Externally-Led Patient Focused Drug Development (EL-PFDD) meeting on LGMD Subtypes 2C, 2D, 2E, 2F, 2A and 2i

MEETING DATE:
September 23, 2022

MEETING HOSTED BY:
Coalition to Cure Calpain 3, the Kurt+Peter Foundation, the LGMD2D Foundation, the Speak Foundation, Cure LGMD2i, and the McColl-Lockwood Laboratory for Muscular Dystrophy Research

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Voice of the Patient Report:

Limb-Girdle Muscular Dystrophy Subtypes 2C, 2D, 2E, 2F, 2A and 2i

LGMD Coalition consists of Coalition to Cure Calpain 3, the CureLGMD2i Foundation, the Kurt+Peter Foundation, the LGMD2D Foundation, the Speak Foundation and the McColl-Lockwood Laboratory for Muscular Dystrophy Research. Our collective mission is to seek patient and caregiver perspectives on how limb-girdle muscular dystrophy (LGMD) affects their lives and their attitudes towards treatments so that stakeholders will take the patient voice into account when developing and approving therapies for the LGMDs.

This *Voice of the Patient* report was prepared by LGMD Coalition as a summary of the input shared at the externally-led patient-focused drug development (EL-PFDD) meeting on LMGD subtypes 2C, 2D, 2E, 2F, 2A and 2i. This meeting was hosted virtually on September 23, 2022.

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Consulting Partners include James Valentine, Esq. and Larry Bauer, RN, MA, from Hyman, Phelps & McNamara, P.C.

Disclosures: LGMD Coalition consists of Coalition to Cure Calpain 3, the CureLGMD2i Foundation, the Kurt+Peter Foundation, the LGMD2D Foundation, the Speak Foundation and the McColl-Lockwood Laboratory for Muscular Dystrophy Research. Each of these organizations is a tax-exempt, charitable organization and is eligible to receive tax- deductible contributions under the IRS Code 501(c)(3). With the exception of the McColl-Lockwood Laboratory for Muscular Dystrophy Research and the Kurt+Peter Foundation, these organizations may receive funding from pharmaceutical companies in the form of unrestricted and restricted grants and sponsorship of programs and events.

James Valentine, Esq. and Larry Bauer, RN, MA are employed by Hyman, Phelps & McNamara, P.C., a law firm that represents patient advocacy organizations and companies that are developing therapeutics and technologies to advance health.

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LGMD Coalition wishes to sincerely thank everyone from our LGMD communities who attended or participated in the EL-PFDD meeting on September 23, 2022. We wish to especially acknowledge those who had the courage to step forward and bravely share their stories by video, zoom, calling in or submitting comments.

LGMD Coalition is incredibly grateful to have had the opportunity to share our experiences with a wide audience. We sincerely thank the FDA staff who attended, and give special thanks to Shannon Sparklin from the FDA's patient focused drug development staff and Karen Jackler from the Center for Biologics Evaluation and Research who guided us through the process.

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We wish to also thank our many community members and partners from advocacy and professional organizations, drug companies, federal agencies and universities from across the world who attended our meeting and are helping us work towards therapies for LGMD subtypes 2C, 2E, 2D, 2E, 2A and 2i.

Contents

LGMD Insights

Key themes that emerged throughout the September 23, 2022 EL-PFDD meeting are listed below. Although the EL-PFDD meeting addressed six different LGMD subtypes, these messages were common to all.

1. **LGMD affects multiple body systems.**
   Impaired mobility is the most impactful symptom, reflected by problems with walking and balance, difficulties getting up from sitting, and challenges using the stairs. Other impactful symptoms include fatigue, difficulties using hands and arms, and social/emotional challenges. For many individuals living with LGMD, constant pain, urinary and bowel issues, poor sleep, muscle contractures, pulmonary and cardiac issues are a way of life. Symptoms can vary from one day to another.

2. **Many with LGMD are severely affected.**
   LGMD affects every aspect of life and robs individuals of their independence. Most rely heavily on their caregivers or family members for activities of daily living, and some require 24-hour care. Many described catastrophic falls, which then resulted in higher care requirements.

3. **All individuals with LGMD progress, but at different rates.**
   Individuals living with LGMD worry about their continuing progression and eventually losing all independence. Adapting to disease progression is extremely challenging and individuals living with LGMD worry about whether they will have someone who will assist them in the future.

4. **LGMD is stigmatizing.**
   Discrimination and social exclusion are part of life. Many are adversely impacted by the limitations they experience compared to their peers. Some try to hide their disability from others. Anxiety and depression are common, and feelings of grief and loss are constant as symptoms progress.

5. **There are currently no FDA approved treatments for any form of LGMD.**
   Many individuals with LGMD described their fears, frustrations, and anger that despite years of research there is no treatment that can slow or halt the disease progression.

6. **Treatment approaches are palliative only and do not change the course of the disease.**
   Approaches include dietary supplements, medications to help manage different symptoms, a wide range of mobility aids, extensive home and vehicle modifications, physical therapy and exercise including aqua therapy.

7. **People living with LGMD urgently and desperately need better treatments.**
   Short of a cure, most would like a treatment that would help regain strength and/or muscle function, followed by a treatment to slow or stop the loss of muscle function, not only to maintain mobility but to support cardiac and pulmonary functions.

8. **Individuals living with LGMD want to participate in clinical trials.**
   Many desire that the FDA and clinical trial sponsors consider: shorter placebo durations or no placebo control arms; would accept a small number of trial participants; include non-ambulatory patients; more meaningful endpoints including arm strength or respiratory function; address the specific needs of each LGMD subtype and each individual's level of progression in the course of the disease.

Introduction

On September 23, 2022, a coalition of patient-focused limb-girdle muscular dystrophy (LGMD) organizations held an Externally-Led Patient Focused Drug Development (EL-PFDD) meeting for six LGMD subtypes: 2C (R5), 2D (R3), 2E (R4), 2F (R6), 2A (R1), and 2i* (R9). The LGMD Coalition includes the following organizations: Coalition to Cure Calpain 3, CureLGMD2i, Kurt+Peter Foundation, LGMD2D Foundation, McColl-Lockwood Laboratory for Muscular Dystrophy Research, and the Speak Foundation.

The EL-PFDD meeting was designed to engage patients and elicit their unique perspectives on the health effects, daily impacts, treatment goals, and decision factors considered when seeking out or selecting a treatment for symptoms and burdens associated with LGMD subtypes 2C, 2D, 2E, 2F (collectively termed sarcoglycanopathies), LGMD2A and LGMD2i. The meeting was held virtually to enable as many community members to participate as possible and to allow many different voices to be heard.

