical experiences. However, when probed, they all shared using words such as *"devastating, cold, rude, shocked, afraid, and frustrating."* One individual shared that their first doctor told them they *"would be dead within three years".* There do not appear to be publications specifically addressing lifespan in dysferlinopathy. However, it is generally accepted that dysferlinopathy does not affect life expectancy, given that cardiac and respiratory muscles are not significantly involved or can be symptomatically treated very effectively (Moore, et al. 2022). What kind of toll does that level of misinformation take on a patient?

Another participant went further during their interview to provide insights on additional communicative, supportive opportunities through education in the clinic. They shared that it was challenging for them to explain the genetics and prognosis to family and friends. They said offering supportive suggestions on how to summarize what dysferlinopathy is and how it impacts on a person's muscles would have helped ease some of the social burdens they experienced.

Beyond the mental health needs of the participants, there were stories shared about resilience, strength, and courage through trial-and-error learning. With subtle changes to strength happening constantly, there are new challenges happening regularly. These self-taught survival skills of the participants, such as how to get from point A to point B without needing emergency care from falling (becoming stranded on the ground after a fall) and without the musculature to lift

themselves up from the ground, were shared by all participants. The fear of falling is not easily comprehended by able-bodied people. All but one participant shared stories of falls, described how they recovered, and the dramatic ways that they tried to prevent more falls through hypervigilance. *"When you fall, you just collapse. It's hard to imagine when you are a normal, healthy, able-bodied person. But there's no kind of way to be able to catch yourself. Your muscles just don't have it in them; they don't respond the same way."*

The interview excerpt below is the description this individual gave about their experience trying to get the courage to walk into work from the parking lot. *"I was willing myself to take the first step. But I was emotionally and mentally paralyzed because of this anxiety and the fear, and that's just not something they (the providers) see or take into consideration, I don't think. Without the support of your muscles, a fall is very shocking".*

Another individual shared their experiences and that emergency services had to be called because there was no one to help them up, which requires extraordinary physical strength since many individuals with dysferlinopathy don't have full use of the muscles needed to assist in getting up from a fall to the ground, even with help. And another participant shared that they fell outside while alone, became injured, and had to scoot their body towards an object to then try to pull themselves up after trying to take out the trash.

There are layers to the clinical experience that participants shared, adding to a feeling of disconnection, and lack of understanding, which in turn can reinforce the negativity associated

with annual neurological examinations. For example, a participant shared an insight that they do not feel the clinical assessments can show the stamina challenges the condition brings. *"It's way different; 10 seconds of pushing and pulling are very different than going to the zoo or spending a whole day out and about with your family and friends or living your life."*

Another participant shared that even having only one clinical champion involved in their care management improved multiple areas of their life. This participant shared that they feel supported and prepared when their clinical care team works together. Multiple experiences shared by this participant illustrated how a type of care pathway facilitated access to essential components of life for this person. In their own words, *"...they were able to start working together a lot. And, you know, discuss, I guess, my case outside of me being there….I know they just started working together…the neurologist contacted the PT department. And, then after the hospital people work with the PT people, they then work with the medical equipment people and like, they are all working together so, yeah…they reached out to me. My PT just reached out to me last week to say, hey, do you need anything?"*

This participant went on to give examples of how their care team had helped them prepare to be as physically independent as possible and even helped explain their progression to their family when they weren't able to communicate effectively with their family about dysferlinopathy. This type of successful, well-rounded care demonstrates the power that combining collaborative neurological teams through PT services, medical equipment supportive services, and social work. The benefits of clinical teamwork include helping the individual have more physical and mental confidence than they would without their supportive clinical care team. This experience

contrasted with another participant's when they shared that in 18 years of receiving clinical care at a neurology clinic, not once had anyone reached out to them to ask how they were doing, provide any research study updates, or community news. *"I don't hear anything from my doctor except the call to tell me that my appointment is tomorrow."*

Learning about accessible equipment options, services and strategies was mentioned as important. It also relieves the burden and potentially lifts some anxiety from the patient to receive timely support. *"I think it is so important to be tuned in with a coordinator who not only knows what is available in the area and how to reach those individuals. I mean, it's tough; as much as the clinic helped, I had to do a lot of research on my own…. it's tough for the individual, but it's also tough on the family."* Teaching the patient about how to access the services locally is the nuts and bolts of making the support tangible in ways that impact the patient's quality of life. Perhaps this would build a stronger relationship between the individual and their care team, which could influence how likely they are to seek the care that they need.

Limitations and Strengths

It should be acknowledged that this study gathered individuals' perspectives and lived experiences at a set point in time and that its observations may be specific to the clinical care options dysferlinopathy care options in the U.S. at a set point in time. Additional studies might be warranted as a result to contribute to the development of collaborative assessment instruments which include patient perspectives.

Individual experiences are contextual and dynamic. The ability to dive deep into personal sharing in interviews takes trust between the participants and the researcher or the organization conducting the research. All participants in this study had between 2-15 years of interactions with the Jain Foundation staff which established a baseline for the conversations to be candid. This creates an environment that is unique and not easily reproducible.

Researcher bias was important to carefully manage during the interviewing and analysis. Reflective bracketing, journaling, and thematic mapping were grounding practices that helped to keep preconceived beliefs at bay. Listening and gently probing were key components during the interviews to keep from leading the conversations. The in-depth knowledge and long-term relationships between the organization staff and the study participants synergized with the phenomenological study design. Further, despite the challenge surrounding the topic of bias that can come with knowing the community well, this familiarity also fosters an atmosphere of validation, comfort, and respect, which promotes in-depth sharing. The willingness of the participants to candidly share their experiences, feelings, and insights on very sensitive topics added strength to the study.

Conclusion and Implications

Some of the clinical burdens experienced by individuals with rare diseases can be caused by "insufficiency" of clinical expertise (Budych, et al. 2012). Without a mechanism to circulate natural history findings, a lack of disease-specific standards of care, and no universal approach to disseminating rare disease research findings to health care providers, we can expect similar

conclusions when evaluating the clinical experiences of individuals with the ultra-rare form of dysferlin-associated LGMD. Understanding where negative clinical experience originate (from a patient's perspective) can provide opportunities to develop better clinical practices.

Insights shared by participants in this work suggest the need for clinicians to focus on how individuals are coping, customizing ways that they can care for their bodies, prescribing therapy sessions of mixed disciplines, and recording the progression of weakness in the chart without making it the focal point of the examination. Providers can involve patients during the examination by asking questions, actively listening, and providing a productive follow-up plan. Additionally, neuromuscular clinical teams who care for individuals with dysferlinopathy could consider taking an inventory of their patient community, determine appropriate methods to begin to build or reinforce their team coordination, patient relations, education, and participate in trauma-informed care training. Clinical intervention tactics are needed to support keeping neurologists in the U.S. up to date on research and what is known about dysferlinopathy.

Lastly, with over 7,000 different rare disease and more being discovered, it is impossible for clinicians to have enough resources to provide tailored care for their rare disease cohort of patients (National Institutes of Health). Specialized knowledge about dysferlinopathy, for example, is either harbored in research silos, or missing an accessible structure for incorporating the data into clinical care. Educating across sectors about what is known, what challenges to be aware of, and the experiences of the patients, will be key to improving clinical care. A first step to empowering individuals with dysferlinopathy is to prioritize their perspectives and keep them at the forefront of awareness, as stakeholders reach for progress.