The meeting was conducted as a parallel effort to FDA's PFDD initiative, a commitment under the fifth authorization of the Prescription Drug User Fee Act (PDUFA V) to more systematically gather patients' perspectives on their conditions and available therapies to treat their conditions. The EL-PFDD meeting outcomes are summarized in this *Voice of the Patient* report, a high-level summary of the perspectives generously shared by individuals living with these six LGMD subtypes who participated in the September 23, 2022 meeting. The report also includes selected patient comments captured in a pre-meeting survey and collected in an online portal.

The information in the *Voice of the Patient* report may be used to guide therapeutic development and inform the U.S. Food and Drug Administration (FDA) benefit-risk evaluations when assessing therapies to address specific LGMD subtypes. The hope is that including the perspectives from individuals living with LGMD will enable patient-informed development and review of LGMD therapies to meet the needs and expectations of our patient community.

The LGMD Coalition has provided this report to the FDA, government agencies, regulatory authorities, medical products developers, academics, and clinicians, and it is publicly available for the many stakeholders in the LGMD community. The September 23, 2022 discussion was limited to patients, family members, and other direct caregivers with LGMD subtypes 2C, 2D, 2E, 2F, 2A and 2i, however, there will be opportunities for other voices to be heard in future meetings. The input received from the September 23, 2022, EL-PFDD meeting reflects a wide range of experiences, however not all symptoms and impacts may be captured in this report.

The final report, the patient comments, the meeting transcript, and a recording of the meeting can be found at LGMDPFDD.com along with a list of supporters.

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* LGMD2i is notated with a small "i" to prevent confusion with LGMD2L.

Clinical Overview of LGMD subtypes 2C, 2D, 2E, 2F, 2A and 2i[1]

Overview of Conditions

LGMDs are a diverse group of disorders that primarily affect the muscles in the shoulders and hips, especially those muscles closer to the center of the body. This group of disorders collectively form the fourth most common cause of genetic muscle weakness with a prevalence estimated between 1 in 14,500 to 1 in 123,000 individuals. LGMD is an umbrella term first used in 1954 to describe a variety of individual muscular dystrophies, each associated with a distinct causative gene, that broadly share predominant clinical symptoms of progressive weakness and atrophy in the limb-girdle muscles due to the loss of muscle fibers. In some cases, people develop cardiomyopathy and breathing-related issues. Additional symptoms may also include joint stiffness, muscle cramps and pain, enlargement of calf muscles, fatigue, delays of motor development, swallowing difficulties, scoliosis or lordosis, rhabdomyolysis, and involvement of the distal body muscles such as those in the hands and feet. Many people progress to loss of ambulation a few years after onset.

Natural History

Individuals with LGMD will often present with proximal muscle weakness, which may cause difficulties running or climbing stairs, or increased falling. Sometimes patients may not have weakness but will have an incidental finding of elevated AST and/or ALT laboratory results, which could indicate muscle damage. Others may present with muscle pain or fatigue.

A clinical diagnosis of LGMD can be made based on a pattern of weakness in the hip and shoulder girdles. However, a genetic LGMD diagnosis cannot be made by history and examination. Genetic testing via a panel of genes associated with neuromuscular disease is necessary to determine an individual's subtype. At least 30 genes cause LGMD, and there is considerable clinical heterogeneity between the subtypes. A new nomenclature was introduced in 2017, which is described in the paragraph below in bold type. Throughout this report, the older nomenclature, which is still most common, is used.

LGMD types 2C/**R5 γ-sarcoglycan-related**, 2D/**R3 α-sarcoglycan-related**, 2E/**R4 β-sarcoglycan-related**, and 2F/**R6 δ-sarcoglycan-related** are collectively termed sarcoglycanopathies and associated with mutations in SGCG, SGCA, SGCB, and SGCD respectively. In addition to the sarcoglycanopathies, LGMD2A/**R1 Calpain 3-related** (associated with mutations in CAPN3, also called calpainopathy), and LGMD2i/**R9 FKRP-related** (also called dystroglycanopathy) were the focus of the September 23, 2022 EL-PFDD meeting.

The prevalence of each of the six subtypes, per million people (listed in descending order of prevalence): LGMD2A, 8.4; LGMD2i, 4.5; LGMD2D, 3.4; LGMD2E, 0.8; LGMD2C, 0.12; LGMD2F, 0.07.

Key symptoms and characteristics of the subtypes are as follows:

- **Sarcoglycanopathies**
  - Onset of weakness common in childhood
  - Weakness begins in proximal lower extremities followed by proximal upper extremities
  - Calf hypertrophy common
  - Majority of patients lose ambulation in teenage years into young adulthood
  - Heart and pulmonary involvement are common, apart from LGMD2D which rarely affects the heart
  - Can result in shortened life expectancy

[1] Landscape Assessment was prepared by Jennifer Levy, PhD, Scientific Director, Coalition to Cure Calpain 3 with additional information provided from the September 23, 2022 presentation by Katherine Mathews, MD, Professor of Pediatrics & Neurology, University of Iowa, Carver College of Medicine.

- **LGMD2A**
  - Onset in childhood through early adulthood
  - Weakness in knee flexors, hip extensors, and hip adductors
  - Joint contractures common in ankles, hips, knees, and elbows
  - Scapular winging common
  - Loss of ambulation often occurs two decades after disease onset
  - Heart is usually not involved

- **LGMD2i**
  - Variable onset ranging from early childhood through older adulthood
  - Patients homozygous for the common c.826C>A mutation present with milder disease than other genotypes
  - Weakness most commonly presents in proximal lower extremities
  - Scapular winging, calf hypertrophy, and tongue hypertrophy occur sometimes
  - Exercise induced muscle pain is common
  - Heart and respiratory involvement are common

Developing and Available Treatments

There currently are no FDA approved specific treatments for sarcoglycanopathies, LGMD2A, or LGMD2i. Current treatments are only supportive and no disease modifying treatments exist. Supportive therapies that may help these LGMD subgroups are physical therapy, speech therapy, pacemakers, braces, non-invasive ventilatory support systems, walkers, wheelchairs, and other assistive devices. The goals of these treatments are to try and slow the complications of LGMD and/or maintain quality of life. People with severe swallowing difficulties may require the placement of a feeding tube to maintain adequate nutrition. Skeletal deformities or joint contractures may require surgical correction.

LGMD Coalition is hopeful that we will soon transition from supportive care to disease modifying treatments for LGMDs. Small molecules, gene replacement, and gene editing therapies are in various stages of development. Most approaches are substrate specific, and therefore must be tailored for a specific LGMD subtype. Current interventional clinical trials include substrate loading for LGMD2i using the sugar ribitol and gene replacement therapy for LGMD2E. Gene replacement therapy is in development for several other LGMD subtypes including LGMD2A, LGMD2C, LGMD2D, and LGMD2i. This approach utilizes systemic delivery of viral vectors carrying a replacement copy of the affected gene.

Meeting summary

The LGMD community conducted an Externally-Led Patient-Focused Drug Development (EL-PFDD) meeting on Friday, September 23, 2022, for six limb-girdle muscular dystrophy (LGMD) subtypes: 2C, 2D, 2E, 2F,2A, and 2i. The EL-PFDD meeting was co-moderated by Jennifer Levy, PhD, Scientific Director, Coalition to Cure Calpain 3 and James Valentine, MHS, from Hyman, Phelps and McNamara.

Kathryn Bryant Knudson, Founder of the Speak Foundation and an individual living with LGMD2i, opened the meeting by welcoming and thanking meeting participants for their attendance. She introduced the six organizations that make up the LGMD Coalition, provided a short introduction to LGMD, and encouraged all people living with LGMD and their loved ones to participate in the meeting.

Dr. Wilson Bryan, Director of the Office of Tissues and Advanced Therapy in the Center for Biologics Evaluation and Research (CBER) at the U.S. Food and Drug Administration, offered some opening remarks on behalf of the FDA. He emphasized how important it is for the FDA to hear from patients in order to help them to think about how clinical trials should be designed, what endpoints are meaningful to patients, and how to balance benefits and risks of a new product. Dr. Katherine Mathews, MD, Professor of Pediatrics & Neurology, University of Iowa, Carver College of Medicine provided a high-level clinical overview of LGMD.

Dr. Levy and James Valentine provided an overview of the meeting structure and encouraged individuals living with LGMD subtypes 2C, 2D, 2E, 2F, 2A and 2i, as well as family members and caregivers of people living with these six subtypes to contribute to the dialogue via online polling, calling in by phone, and contributing written comments using the online portal. The meeting agenda is presented in **Appendix 1**.

Online polling was used to determine the demographics of the meeting attendees who were representing those living with LGMD and are presented in **Appendix 2**. Almost two-thirds of poll respondents were individuals living with LGMD and just over one third were parents and caregivers. Two-thirds of poll respondents were from the U.S., with representation from the Midwest, Northeast, South, West, Mid-Atlantic and Mountain regions. Almost 20% were from Europe or United Kingdom, with the remaining attendees from Asia, Canada, Africa, Central or South America, Australia or New Zealand and other.

A wide age range of ages of individuals living with LGMD were represented. The largest group were individuals in the 30-39-year age range, followed by individuals in the 18-29 and 40-49 year age ranges, with representation by individuals who are over 50 years and 0-17 years. The numbers of individuals who identify as female and male were fairly evenly split.

Two-thirds of poll respondents reported that they were diagnosed with LGMD more than 10 years previously. There was fairly equal representation by individuals who were diagnosed within the past five years and between 5-10 years ago, with only a small fraction unsure of when they were diagnosed. The subtype representation mirrors the prevalence of each subtype. Those living with LGMD2A had the strongest representation, followed by LGMD2i. Individuals living with LGMD subtypes 2C, 2D, and 2E were also well represented, but LGMD2F was not represented in the polling results, as expected due to the very low prevalence of this subtype. Although a few attendees had a genetically confirmed subtype that was not listed, or were unsure about their subtype, the EL-PFDD meeting and this *Voice of the Patient* report are focused on those who have a genetic diagnosis of one of the six subtypes.

The meeting was attended by 626 individuals, including 278 individuals living with LGMD, 126 family members including parents, grandparents and partners, 47 caregivers, 32 friends. The meeting was attended by 27 FDA and 48 industry representatives, 22 healthcare providers, 15 representatives from non-profit groups, more than 20 scientists, researchers and students, as well as representatives from allied organizations, and consultants.

The EL-PFDD meeting was structured around two key topics divided into three sessions. The morning session was Topic 1: *Symptoms, Health Effects and Impacts on Daily Life*. Session 1 focused on *Living with Sarcoglycanopathies (LGMD2C, 2D, 2E, 2F)* and Session 2 focused on *Living with LGMD2A and LGMD2i*.[2] Session 3 included a discussion of Topic 2: *Current Approaches to Managing LGMD*, and included patients with all six LGMD subtypes. Each of the three sessions started with pre-recorded panelists who were selected to represent a range of experiences of living with LGMD. James Valentine moderated a discussion between a live Zoom panel of discussion starters and people who dialed in by phone. Additional relevant comments entered through an online submission form were read by Dr. Levy. The questions provided for meeting discussion are in **Appendix 3**. The names of panelists and callers are listed in **Appendix 4**.

Online polling results from Session 1: *Living with Sarcoglycanopathies (LGMD2C, 2D, 2E, 2F)* are included in **Appendix 5**, with a further breakdown of results included in **Appendix 6**. Online polling results from Session 2, are separated into *Living with LGMD2A* in **Appendix 7** and *Living with LGMD2i* in **Appendix 8**. Online polling results from Session 3: *Current Approaches to Managing LGMD* are in **Appendix 9**. To include as many voices as possible, an online survey was open several months prior to the meeting and an online comment submission portal was open for four weeks after the meeting. Selected comments are included in the body of this report, and all survey responses and submitted comments are included in an accompanying PDF.

[2] The live transmission of Session 2 was briefly interrupted due to a world-wide YouTube shutdown, however the complete meeting proceedings were captured in the meeting recording and transcript. Live transmission resumed concurrent with the start of Session 3.

Session 1:
Living with Sarcoglycanopathies (LGMD2C, 2D, 2E, 2F) — Symptoms, health effects and impacts on daily life

Individuals living with LGMD subtypes 2C, 2D and 2E or their parents and caregivers used online polling to answer questions related to their symptoms, health effects and impacts on daily life. The outcomes of the poll results are summarized in the sections below and illustrated with patient comments. The full poll results are included in **Appendix 5** and responses are shown by subtype in **Appendix 6**.

Of note: Many individuals attending the EL-PFDD were younger patients so the full range of symptoms and severity may not be represented. Most living with LGMD2C and LGMD2E do not have long lifespans.

Impaired mobility is the symptom with the most significant impact on individuals living with sarcoglycanopathies, followed by difficulty using hands and arms, and fatigue.

Poll results are shown in **Appendix 5, Q1**.

Impaired mobility – including trouble walking, standing and transferring – was the top symptom for individuals living with sarcoglycanopathies. Often difficulties keeping up with their peers was an initial symptom with continued progression developing over years resulting in the loss of ambulation. Many have difficulties standing from sitting, climbing stairs, maintaining balance, and preventing falls early on in the disease progression.