Appendix A: Interview Guide

1. Introductions: Each interview began with introductions and time for establishing norms (Rapport building, maintaining trust)
2. Background: Participants had opportunity to share about themselves, their family, their work, and how they are doing in general which is typical of Jain Foundation communications with patients.
3. Probing: Probing techniques were utilized through open-ended, direct questions as well as non-verbal probes (posture, facial expression, deep listening) to facilitate understanding the context and to explore the details offered.

Probing questions covered the below six categories to contextualize the experiences that were shared. During transcription, these categories were used as a template for documenting contextual themes within the interview discussion.

What?	When?	Where?	How?	Who?	Why?

Interview question template:

Access to care	Will you share your experience accessing supportive services related to dysferlinopathy?
Current clinical care	Do you currently have a care team?
Frequency of care	How often do you receive clinical care?
Prognosis	How have you accessed guidance about caring for yourself as the disease has progressed?
Education	What are your thoughts about being offered educational materials about dysferlinopathy at your clinic visits?
Barriers	Is there any care that you feel is not addressed in clinic visits?
Assistive Devices	What is your experience with using assistive devices?
Mental Health	Have you experienced stress and anxiety related to dysferlinopathy?
Genetic counseling	Will you describe the pattern of inheritance of dysferlinopathy and how you learned about it?
Advocacy	Have you connected with other people who have dysferlinopathy?
Physical therapy	Have you tried any physical therapy or occupational therapy?
Falls	Have you experienced any falls?
Injury	Do you experience any injuries related to dysferlinopathy?
Insights	Are there any other clinical experiences you would like to share?

Appendix B: Thematic Maps (1-8)

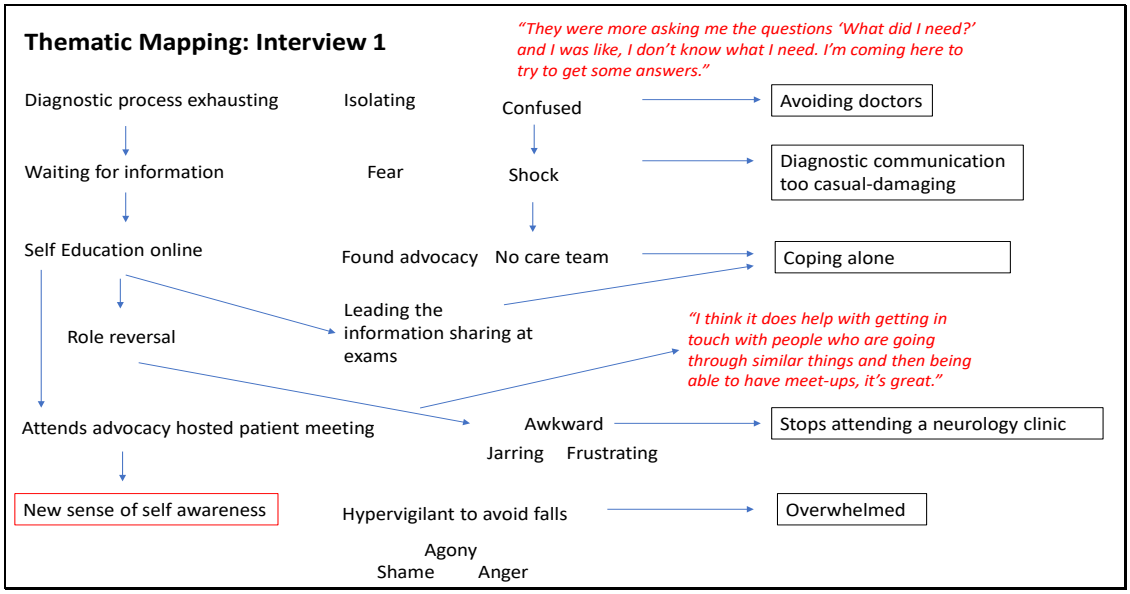
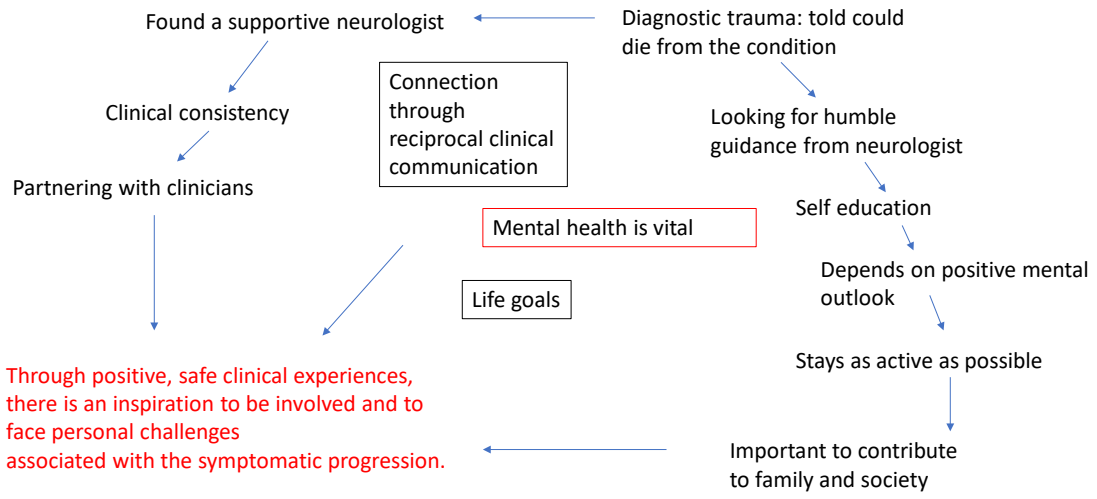
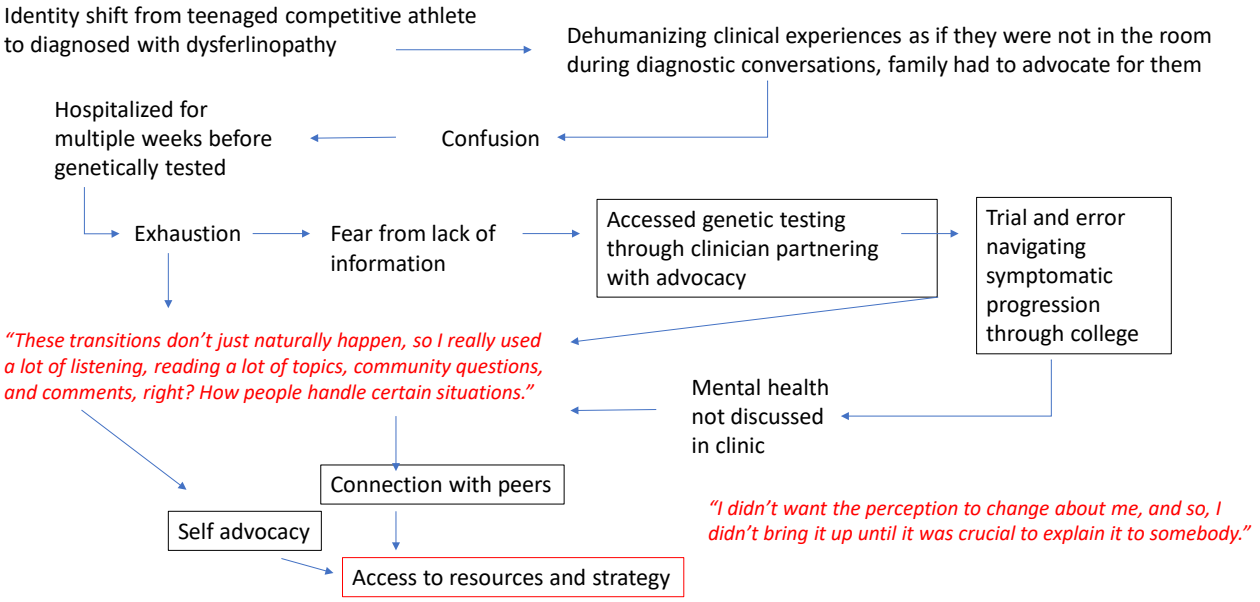