> *"The first symptoms I remember were tightness in my ankles and getting tired faster than other kids. … In third grade, I noticed more differences between me and the other kids. I was much slower, and climbing into cars was challenging because I could not lift my leg up into them, and I was not tall enough to just sit down. In fourth grade, stairs became challenging and carrying my cello was difficult. … By fifth grade, stairs became very difficult, and I was using the elevator. I also couldn't climb playground equipment."*
>
> –**Peter**, 14-year-old male living with LGMD2C

> *"He is unable to even play a game of tag without falling. His ability to stabilize his body with the smallest nudge or stumble leads to frequent falls, some of which has led to a strong impact to his head and limbs. We fear that he will break a bone and be unable to use that limb leading to more muscle loss that he will be unable to recover."*
>
> –**Faran**, mother of a nine-year-old son living with LGMD2D

> *"I was never able to run as fast as other kids, wasn't as strong as other kids. I noticed this around the third grade. When I was 12, I started to walk with a gait, swinging my hips, and then I was diagnosed with scoliosis. The doctors thought [scoliosis] was causing my gait, but actually it was my muscular dystrophy. When I was in my late twenties to early thirties, it became harder for me to walk and stand up."*
>
> –**Donavon**, 59-year-old man living with LGMD2D

> *Last week in school he wrote he wanted to 'run faster' as something to work on this week. When I asked him about his response, he said he is always behind his peers when running in gym.*
>
> —**Rachel**, mother of a five-year-old son living with LGMD2D

> *From ages seven to 10, my symptoms progressed quickly. I began to toe walk with a distinct waddle while arching my back because I would struggle to be able to lift my leg with each step and to keep my balance while standing. When I fell, I was never able to break my fall.*
>
> —**Elizabeth**, 42-year-old woman living with LGMD2C

A 64-year woman living with LGMD2F said that her top symptoms include, *Managing stairs and getting up from the floor or chair.*

Difficulty using hands or arms was the second most impactful LGMD symptom for those living with sarcoglycanopathies. Most individuals living with sarcoglycanopathies experience difficulties with activities involving both upper extremities and lower extremities and core, as confirmed in the second poll question, in **Appendix 5, Q2**. Difficulty using hands or arms profoundly impacts independence.

> *Weakness has taken away my ability to be self-sufficient. I no longer can toilet myself, bathe myself, dress myself, prepare meals myself. I no longer have enough strength to put my hair up in my desired style since I can not elevate my arms. I slouch and prop my arms on counters to brush my teeth, to feed myself.*
>
> —**Vanessa**, woman living with LGMD2C

> *I am not able to walk or do any activities that involve body transfers or strength, including using my arms for any activities requiring lifting, carrying, pulling or pushing anything with my arms, which is very frustrating. … I used to be able to play the violin as I come from a music background family, and now I can't lift my arms to even hold my toothbrush in the mornings.*
>
> —**Nahira**, woman living with LGMD2C

> *The disease is gradually progressing over the years, the strength in the lower limbs started to decline at first and then the core and then gradually the arm strength.*
>
> —**Prakash**, living with LGMD2D

> *My son does not move his legs and arms, he can only move his hands and fingers with difficulty. This limits him in all activities that require movement. He has to be fed, washed, dressed, moved in the car, he is only independent in using the wheelchair with a joystick, mobile phone and PC.*
>
> —**Beatrice**, caregiver of a son living with LGMD2E

> *Just trying to fix my hair or even brush my hair can be difficult because my arms tire out very easily. I have to lean on something to be able to so much as wash my face. Any kind of movement is very difficult.*
>
> —**Tomie**, 50-year-old woman living with LGMD2F

Fatigue is the third most impactful symptom for those living with sarcoglycanopathies, and for many is one of the first symptoms. Individuals living with sarcoglycanopathies also described muscle weakness and how fatigue can be exacerbated by pulmonary issues.

> *From ages 25 to 35, … I noticed how incredibly tired I'd be by the end of the day. I began developing constant headaches, but looking back, it was a symptom of too much carbon dioxide in my blood due to my vessels weakening around my lungs and my diaphragm.*
>
> –**Elizabeth**, 42-year-old woman living with LGMD2C

> *Fatigue varies by day and the kids can really tire out on some days much more than others, and so one has to see how people feel each day, with how much they can do. That is definitely an issue. … Some days, kids really struggle to get to things, setting aside the physical barriers that may exist.*
>
> –**Scott**, father of two male teens, age 16 and 14, living with LGMD2C

Bryan's fatigue is increasing. *In my advanced age now being an old man, you wake up, and it feels like gravity has been turned up, and you have no way of knowing what you wake up to. Some days are stronger than others, but they're less and farther between the older you get.*

–**Bryan**, 55-year-old man living with LGMD2D

> *The symptom I have struggled the most with is the diaphragm weakness and its role in lung function. …The loss of lung function has been devastating. You never realize how much you appreciate the ability to breathe until it is a struggle.*
>
> –**Kelly C.**, Individual living with LGMD2D

> *After my workday, my energy level is very low, and that I have no strength to do anything else but to relax in bed the rest of the night.*
>
> –**Rania**, 35-year-old woman living with LGMD2E

Social/emotional concerns (isolation, depression, anxiety) are the fourth most impactful symptom for those living with sarcoglycanopathies. Some described the emotional challenges of coping with a disease that is continually progressing and that is variable from one day to the next. Several described the burden of exclusion and stigma, and some tried to hide their disability for as long as possible.

> *Our 13-year-old son struggles emotionally. Not being able to play with friends, go to birthday parties, play sports or even have fun at recess. He has a great group of friends, but other kids are not as understanding, mean almost. He constantly feels like a burden and apologizes often. Walking and daily functions are a struggle. He just wants to be able to hang with his friends and not feel like crap for the next few days.*
>
> –**Nikki**, parent of a son with LGMD2C

> *This disease is life-altering, but you roll with the punches... you have to. The progressive nature of this disease is what makes this disease so hard physically and emotionally. What will be the next ability that I lose?*
>
> –**Michelle**, woman living with LGMD2D

> *Am I angry? You bet. Am I sad? Sure. Do I question why muscular dystrophy chose me? Every day. Just like all of you, some days the glass is half-full, some days it's half empty, and some days I just wish the glass was bigger.*
>
> —**Patrick**, 49-year-old man living with LGMD2E

Other significant symptoms for those living with sarcoglycanopathies selected in the online polls: **pulmonary (breathing) issues; curvature of the spine (lordosis or scoliosis) or scapular winging; contractures (permanent muscle tightening); cardiac (heart) issues; poor sleep; pain; and urinary/bowel issues including (incontinence, constipation, urinary track infections (UTIs) and rhabdomyolysis)**. These are highlighted with selected patient quotes below.

> *I have ongoing muscle weakness especially now that it is taking away my air. The inability to take a full deep breath, the inability to hold a conversation without gasping for air, the need to be hooked up to non-invasive ventilation, the need to carry such device everywhere I go and the need to not only use it at night but for a portion of my day.*
>
> —**Vanessa**, woman living with LGMD2C

> *My weakened lung and diagram muscles severely reduce my lung capacity which means I cannot lay flat in a bed anymore or fly on an airplane without my ventilator. If I drink too much water or eat a little too much, it puts pressure on my diaphragm and makes it harder for me to breathe, so then I need to use my ventilator for a while to give my lungs a rest.*
>
> —**Donavon**, man living with LGMD2D

Makayla experienced both pain and lack of sleep before her recent diagnosis. *I was 12 when I started to notice the pain. …Later on down the road, I did start noticing weakness. …The pain I have is more achy type feeling. … I'm in constant pain all the time, and with activity, it just worsens.*

—**Makayla**, 17-year-old woman living with LGMD2E

> *It's also difficult to sleep flat in a bed. I spent 12 years sleeping in a lift chair because beds that will sit you up are quite expensive and the recliner was a cheaper option.*
>
> —**Tomie**, 50-year-old woman living with LGMD2F

> *She has rhabdomyolysis with fevers, and so she was at a really high risk. …She's had to be hospitalized for every fever she's ever had. And, for a young kid, constant hospitalization is kind of traumatizing and painful. And, there have been a few times where we've had CK tests done in the hospital where she's at this peak of rhabdomyolysis, and her CK got like 120,000. It's so high, and we just worry about the sort of rapid muscle breakdown that's happening at that time. It's just not healthy for her organs. So, we try and avoid that kind of exposure. And, we also wanted to make sure she was able to be vaccinated before we started exposing her.*
>
> —**Alexa**, caregiver of eight-year-old daughter with LGMD2C

Urinary/bowel issues can be physical (rhabdomyolysis) or can result from a lack of accessible washrooms. *During my workday, I limit and monitor my water intake since I cannot use the restroom at work. I hold my bladder daily for eight hours since the only way for me to use the bathroom is at my house by using the patient lift.*

—**Rania**, 35-year-old woman living with LGMD2E

Points mentioned in the comments but not captured in the polls: symptoms can be variable from one day to the next and can be affected by changes in the weather.

Many individuals living with sarcoglycanopathies are dependent on a caregiver or family member for activities of daily living.

Poll respondents were asked to select the top three activities of daily living that they depended on a caregiver for assistance. Each respondent selected an average of 2.7 responses. Almost 60% of individuals living with sarcoglycanopathies require assistance with **transportation**, **meal preparation**, and **household chores**. Many described requiring caregivers 24/7. Poll results are shown in **Appendix 5, Q3**.

> *"I need help getting to various activities that most teenagers take for granted. For example, one of my parents had to come along to a friend's birthday party to help me in and out of a fun party bus."*
>
> –**Peter**, 14-year-old male living with LGMD2C

> *"The most significant impact in my life is how I have seen that over time I lost my ability to be independent and I am not able to do basic activities of daily living such as getting in and out of the bed, dressing, bathing, using the toilet, grooming, doing my hair, doing house chores, meal preparation, among others. … It has been difficult to depend on family members to be able to continue living my life. My caregiver is my mother, and she lives day-by-day just caring for me and attending to needs 24 hours a day."*
>
> –**Nahira**, woman living with LGMD2C

> *"I've always loved to be independent in my life, to do whatever I want to and to go wherever I want to, without anyone else's help. But LGMD has made it impossible for me to even accomplish the most basic activities of my life without someone else's help."*
>
> –**Prakasa**, 32-year-old man living with LGMD2D

> *I have daily in-home caregivers during the day, my wife cares for my needs overnight.*
>
> –**Paul J.**, a 65-year-old man living with LGMD2C

While only a third require **assistance with going to the bathroom**, this activity generated many comments. Fewer require **assistance with eating**, **dressing**, **bed mobility (getting in and out of bed, rolling over)** and **bathing**, however these topics also generated many comments.

> *I really miss having the ability to bathe and toilet myself. It's so difficult to keep having strangers help with something so intimate. Needing the help to lotion your body and get dressed. It's awful to constantly depend on someone to place you on the toilet or help with a urinal. I cannot say how many UTI's I've had since you end up dehydrating yourself when you're out to not use the facilities and hold it for long periods because no one is around.*
>
> –**Vanessa**, woman living with LGMD2C

> *Today, at the age of 59, I've lost all independent living, as I do require a person to get me in and out of bed, help me bathe, and help me on the toilet. … My wife dresses me and helps me throughout the day. My wife is unable to work outside the home because she's my caretaker.*
>
> –**Donavon**, 59-year-old man living with LGMD2D

> *After my [spinal fusion] surgery I became 100% dependent on my family for my care, because I could no longer stand to walk, and I needed total assistance getting out of bed, bathing, using the bathroom, getting dressed, and grooming. This was a realization for my family that I could no longer be left alone and needed someone with me at all times. … My mom is my primary caregiver and helps me get out of bed using a patient lift. She helps me brush my teeth, showers me, and gets me dressed for work.*
>
> –**Rania**, 35-year-old woman living with LGMD2E

The everyday activities most impacted for those living with sarcoglycanopathies include going out, socializing, traveling and personal hygiene.

Poll respondents were asked to select the top three everyday activities, that they could not do at all or as fully as they would like because of LGMD. The top selected option was **going out**, **socializing** and **traveling** and **personal hygiene**. Poll results are shown in **Appendix 5, Q4**.

> *My two biggest frustrations are losing the ability to reach for heavier things with my arms and not being able to climb the couple of stairs, which frequently prevent me from entering someone's home or getting on a bus. If I had to choose one activity that I wish I could do it is to stand up by myself. Although, I can still get out of some chairs, most couches and chairs are too low for me to get out of by myself.*
>
> –**Peter**, 14-year-old male living with LGMD2C

> *I leave the house four, or five times a month for doctor appointments and very rarely to visit friends.*
>
> –**Paul**, 65-year-old man living with LGMD2C

> *Muscular dystrophy affects every aspect of my life, including socially. I'm unable to visit most friends because of stairs. Any place we go, I have to make sure we have access to the bathroom. … When we travel, my wife has to do a lot of extra work as I need a Hoyer lift, cough assist machine, and my Trilogy. Most of the time, I sleep in my wheelchair, as I need to adjust my legs during the night.*
>
> –**Donavon**, 59-year-old man living with LGMD2D

> *It affects me a lot. I feel sad every day every moment. I can't hang out with friends nor enjoy the life you enjoy. My worst days are the days when friends go on vacations and picnics and mountain climbing and I can't go. And the best days never exist. Yes, there are a lot of activities that I can no longer do because of LGMD2D. First of all, running and walking independently, climbing stairs, riding a horse, skating, getting up, sitting, visiting friends and patients, watching matches, shopping, hiking, and every activity that requires healthy muscles.*
>
> –**Anwar**, 27-year-old living with LGMD2D

> *A significant impact on every aspect of life both physically and emotionally, huge impact on her childhood is 'catching up' with her friends. …We had to gather lot of information ourselves to support us in making reasonable adjustments to continue at same school. We are successful in making our daughter complete her primary school in a normal school.*
>
> –Parent/guardian/caregiver of a 11-year-old female living with LGMD2E

> *Mobility. Being able to play with my granddaughters, being able to travel. Travel is very difficult. … Movement is very difficult.* Tomie said that any type of movement in her body is painful. *Walking is extremely difficult. There's a lot of pain involved. No stairs. I can't navigate stairs at all.*
>
> –**Tomie**, 50-year-old woman living with LGMD2F

Other everyday activities impacted by LGMD that were selected in the polls: **exercising**, **walking**, **attending school** or **working**, **being intimate with a partner**, **driving a motor vehicle**, **performing household chores**, **meal preparation** and **childcare** are all activities that individuals living with sarcoglycanopathies cannot do at all or as fully as they would like.