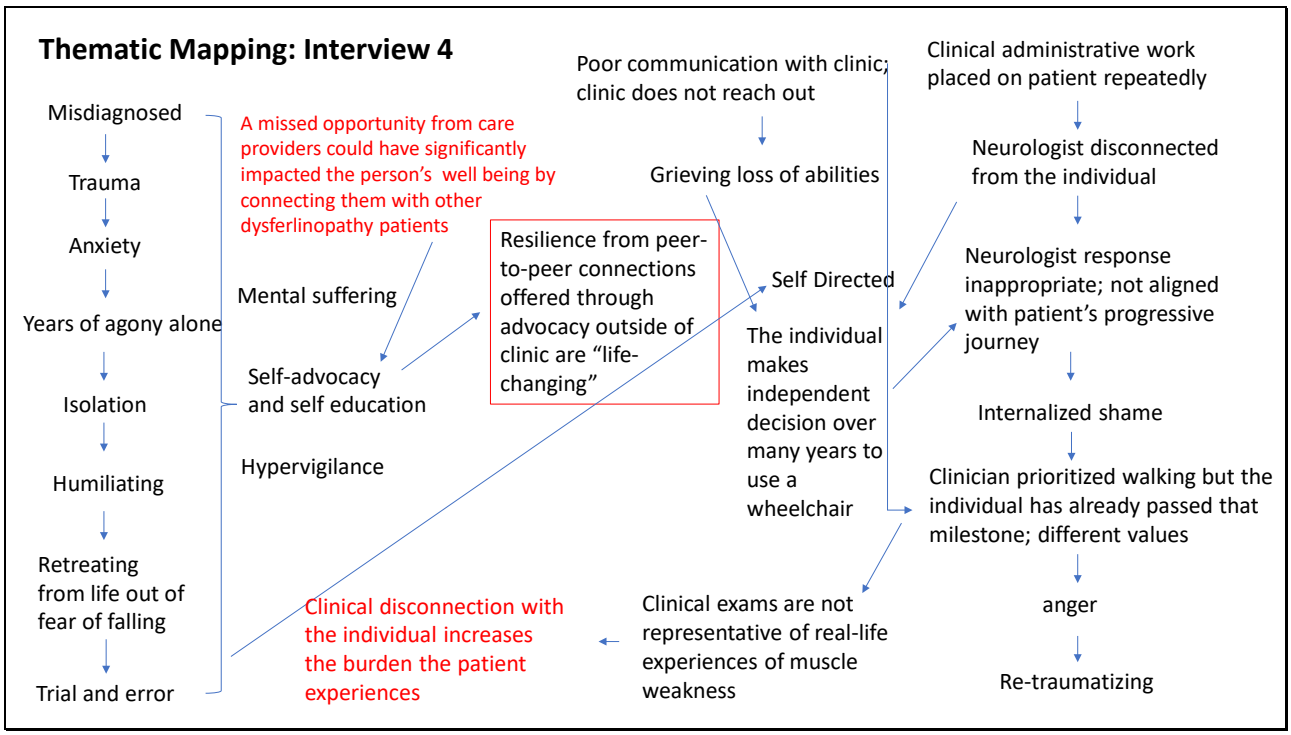
Fig. 1 Thematic mapping from Interview #1. Interview coding is listed on the left with arrows indicating how the data lead to themes which are listed to the right. Blue arrows pointing right indicate how codes/themes translated to behaviors and actions experienced by the participant. Content in red and italics are quotes from Interview#1. The red box signifies an empowering experience.

Thematic Mapping: Interview 2

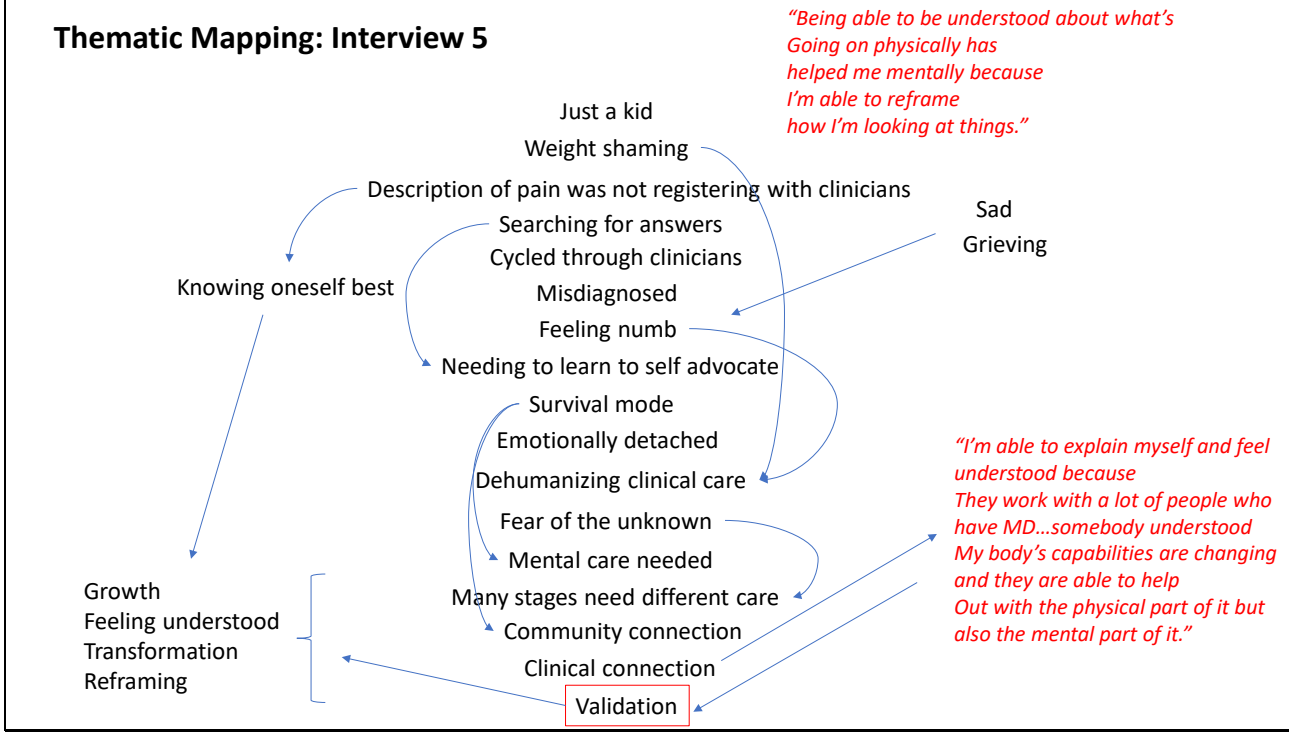


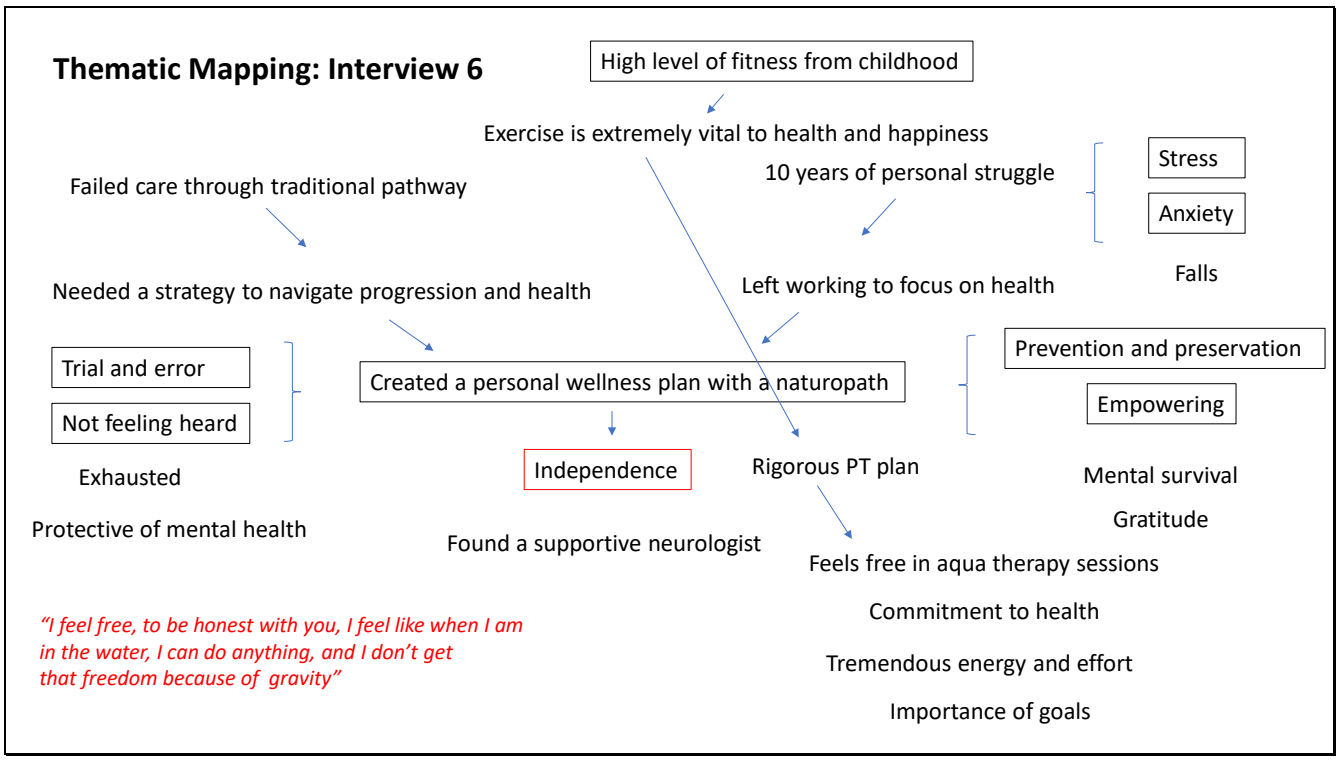
Thematic Mapping: Interview 3



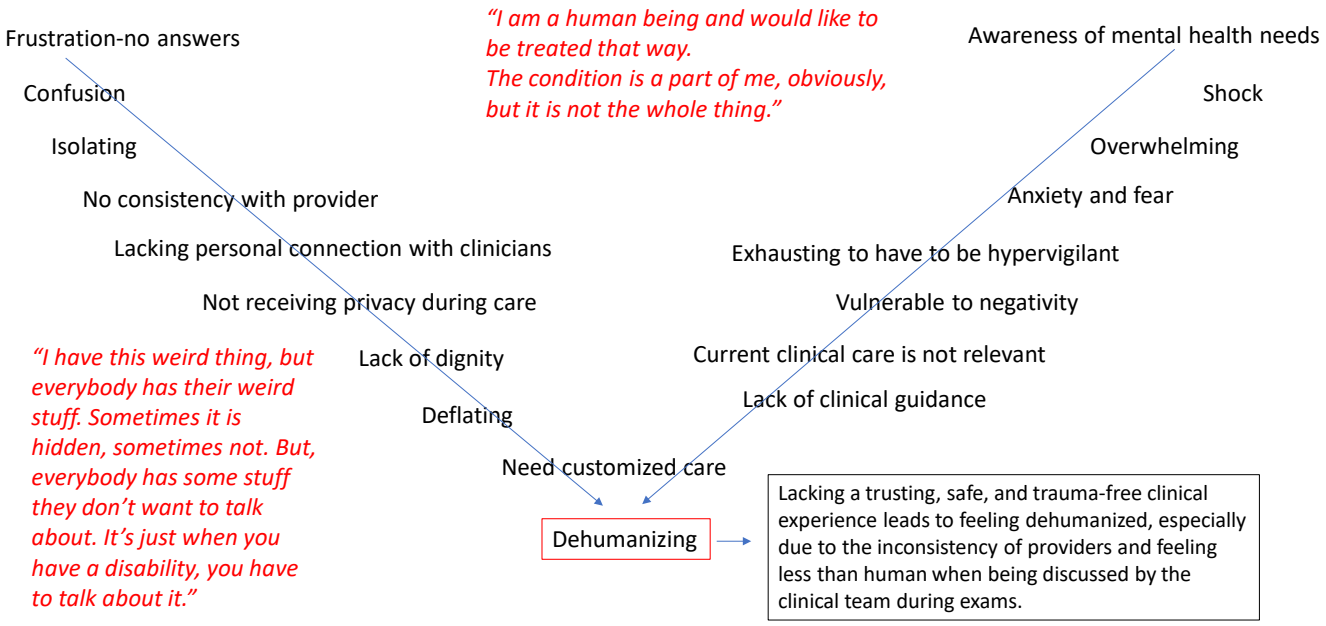

Thematic Mapping: Interview 4
Misdiagnosed
Trauma
Anxiety
Years of agony alone
Isolation
Humiliating
Retreating from life out of fear of falling
Trial and error
A missed opportunity from care providers could have significantly impacted the person's well being by connecting them with other dysferlinopathy patients
Mental suffering
Self-advocacy and self education
Hypervigilance
Resilience from peer-to-peer connections offered through advocacy outside of clinic are "life-changing"
Clinical disconnection with the individual increases the burden the patient experiences
Poor communication with clinic; clinic does not reach out
Grieving loss of abilities
Self Directed
The individual makes independent decision over many years to use a wheelchair
Clinical exams are not representative of real-life experiences of muscle weakness
Clinical administrative work placed on patient repeatedly
Neurologist disconnected from the individual
Neurologist response inappropriate; not aligned with patient's progressive journey
Internalized shame
Clinician prioritized walking but the individual has already passed that milestone; different values
anger
Re-traumatizing