> *I could not walk distances between classrooms and get around campus without getting knocked down. I was nervous about going to a new middle school with a wheelchair. I had been increasingly using a wheelchair through sixth, seventh, and eighth grades.*
>
> –**Peter**, 14-year-old male living with LGMD2C

> *From ages 35 to 42, present day, my symptoms have progressed significantly. I can no longer be alone for more than a few hours. I went from working full-time to part-time as well as transitioned to working remotely.*
>
> –**Elizabeth**, 42-year-old woman living with LGMD2C

> *I am a lawyer and I find myself in court giving lengthy oral arguments and it is difficult to talk for long periods of time due to my breathing difficulties. This latest symptom has had the most debilitating impact on my life.*
>
> –**Kelly C.**, individual living with LGMD2D

> *Jacob's only current restriction is from playing team sports, not because he can't physically, but because of the strain, if he's pushed too much. Team sportsmanship, camaraderie and a sense of togetherness among peers, is so important at his age and as he grows.*
>
> –**Rachel**, mother of a five-year-old son living with LGMD2D

> *If I have any meetings at work, I look for available coworkers who can assist me in getting up the elevators and opening up the doors for me.*
>
> –**Rania**, 35-year-old woman living with LGMD2E

> *I can't flop on the couch and kick my shoes off after a rough day. I cannot cruise through a drive-up window and get a coffee. And I certainly, cannot pick up my young children to hug them, give them piggybacks, or teach them to play catch.*
>
> –**Patrick**, 49-year-old man living with LGMD2E

A 64-year-old woman living with LGMD2F described the specific activities she can no longer do.
> *Walking, holding my grandchildren.*

People living with sarcoglycanopathies have many worries: becoming a burden; developing or worsening pulmonary/respiratory issues; developing or worsening cardiac issues.

These three top worries – **becoming a burden**, **developing** or **worsening pulmonary/respiratory issues**, **developing** or **worsening cardiac issues** – were selected equally by poll respondents, poll results are shown in **Appendix 5, Q4**.

> *This disease has slowly robbed my ability to live independently, and I can no longer voluntarily move my body, and I now require full-time assistance and I fear I'll ultimately die from respiratory or heart failure.*
>
> –**Elizabeth**, 42-year-old woman living with LGMD2C

> *Losing these physical mobile abilities is hard, but during the past few years I have now realized the next ability that I'm losing is the ability to breathe. I've cried so many tears about this and have come to terms with it.*
>
> –**Michelle**, woman living with LGMD2D

> *As an adult living with limb-girdle muscular dystrophy, my greatest fear is the day my elderly parents, who are currently in their 70s, can no longer provide regular care for me. This would have a significant impact on my independence and quality of life. It will mean the difference if I can reliably get to work on time or how frequently I can leave my house to run errands. Not only is this stressful, but it also scares me.*
>
> –**Rania**, 35-year-old woman living with LGMD2E

> *When I can't move my hands and someone has to feed me, who's going to be there when I can't get up and go to the bathroom?*
>
> –**Tomie**, 50-year-old woman living with LGMD2F

The other worries selected in the poll include (in descending order): **dying prematurely**, **losing independence**, **losing the ability to use my arms and hands**, **losing mobility and the ability to walk**, **being placed in a nursing home or other care facility**, **losing ability to communicate and/or swallow**, **losing social connections** and **coping with pain**. Other worries that were mentioned in the comments include worries about **choking and being unable to swallow**, and **running out of resources**.

Session 2A:
Living with LGMD2A — Symptoms, health effects and impacts on daily life

Individuals with LGMD2A and their caregivers used online polling to answer questions related to their symptoms, health effects and impacts on daily life. The full poll results are in **Appendix 7** and illustrated below with patient comments.

Impaired mobility is the symptom with the most significant impact on individuals living with LGMD2A, followed by difficulty using hands and arms and social/emotional concerns.

Poll results are shown in **Appendix 7, Q1**.

Impaired mobility was the most impactful symptom for individuals living with LGMD2A. Many described challenges navigating stairs and standing up from sitting. Several described how their lack of balance has resulted in falls, which can be difficult to get up from, and have led to serious injury.

> *"The symptom that bothers me the most is how I walk funny. … Because of limb-girdle, I can't walk upstairs anymore except a few. And it takes me a long time and a lot of effort. So, I must take the elevator at school to avoid the stairs... I can't pick myself up from the ground, … so I have to wait for help from teachers or friends that know me well enough to know how to properly lift me under my arms. The common reaction to a fall is to lend the person a hand to grab, but I don't have enough strength in my arms to get up that way. It's so embarrassing."*
>
> –**Brooklyn**, 15-year-old female living with LGMD2A

> *"By the time I graduated from college, stairs were impossible, getting up from a seated position was exceedingly difficult, and my gait was quite precarious, which resulted in many falls from which I couldn't get up without help and included some injuries."*
>
> –**Carol**, 61-year-old woman living with LGMD2A

> *"I constantly lose balance both in private and in public which have hurt me. I can not walk for long periods and feel my legs getting tired very fast. I can't get up from a seated position easily and I can't get up off the floor at all on my own. So, when I fall, I need someone to help me up."*
>
> –21-year-old woman living with LGMD2A

> *"I'd say the most important aspect for 2A would be reducing or pausing the effects on mobility, especially on the hip flexors/legs. Watching my wife fall and having to lift her off the ground, often in front of crowds, is dreadful for her to endure. I also have to help her up from many chairs and toilets, as well as into and out of zero-entry swimming pools when a lift is not available."*
>
> –**Christopher**, spouse of individual living with LGMD2A

Many with LGMD2A also described how they were unable to bend over. Many stated that their mobility was particularly affected by colder temperatures.

Difficulty using hands or arms is the second most impactful symptom of LGMD2A. Most individuals living with LGMD2A experience difficulties with activities involving both upper extremities and lower extremities and core, as was shown in the poll, **Appendix 7, Q2**. They described how their challenge was due to muscle weakness, which became worse as the disease progressed. Many were unable to lift objects or even transfer in and out of a wheelchair. Heartbreakingly, a common theme for many individuals living with LGMD2A is the inability to hug family members, grandchildren and pets.