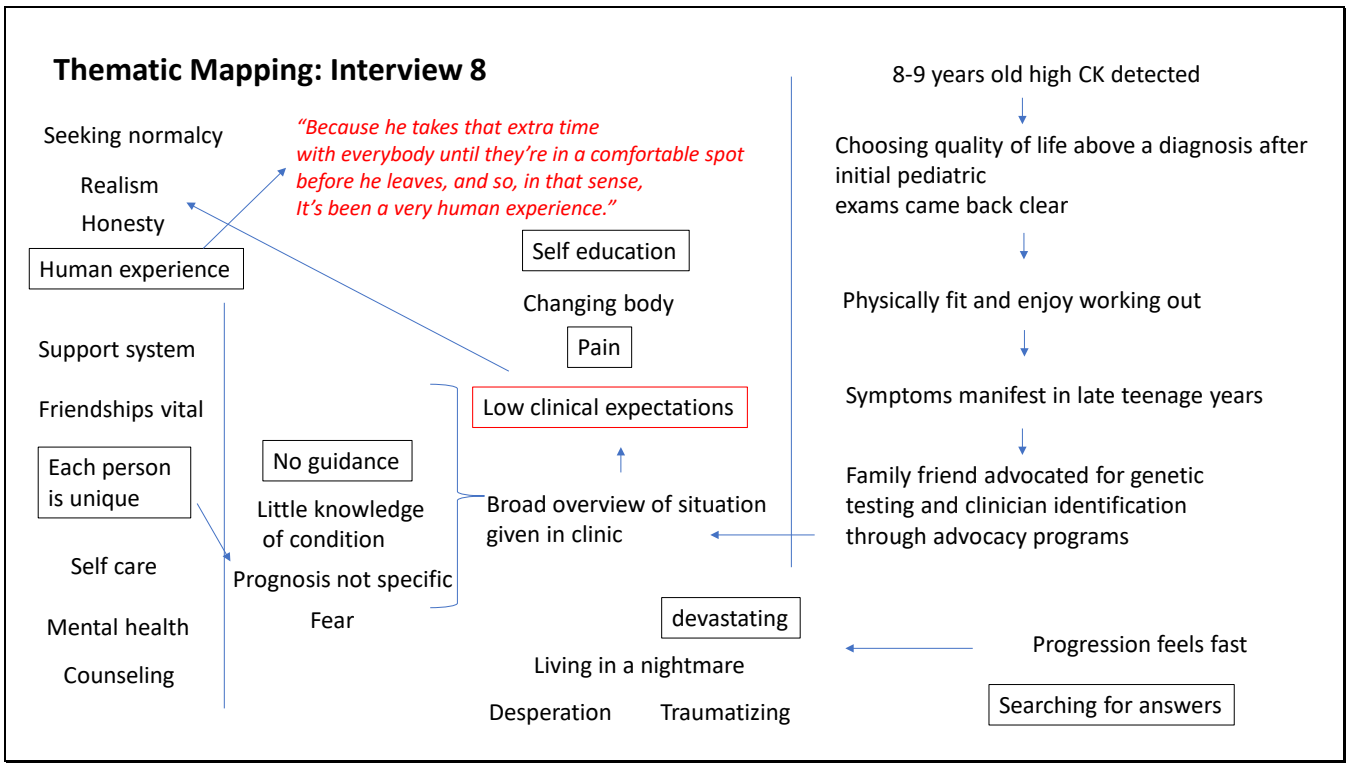
Thematic Mapping: Interview 5




Thematic Mapping: Interview 6
High level of fitness from childhood
Exercise is extremely vital to health and happiness
Failed care through traditional pathway
10 years of personal struggle
Stress
Anxiety
Falls
Needed a strategy to navigate progression and health
Left working to focus on health
Trial and error
Not feeling heard
Exhausted
Protective of mental health
Created a personal wellness plan with a naturopath
Independence
Found a supportive neurologist
Rigorous PT plan
Prevention and preservation
Empowering
Mental survival
Gratitude
Feels free in aqua therapy sessions
Commitment to health
Tremendous energy and effort
Importance of goals
"I feel free, to be honest with you, I feel like when I am in the water, I can do anything, and I don't get that freedom because of gravity"

Thematic Mapping: Interview 7




Thematic Mapping: Interview 8
8-9 years old high CK detected
Choosing quality of life above a diagnosis after initial pediatric exams came back clear
Physically fit and enjoy working out
Symptoms manifest in late teenage years
Family friend advocated for genetic testing and clinician identification through advocacy programs
Progression feels fast
Searching for answers
devastating
Living in a nightmare
Desperation
Traumatizing
Broad overview of situation given in clinic
Low clinical expectations
Self education
Changing body
Pain
"Because he takes that extra time with everybody until they're in a comfortable spot before he leaves, and so, in that sense, It's been a very human experience."
Seeking normalcy
Realism
Honesty
Human experience
Support system
Friendships vital
Each person is unique
Self care
Mental health
Counseling
No guidance
Little knowledge of condition
Prognosis not specific
Fear

Appendix C: Interview summaries and highlights

**165 pages of transcriptions from the 8 interviews are summarized to offer immediate access to portions of the interviews.*

Interview #1: pages 1-28

The individual (approximately 40 years old) experienced diagnostic trauma over a period of years between the ages 17 and 27 from when symptoms first began to when a genetic test confirmed the cause of the symptoms. There had been subtle changes in strength since the late teenage years, but it had not slowed the individual down as they were still able to work out at the gym lifting weights, and work jobs that required standing or walking for 8 hours at a time. This individual felt mentally fatigued from feeling deflated when trying to build muscle, struggling to get up from a squat position, after having been a high school athlete with an active lifestyle. They were getting weaker when they felt they should be getting stronger at that time in their life. During this period, the participant experienced feelings of confusion about why no one else in their circle was experiencing similar body changes and avoidance of doctors. The most impactful experience relating to clinical care for this participant over the diagnostic journey was having received their diagnosis over email which they described as a *"nice enough, but kind of, a rude manner, I don't understand why he wrote an email to me, it kind of shocked me".* The participant articulates that a general diagnosis of possible muscular dystrophy sent them into a state of fear not knowing if this was life-threatening, if their cardiac function was healthy, with the only muscular dystrophy point of reference at the time, being the MDA telethons with pediatric examples of terminal forms of muscular dystrophies. The experience was too casual for the individual given the magnitude of the diagnosis and the ambiguity of the process of caring for their dysferlin deficient muscles. This person was not offered any support mentally or physically

and describes those early years of symptomatic manifestation as if the experience was recent despite, it having taken place about 18 years earlier.

Over the course of the interview, the participant described experiential progression milestones from early symptoms to using assistive devices, to parenting young children, to transitioning to using a power wheelchair. Right out of the gate and throughout the years, the individual shared that they had to resort to internet searching to try to make sense of their diagnosis and find information. They tried connecting with other patients through an MDA event offered at a neurology clinic. However, they shared that the experience was awkward since they were the only adult at the event which was populated by children with different types of muscle conditions.

Even after having a diagnosis, this individual was still isolated and had no support offered besides that which was received after self-advocating to connect with their disease-specific foundation via online searches. A summary of the clinical experiences of this individual over the years could include feelings of trauma, shock, confusion, avoidance, isolation, disappointment, trial and error, pain, frustration, and resignation. The individual has demonstrated personal resilience and strength both mentally and physically but this has repeatedly taken a toll on the individual. When asked about why they currently do not choose to see a neurologist for care, they shared, *"I just, you know, quit going because I didn't feel like it was benefiting anything…there just wasn't any information out there".*

Without clinical care offered in such a way that the individual feels it is worth the cost, time, and effort to go, the individual ended up personally taking on all of the responsibility of their care or relying on natural history study participation to have neurology checkpoints over the years.

Interview #2: Pages 29-41

An individual in their 60's who had a later symptomatic onset (at age 47) who is ambulant, lives with family and went through a series of diagnostic errors such as multiple (3) liver biopsies that due to elevated “liver enzymes” that were actually related to the muscular dystrophy, not liver disease. Part of their clinical trauma during that time was defending themselves from clinicians who believed that they were hiding substance abuse because of their high “liver enzymes”. They ultimately connected with a neurologist that they trust, can relate to, and feel is supportive. They articulated the contrast between their current care provider and previous providers who misunderstood dysferlinopathy to be life-threatening (other forms of muscular dystrophy can cause early death).

They also gave examples of providers who they could not connect with based on their demeanor highlighting the importance of a positive patient/provider connection when accessing care. Themes of frustration, shock, and fear were noted during the portions of the interview that demonstrated a lack of clinical knowledge of dysferlinopathy or poor bedside manner. This individual articulated that they rely on their positive mindset as if their life depended on it. One of the strategies they use to remain healthy in mind and body is to stay as active as possible, finding ways to feel useful to *"family, life, and society"*.

They shared that their health has been a journey and that when they were first diagnosed, they broke down mentally. They articulated that, *"there are a lot of parts to being healthy, and part of it is the mental attitude".* Through their repeated examples of how their current neurologist has helped them, the significance of the connection they have with their provider was illustrated. The

individual shared how they approach outings and movement with extreme care (hypervigilance) to avoid falling. Despite having experienced serious misdiagnosis early on, this individual focused most of their interview on the importance of having a healthy mindset.

Interview #3: Pages 42-67

This participant is in their late 20's, has established long-term employment, and is becoming a parent for the first time. The individual shared their experiences from first symptoms to transitioning to using a power wheelchair full time. They first began exploring the cause of their muscle weakness during high school when they went from being invited to play as a youth team U.S.A. basketball competitor to losing the ability to compete at a high level after a series of physical therapy approaches over many months. After a blood draw, the individual was admitted to the hospital and was kept there for 2-3 weeks.

Without a definitive diagnosis, the individual went to college where they began to learn (through trial and error) about self-advocating. Themes of confusion, resilience, determination, and strength were threaded throughout this interview covering topics of the diagnostic odyssey, self-identity, proactively keeping interpersonal relationships healthy, and the importance of accessing supportive systems and devices to maintain independence. This individual spoke about the mental aspects of dysferlinopathy, the physical changes, how they prepared themselves for life events and milestones, and experiences they have had dealing with the reaction of the public to their disability.

They articulated that the physical and mental changes and need for assistive devices don't *"just happen naturally", "So, I really used a lot of listening, reading a lot of topics, community questions and comments, right? How People handle certain situations, that definitely played a factor into, um, you know, (learning about) resources that were available".* Learning how to prepare and avoid falls, protecting family relationships, and accessing supportive services were the highlight of this interview.

There were also experiences shared that suggested an internalization of the disease progression at various stages of the symptomatic journey. Specifically, during physical transitions when the individual went from using crutches, to lofstrands, to a manual wheelchair, to a power wheelchair and Hoyer lifts for transitions (over the course of 5-8 years). There were multiple aspects to each of the transitions mentally and physically. What the individual shared that was most important to them was the ability to access resources and remain as independent as possible during each stage of progression. Much of their ability to access the resources they have needed came from personal research which added to their level of stress and anxiety.

Interview #4: Pages 68-91

This participant is in their 30's and has had symptoms of dysferlinopathy since age 16. Despite this participant having been cared for by a prominent neurologist who has been directly involved in dysferlinopathy research, the primary theme of this interview was the consequences that clinical disconnection: internalized shame, anger, sadness, disappointment, mistrust, and anxiety surrounding clinical care.

The individual continues to see the same neurologist (for about 18 years) since they believe that by doing so, they will be more likely be able to access a future treatment for dysferlinopathy through this clinician. However, they shared multiple experiences that demonstrate the ways they are repeatedly traumatized at the clinic: provider not anticipating their needs, emotional responses from the provider about their muscles getting weaker, not having access to accessible clinical equipment, providers not being familiar with their file despite years of attendance, providers not reviewing their history before exams, lack of any follow-up, and providers depending on them to re-state their history and diagnostic journey annually, for example. When describing the anger felt upon their provider being surprised about their transition to using a wheelchair the participant shared, *"When I decided to transition, I had losses for, noticeable losses, for at least two decades. And, so, it's like, no, don't tell me that- and then it makes me feel that I've done something wrong like if I had just kept going if I had just, I don't know, that I look worse off than other people when really, I'm just trying to live my life the best way that I can".*

Interview #5: Pages 92-112

The symptomatic journey began in high school for this individual, now in their mid 20's. They first noticed changes in the form of leg pain that they now reflect on as pain related to muscle wasting. There were accounts of being *"cycled through many resident clinicians"* and it ended up being their elevated CK levels that lead to a general diagnosis of muscular dystrophy and eventually, access to advocacy programs for free genetic testing which confirmed their dysferlinopathy. The transition from being seen for the purpose of diagnostic support to being evaluated specifically for dysferlinopathy was recounted by the individual as *"it was like, a weird*

moment because it was like, ok, you guys know what's wrong, let's just take this further and research her a little bit more, um, honestly, I start to feel like a guinea pig at that point."

Over the 15 years since the individual has been experiencing symptoms, they have learned to self-advocate. They shared that some clinicians did a great job including them in clinical communications. Later, when they were asked to participate in research led by the government, they felt dehumanized during the research process. Specifically, they spoke about the need for mental health support during and after the diagnostic process. They described the process of participating in research as both *"exciting and depressing"* because they were at a research hospital where there were visibly ill individuals, and they recall feeling the magnitude of their diagnosis.

A significant point made by this individual and articulated through examples, was the positive impact 1-2 champion clinicians have had on their life. Their initial neurologist was supportive through the early diagnostic process. Later, their physical therapist became a primary source of support ranging from help accessing equipment, help with communicating with family members a description of the condition, putting them in touch with other supportive services such as mental health counseling, and even calling to check-in in with them asking how they are doing. This individual shared insights about clinical care that their PT suggested to them surrounding reframing how they perceive the progression of the condition, *"...you shouldn't be measuring what you are accomplishing by your ability to walk. You should be measuring it by, like, what you are able to do now that you are in a wheelchair."* The participant articulated that this ability to reframe their perspective about mobility came from a clinician who deeply understood what

was going on physically, which in turn, has helped the individual mentally because *"I'm able to reframe how I'm looking at things because I'm able to get a lot more done."*

Interview #6: Pages 113-115

This is an individual who had a later onset of weakness and who has taken it upon themselves to personally create a specialized health routine that includes regimes focused on nutrition, multiple physical therapeutic approaches, and attention to mental health impacts on their physical health. Early in the interview, when asked about their neurology exams, they shared that they are attending their neurology clinic every 6 months, but not much is offered to them or even shared about their condition. The individual shared that even though their condition has progressed in the 9 years since symptomatic onset (they are currently in their late 30's), they are feeling "better than they ever have," which they credit to the supportive services that they receive through a naturopath which include: infrared sauna, vitamins, supplements, water exercise, cranial-sacral massage, that are consistently done each week.

They shared that their lifestyle changed when they left their corporate job and dedicated their time to their health. Towards the end of their career in the insurance industry, they were experiencing falls while at work, and sitting down for work 8-10 hours a day for about 17 years had left limited time for them to prioritize their health. Their partner was *"carrying me into the building when the weather was bad…would have to follow me to work, go to my car, pick me up, carry me into the building so that I didn't fall down with the ice and snow. If I fall, there's no walking again, and I just don't go out, I just stay indoors."* The anxiety surrounding falling is at the forefront of their mind and was a consideration when they chose to leave their job.

They went on to describe their PT regime in detail and how they attribute it to their ability to manage their progression. They spent considerable time during the interview sharing their perspective on the importance of having a positive mental outlook.

This individual also described the family culture they were raised with which included above-average levels of physical activity from childhood. They were extremely physically accomplished in cycling, running, and other sports over the years. Of note were the reflections on being a patient at a teaching hospital: *"I'll be honest with you, I don't like feeling like you're sitting there and they are examining you, and there's people around you. Yeah, honestly, they're studying me, he's trying to teach, it's a teaching thing, you know, I know that I just wasn't comfortable being that person. I prefer to go to only one regular neurologist with just him and me in the room. I didn't like, you know, the guinea pig, with all that going on…he wasn't listening to me."* Themes of self-empowerment, dignity, open-mindedness, respect, and vulnerability were articulated, among others.