> *"LGMD2A impacts every activity in my life. For me, the severe muscle weakness that has significantly affected my upper extremities within the past 10 to 15 years has been by far the most difficult to adjust to. Imagine life when you cannot raise your hands off your lap or reach for something beyond six to eight inches away."*
>
> —**Carol**, 61-year-old woman living with LGMD2A

> *"I can no longer walk upstairs, carry a pet or a child, ambulate without a rollator, lift my arms above my head, do a squat, dance, walk on the beach, roll over in bed unassisted, get up independently from a seated position, or give a proper hug."*
>
> —**Jill**, 43-years-old living with LGMD2A

A 61-year-old woman living with LGMD2A described how she was unable to participate in, *"Independent self-care (bathing, dressing, toileting), driving, food prep/eating, and hugging my family members and friends."*

Noni's difficulty in using her arms are becoming her most impactful symptom. *"Initially, it was more mobility, transferring, just walking, getting upstairs, but it has progressed now. It has affected my arms quite a lot. …I can still feed myself but only if I can put my elbows against something. … It is consistent and just getting worse, so eventually, I probably won't be able to feed myself. … Not looking forward to that."*

—**Noni**, 55-year-old woman living with LGMD2A

Social/emotional concerns (isolation, depression, anxiety) is the third most impactful symptom for individuals living with LGMD2A. Some described how living with a progressive disease has mental health implications. Others experience stigma and discrimination, and some try to hide their disability from others.

> *"Living with a progressive muscle wasting disease never gives you the peace of mind, [you are] constantly in fear of what the next step will be. 'What will I lose next? How will I have to adjust and cope, and what will the impact be on my family?'"*
>
> —**Andrew**, 41-year-old man living with LGMD2A

> *"One of the hardest parts is slowly losing your independence and mobility. It is really hard to continually adjust my expectations for my life. It is hard to not feel defeated when I have to keep letting go of activities I used to be able to do. And I'm especially scared of the future because my muscles will only grow weaker without treatment."*
>
> —**Matt**, man living with LGMD2A

Jessica's young daughter, *"Is fully aware of her muscle strength decline due to her LGMD/2A diagnosis and it scares her and causes immense anxiety."*

—**Jessica**, mother of a nine-year-old daughter living with LGMD2A

"I did not experience symptoms until I was 18 years old, so it is easy to remember what being 'normal' was like. My bad days I feel tired, but able. My worst days, I am still able but plagued by sadness and depression. In public, not only do I walk slower and with a gait, but I feel a deep shame and oftentimes feel like everyone is watching me (although, this is becoming easier to cope with)."

—**Peter**, 23-year-old living with LGMD2A

"The continued progression of this disease is like a ghoul always hovering over me. What will be stripped away next? What new pain will crop up and become a constant reminder of the devastation that is happening to my physical self? I am worried that if my caregiver becomes hurt or unable to care for me, I will be in an immediate state of horror. I have moved through this before and it is a nightmare. Caregivers do not fall out of trees, they are expensive and they are usually nowhere near as skilled as someone you have worked with for years."

—49-year-old woman living with LGMD2A

"People in high school asked me why my back looks like a boat, why I walk weird, why I can't run. I even got called a cripple this year."

—**Brooklyn**, 15-year-old female living with LGMD2A.

Fatigue/muscle weakness was the fourth most impactful symptom of LGMD2A, but for many it was one of their main concerns.

"Muscle weakness has impacted every aspect of my life. It's hard to imagine getting any weaker. I am so weak already that the unrelenting disease progression just continues. After 56 years of LGMD2A impacting my life, I am truly running out of ways to adapt."

—**Carol**, 61-year-old woman living with LGMD2A

"The symptom with the most impact on me is the muscle weakness. Due to muscle weakness I have a high risk of falling and need supports to get up from a seated position, which limits my ability to participate in activities professionally and socially."

—**Melissa**, woman living with LGMD2A

Other symptoms with significant impacts for those living with LGMD2A selected in the online polls include (in descending order): **urinary/bowel issues including (incontinence, constipation, UTI and rhabdomyolysis); pain**; **curvature of the spine (lordosis or scoliosis) or scapular winging**; **contractures (permanent muscle tightening)**; **poor sleep**; and **speech and/or swallowing difficulties**. Of all of these symptoms, **pain** was the one that was most frequently mentioned in the quotes. These are illustrated with selected patient quotes below. None of the individuals with LGMD2A selected pulmonary (breathing) issues or cardiac (heart) issues.

Carol suffers from severe lordosis. *"My spine is so arched that I am actually looking behind me when my husband stands me up."* Her sleep is affected by LGMD2A. *"LGMD2A affects my ability to even sleep comfortably. I have no independent bed mobility, so I only sleep in an adjustable frame bed or in my power wheelchair. …I sleep with my hands on my chest, clenching the bed, remote control, and a personal urgent response device."*

—**Carol**, 61-year-old woman living with LGMD2A

"I have heel cord contractures, so when I was walking that obviously made me much less stable and made it much more difficult to walk. But even other muscle contractures affect how well you're able to reach things, hold things and so on."

—**Jordan**, 36-year-old man living with LGMD2A

"On bad days [my daughter] can't get out of bed for two days, she has severe pain, cramping, and chest pain."

—**Jessica**, mother of a nine-year-old daughter living with LGMD2A

Impactful symptoms mentioned in the comments but not captured in the polls: **edema**, **thinning skin** and **pressure sores**.

"I am in a wheelchair 100% of the time and can't walk anymore. Loss of strength in my arms and getting pressure sores because skin is so thin on my behind, it hurts every day. I'm always cold and very stiff. My legs and arms just don't work for me anymore."

—70-year-old woman living with LGMD2A

The majority of individuals living with LGMD2A are dependent on a caregiver or family member for activities of daily living.

Poll respondents were asked to select the top three activities of daily living that they depended on a caregiver for assistance. Each selected an average of 4.2 responses. More than 80% of individuals living with LGMD2A require **assistance with household chores** including **shopping**, **cleaning** and **laundry**. More than half require **assistance with dressing**, **bed mobility**, and **bathing**. Some require full-time care. Poll results are shown in **Appendix 7, Q3**.

"I cannot do grocery shopping for items on tall shelves."

—63-year-old woman living with LGMD2A

"The list of things I can no longer do far outweighs what I am still able to do. Some specifics are — the inability to: use the bathroom independently, dress myself, bathe myself, reposition myself/apply medicine/use devices in order to reduce pain, hold my head up, get in/out of bed, cook/make meals, drive for long distances, independently go where I would like and be able to do what I would like when I got there...the list could go on."

—49-year-old woman living with LGMD2A

> *I always tell Brooklyn that she is closer to her mother than any 15-year-old wants to be. Some of the daily tasks I help her with are showering, lifting her up out of the bathtub, shaving her legs and armpits, drying her off, helping get her bra and shirt over her head, and bending down to get her underwear and bottoms on. I help her with her hair, getting up from the couch and chairs, making her bed, doing laundry, getting on leg braces at night and more.*
>
> —**Melina**, mother of a 15-year-old daughter living with LGMD2A

Other activities identified in the polls as activities that individuals living with LGMD2A are dependent on others for include **meal preparation**, **going to the bathroom**, **transportation**, and **eating**.