Interview #7: Pages 136-151

This person is in their mid-40's and has had a late onset of symptoms which were first noticeable to them at about age 30. They are ambulant with assistance and described what receiving neurology care at the Veteran's Affairs (VA) hospital has been like for them. They shared experience with teaching neurology examinations and have tried various sessions of physical and occupational therapy. *"I didn't feel like it was tailored for me, you know."* They shared that they do not participate in regular PT sessions but that they are finding the appointments where they

are receiving interventional support the most productive such as wheelchair fittings or accessibility communications.

When asked about their experiences getting their annual neurology examinations, they shared that, *" I went in and I'm in there with the guy, who is the head guy, and he's bringing in all these other people, to kind of see me and kind of how I function so it's a little bit kind of a lab rat feeling, like, oh, this is such a rare condition, so we need to like show everybody what this is because it's unique. But, it's kind of unpleasant and uncomfortable to do that."* The individual shared that they feel the desire to help clinicians understand dysferlinopathy, but that at the same time, the experience for them in the clinic is dehumanizing and not something they feel is helpful to them. This is exacerbated when there are different clinicians providing the examinations each year which blocks the individual from forming a relationship with their neurologist over time.

Consistency was desired and lacking with the clinical care framework that this individual experiences through the VA. However, they are able to receive extensive support through the VA for equipment and other services that are instrumental in helping this individual remain as independent as possible. When asked about what clinical exams are like, the individual shared, *"it's just frustrating because nobody has any answers, it's just, oh yeah, we're going to check, test your muscle function and we're going to do this and that but nobody can really give me any answers."*

In contrast, they shared that their wheelchair fitting appointments are better because something productive happens. There were stories of multiple system exams that take place annually which

the individual describes as *"frustrating"* and, *"it can be stressful because it's like, there's not really a standard of care. It's just like, ok, we're going to try this, we're going to try that, we're going to see if this works or doesn't work, but it doesn't feel cohesive".* However, out of all the experiences this individual shared from past clinical examinations, what they said was what they would hope clinicians can take away from the study the awareness that patients need to be seen and treated as whole people, not identified as a condition.

Interview #8: Pages 152-165

It has been 3 years since this participant was given their diagnosis but for most of their childhood, their family was aware of their elevated CK and chose to wait to pursue genetic testing until it became relevant to the individual. They are completing graduate work and are in their early 20's, living independently at college, and participating in the dysferlinopathy natural history study (COS). They shared that their clinical experiences have been positive and that one of the reasons their relationship with their neurologist is good is the fact that the neurologist is willing to collaborate with the individual on treatment ideas. There are drugs approved for other conditions that the individual would like to learn more about and/or try. Their neurologist works together with them on exploring options. But, when discussing how they are accessing disease-specific information, they shared, *"I feel like in terms of information I was given, it was broad, it wasn't very detailed either, it was just kind of like, ok, this is kind of what you can expect. In terms of progression, we have no idea."*

This is an individual who has enjoyed working out and has been keeping up a modified exercise routine as best they can during a time when they are noticing changes in their muscles. Of note

are the experiences this individual has had about the mental aspect of the condition, specifically surrounding being mentally prepared to process what the condition is, how they will navigate life, and when they are feeling ready to face certain aspects that come with the condition. They shared that there have been times when they have not been ready to talk about future progression. Even though they have a good relationship with their neurologist, they shared that the exams feel "pointless" because, *"when I go to see them and I don't go much because there's not much to tell me, to be honest. Right? It's like, ok, you lost, this much function, but you already know that there's nothing I can do for you. It's kind of pointless, in a sense."* Themes of integrity, trauma, coping, self-study, mutuality, and realism were threaded throughout this interview.

References

Alase, A. (April 2017). The Interpretive Phenomenological Analysis (IPA): A Guide to a Good Qualitative Research Approach. International Journal of Education and Literacy Studies, Volume 5, Number 2. http://dx.doi.org/10.7575/aiac.ijels.v.5n.2p.9

Braun, V., Clarke, V. (2006). Using Thematic analysis in psychology. Qualitative Research in Psychology, Volume 3, pages 77-101. University of Aukland and University of the West of England. https://doi.org/10.1191/1478088706qp063oa

Budych, K., Helms, T., Schultz, C. (2012). How do patients with rare diseases experience the medical encounter? Exploring role behavior and its impact on patient-physician interaction. Health Policy, Volume 105, issues 2-3, Pages 154-164. https://www.sciencedirect.com/science/article/pii/S0168851012000644

Bushby, K. (1999). Making sense of the limb-girdle muscular dystrophies. Oxford Academic Brain. Volume 122, Issue 8, pages 1402-1420. https://doi.org/10.1093/brain/122.8.1403

Green, B., Saunders, P., Power, E., Dass-Brailsford, P., Schelbert, K., Giller, E., Wissow, L., Hurtado-de-Mendoza, A., Mete, M. (2015). Trauma-Informed Medical Care: A CME Communication Training for Primary Care Providers. Family Medicine. Volume 47 (1), pages 7-14. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4316735/

Groenewald, T. (2004). A Phenomenological Research Design Illustrated. International Journal of Qualitative Methods. Volume 3, Issue 1 https://doi.org/10.1177/160940690400300104

Hall, J., Roter, D., Katz, N. (1988). Meta-analysis of Correlates of Provider Behavior in Medical Encounters. Medical Care, Volume 26, Number 7, pages 657-675. https://www.jstor.org/stable/3765489

Huyard, C. (2009). What, if anything, is specific about having a rare disorder? Patients' judgments on being ill and being rare. Health Expectations. Volume 12 (4), pages 361-70. https://doi.org/10.1111/j.1369-7625.2009.00552.x

Kaplan, M. (1984). The connection between clinical health promotion and health status: A critical overview. American Psychologist, Volume 39(7), pages 755–765. https://doi.org/10.1037/0003-066X.39.7.755

Kremp, O., Dosquet, P., Rath, A. (2012). Professional clinical guidelines for rare diseases: methodology. Orphanet Journal of Rare Diseases. Volume **7,** Article number A12. https://doi.org/10.1186/1750-1172-7-S2-A12

Liu, J., Aoki, M., Illa I., Wu, C., Fardeau, M., Angelini, C., Serrano, C., Urtizberea, J., Hentati, F., Hamida, B., Bohleg,a S., Culper, J., Amato, A., Bossie, K., Oeltjen, J., Bejaoui, K., McKenna-Yasek, D., Hosler, A., Schurr, E., Arahata, K., de Jong, J., Brown, R. Jr.. (1998). Dysferlin, a novel skeletal muscle gene, is mutated in Miyoshi myopathy and

limb girdle muscular dystrophy. Nature Genetics. Volume 20, pages 31-36. https://doi.org/10.1038/1682

Lowes, L., Prowse, M. (2001). Standing outside the interview process? The illusion of objectivity in phenomenological data generation. International Journal of Nursing. Volume 38, Issue 4, pages 471-480. https://doi.org/10.1016/50020-7489(00)00080-8

Mayhew, A., James, M., Moore, U., Sutherland, H., Jacobs, M., Feng, J., Lowes, L., Alfano, L., Lofra, R., Rufibach, L., Rose, K., Duong, T., Bello, L., Pedrosa-Hernandez, I., Holsten, S., Sakamoto, C., Vandevelde, B., DeWolf, B., Maron, E., Gordish-Dressman, H., Hilsden, H., Guglieri, M., Hogrel, J., Blamire, A., Carlier, P., Spuler, S., Da, J., Jones, K., Bharucha-Goebel, D., Campana, E., Pestronk, A., Walkter, M., Paradas, C., Stojkovic, T., Mori-Yoshimura, M., Bravver, E., Diaz-Manera, J., Pegorano, E., Mendell, J., the Jain COS Consortium, Straub, V.. (2022). Assessing the Relationship of Patient Reported Outcome Measures With Functional Status on Dysferlinopathy: A Rasch Analysis Approach. Frontiers in Neurology. https://doi.org/10.3389/fneur.2022.828525

Moore, U., Jacobs, M., James, M., Mayhew, A., Fernandez-Torron, R., Feng, J., Cnaan, A., Eagle, M., Bettinson, K., Rufibach, L., Lofra, L., Blamire, A., Carlier, P., Mittal, P., Lowes, L., Alfano, L., Rose, K., Duong, T., Berry, K., Montiel-Morillo, E., Pedrosa-Hernández, I., Holsten, S., Sanjak, M., Ashida, A., Sakamoto, C., Tateishi, T., Yajima, H., Canal, A., Ollivier, G., Decostre, V., Mendez, J., Praxedes, N., Thiele, S., Siener, C., Shierbecker, J., Florence, J., Vandevelde, B., DeWolf, B., Hutchence, M., Gee, R., Prügel, J., Maron, E., Hilsden, H., Lochmüller, H., Grieben, U., Spuler, S., Rocha, C., Day, J., Jones, K.,Bharucha-Goebel, D., Salort-Campana, E., Harms, H., Pestronk, A., Krause, S., Schreiber-Katz, O., Walter, M., Paradas, C., Hogrel, J., Stojkovic, T., Takeda, S., Mori-Yoshimura, M., Bravver, E., Sparks, S., Díaz-Manera, J., Bello, L., Semplicini, C., Pegoraro, E., Mendell, J., Bushby, K., Straub, V., for the Jain COS Consortium. (2019). Assessment of disease progression in dysferlinopathy. Neurology. https://doi.org/10.1212/WNL.0000000000006858

Moore U., Fernandez-Torron, R., Jacobs, Gordish-Dressman, H., Diaz-Manera, J., M., James, M., Mayhew, A., Harris, E., Guglieri, M., Rufibach, L., Feng, J., Blamire, A., Carlier, P., Spuler, S., Day, J., Jones, K., Bharucha-Goebel, D., Salort-Campana, E., Pestronk, A., Walter, M., Paradas, C., Stojkovic, T., Mori-Yoshimura, M., Bravver, E., Pegoraro, E., Lowes, L., Mendell, J., Bushby, K., the Jain COS Consortium, Bourke, J., Straub, V. (2022). Cardiac and pulmonary findings in dysferlinopathy: A 3-year, longitudinal study. Muscle & Nerve. Volume 65(5), pages 531-540. https://doi.org/10.1002/mus.27524

Morel, T., Cano, S. (2017). Measuring what matters to rare disease patients- Reflections on the work of the IRDiRC taskforce on patient centered outcome measures. Orphanet Journal of Rare Diseases, Volume 12, Article 171. https://doi.org/10.1186/s13023-017-0718-x

Moser, A., Kjorstgen's, I. (2018) Series: Practical Guidance to Qualitative Research. Part 3: Sampling, Data Collection and Analysis, The European Journal of General Practice, Volume 24(1), pages 9-18. https://doi.org/10.1080/13814788.2017.1375091

Noon, E., (2018). Interpretive Phenomenological Analysis: An Appropriate Methodology for Educational Research?", Sheffield Hallman University, UK, Journal of Perspectives in Applied Academic Practice. Vol. 6, Issue 1, pages 75-83. https://jpaap.napier.ac.uk/index.php/JPAAP/article/view/304/447

Oliveira, V., Ferreira, M., Pinto, R., Filho, R., Refshauge, K., Ferreira, P., (2015). Effectiveness of Training Clinicians' Communication Skills on Patients' Clinical Outcomes: A Systematic Review. Journal of Manipulative and Physiological Therapeutics, Volume 38, Issue 8, Pages 601-616. https://doi.org/10.1016/j.jmpt.2015.08.002

Pai, M., Iorio, A., Meerpohl, J., Taruscio, D., Laricchiuta, P., Mincarone, P., Morciano, C., Leo, C., Sabina, S., Akl, E., Treweek, S., Djulbegovic, B., Schunemann, H., and Consortium for the RARE-Bestpractices. (2015). Developing methodology for the creation of clinical practice guidelines for rare diseases: A report from RARE-Best practices, Rare Diseases, Volume 3(1). https://doi.org/10.1080/21675511.2015.1058463

Pai M., Yeung, C., Akl, E., Darzi, A., Hillis, C., Legault, K., Meerpohl, J., Santesso, N., Taruscio, D., Verhovsek, M., Schunemann, H., Iorio, A. (2019). Strategies for eliciting and synthesizing evidence for guidelines in rare diseases. BMC Medical Research Methodology. Article number 67. https://doi.org/10.1186/s12874-019-0713-0

Pavan, S., Rommel, K., Marquina, M., Höhn, S., Lanneau,V., Rath, A. (2017). Clinical Practice Guidelines for Rare Diseases: The Orphanet Database. PloS one, Volume 12(1), e0170365. https://doi.org/10.1371/journal.pone.0170365

Pietkiewicz, I., Smith, J. (2012). A practical guide to using Interpretive Phenomenological Analysis in qualitative research psychology. University of Social Sciences and Humanities. Birkbeck University of London, Department of Psychological Sciences. Czasopismo Psychologiczne (Psychological Journal). Volume 18(2), Pages 361-369. https://www.researchgate.net/file.PostFileLoader.html?id=53c8b90acf57d7ce4b8b45a2&assetKey=AS%3A273565755084817%401442234566451

Sardella, M., Belcher, G. (2018). Pharmacovigilance of medicines for rare and ultrarare diseases. *Therapeutic advances in drug safety*, *9*(11), 631–638. https://doi.org/10.1177/2042098618792502

Sejersen, T., Giovane, C., Filippini, G., Leo, C., Meerpohl, J., Mincarone, P., Minozzi, S., Sabina, A., Schunemann, H., Senecat, J., Taruscio, D., the RARE-Bestpractices consortium. (2014). Methodology for production of best practice guidelines for rare

diseases. Rare diseases and orphan drugs, An international journal of public health, Volume 1, number 1. https://www.rarejournal.org/index.php/rarejournal/article/view/35

Smith, J., Osborn, M. (2006). Interpretive phenomenological analysis. Research Methods in Psychology, 3rd Edition, Chapter 4. https://research.familymed.ubc.ca/files/2012/03/IPA_Smith_Osborne21632.pdf

Stewart M. A. (1995). Effective physician-patient communication and health outcomes: a review. Canadian Medical Association journal = journal de l'Association medicale canadienne, Volume 152(9), pages 1423–1433. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1337906/

Straub, V., Murphy, A., Udd, B; LGMD workshop study group. (2018). Nomenclature and reformed classification. 229th ENMC international workshop: Limb girdle muscular dystrophies Naarden, the Netherlands. Neuromuscular Disorders. Volume 28(8), pages 702-710. https://doi.org/10.1016.j.nmd.2018.05.007

van Breukelen, S. (2016). Patient involvement in the development of rare disease standards of care. EURORDIS Conference, Edinburgh. https://www.eurordis.org/sites/default/files/ws4-5-silvia-van-breukelen-good-clinical-practices.pdf