> *The most frustrating thing which affects my daily life and being able to enjoy life better, is not being able to toilet myself. Affects my social life and my health and is so hard to deal with because it is an activity that is necessary multiple times a day.*
>
> —42-year-old woman living with LGMD2A

> *I require my husband to cut my food and set it within reach at the table. I need a straw for all liquids. I can still feed myself at a taller bar height table because there really isn't much distance for the food to travel from the plate to my mouth. At a normal height table, I need someone to feed me, which is humiliating.*
>
> —**Carol**, 61-year-old woman living with LGMD2A

All everyday activities are impacted by LGMD2A, with going out, socializing, and traveling as the most challenging.

Poll respondents were asked to select the top three everyday activities that they could not do at all or as fully as they would like because of LGMD. **Going out**, **socializing** and **traveling** was at the top of the list, closely followed by **walking**. Poll results are shown in **Appendix 7, Q4**.

Going out, **socializing** and **traveling** and **walking**. Individuals with LGMD2A described what this was like for them and demonstrated just how much advance planning is required for them and their caregivers.

> Peter always uses Google before he goes anywhere. *Anybody living with this disease will tell you the same thing: that you think about it all the time. So whenever I'm going into any setting, even if it's walking to my kitchen or if it's going to the grocery store, I'm thinking beforehand about everything I might encounter, everything that might be there.*
>
> —**Peter**, 24-year-old man living with LGMD2A

> *From a social standpoint, I've really seen Brooklyn be affected by not being able to do things with new friends. Before going anywhere, I have to make sure that people understand her limitations and how to help her if something happens. …Before going anywhere, we Google what does it look like. Are there going to be stairs there in the house? Are there stairs in the building? Is it a two storey? … Is there a lot of walking? We evaluate all social situations to see if it's somewhere Brooklyn can go without the assistance of parents. Mentally, this affects her confidence and sometimes, deters her from going altogether.*
>
> —**Melina**, mother of a 15-year-old daughter living with LGMD2A

> *I do not attend activities at other people's homes because of the risk of falling or possibility of stairs, which I cannot physically do. I avoid traveling with friends; I need assistance to navigate an airport due to the size, airport security is especially time consuming because I have to explain that I cannot get up to walk through. Airplane seating is very tight, which is uncomfortable and I have a lot of difficulty getting up from an airplane seat.*
>
> –**Melissa**, woman living with LGMD2A

> *Impacts often overlooked include increased difficulty getting to doctor appointments, dental care. … I am limited to traveling because of toileting.*
>
> –**Karen**, 62-year-old woman living with LGMD2A

> *Just getting ready for an event takes so long and tires me out so much, I might not be able to enjoy myself when I get to the event. I have greatly limited my outings and doings – especially as I age with this disease.*
>
> –49-year-old woman living with LGMD2A

Exercising and **participating in sports** was the third most selected activity that is impacted by LGMD2A.

> *I would love to dance, but I can't because it requires too much movement which I can't do easily. Exercising as well. Also traveling because a lot of places have stairs, especially in different countries.*
>
> –21-year-old woman living with LGMD2A

> *Over time I have weakened. …We do everything together, my husband helps me wash myself, to go to the bathroom. He gets me out of bed and chair. Helps me cook. We can't dance. Or take a bath alone in the sea. … My husband quit his job and became my assistant.*
>
> –**Rosaria**, woman living with LGMD2A

When asked what specific activities that were important to him that he could not do, one 45-year-old man said, *Bending, gripping things, sitting during a meeting, typing for long, walking stability without falling down. Not to mention the lack of ability to play any sport with my child.*

> –45-year-old man living with LGMD2A

> *I used to do roller skating at a professional level participating in competitions … I would love to walk by the seaside and feel the warm sand under my feet.*
>
> –39-year-old woman living with LGMD2A

> *Before I was a sporty person, playing badminton, dancing, driving doing a job in a restaurant. I am totally dependent on walker now, day by day it's getting worse.*
>
> –**Valley**, 42-year-old living with LGMD2A

Other LGMD2A impacts mentioned in the polls in descending order: **personal hygiene (bathing, toileting, dressing)**, **being intimate with a spouse or partner**, **driving a motor vehicle**, **performing household chores**, **attending school** or **working**, **meal preparation** and **childcare**. For individuals with LGMD2A especially, the use of public restrooms is an issue that interferes with work and travel.

> *Toileting independently in public restrooms, traveling/taking family trips with ease, driving.*
>
> –58-year-old woman living with LGMD2A

> *Extensive muscle weakness and my severe lordosis even impact intimacy. I miss being able to hug or even snuggle my husband.*
>
> –**Carol**, 61-year-old woman living with LGMD2A

> *I was able to drive before. Recently, I cannot drive anymore. … So fortunately, my company has been able to allow me to continue working online. I don't know how much time that's going to happen, but the arm part right now is what's affecting me more. So I can replace my legs a little bit more with a scooter but not the arms.*
>
> –**Noni**, 55-year-old woman living with LGMD2A

A 26-year-old woman is unable to participate in, *Traveling, cooking, gardening, cleaning my home, washing my hair, going up stairs, swimming, yoga, going for walks in my neighborhood, hugging my loved ones.*

–26-year-old woman living with LGMD2A

> *I had to leave work because I couldn't use the toilet at the office.*
>
> –**Karen**, 62-year-old woman living with LGMD2A

> *Due to LGMD, I can no longer work as a nurse especially due to arm weakness. This is saddening and difficult emotionally and financially. I also feel like I cannot travel freely due to limitations on airlines, limited mobility once I get to a travel destination.*
>
> –**Angela**, woman living with LGMD2A

> *I went to and graduated culinary school and worked in restaurants until I couldn't anymore. I miss the calamity of a professional kitchen so much, but I am unable to do that work–what I love–anymore. However, I did move into food journalism and reporting, which is also a line of work I love. It combines my love for food and cooking with my talent of storytelling. I am thankful in a way that my disability led me here.*
>
> –**Peter**, 24-year-old living man living with LGMD2A

Becoming a burden is the top worry for those living with LGMD2A.

Becoming a burden was a top worry and was followed by the closely-related worries of **losing mobility/ ability to walk**, **losing independence** and **losing the abilities to use arms and legs**. Poll results are shown in **Appendix 7, Q4**.

Becoming a burden (physically, financially, emotionally). Many expressed their worries for what would happen to them if they lost their spouses or family members who cared for them.

> *I worry about the disease's impact on my husband and becoming a burden. I worry about how much longer my husband can care for me as he ages. I worry about my quality of life and what will happen to me if something should happen to him. ... I fear that if something should happen to my husband during the night, I wouldn't be able to call for help.*
>
> –**Carol**, 61-year-old woman living with LGMD2A

> *My worry for what will happen after my husband is no longer able to care for me is constantly on my mind. At times it is all consuming and affects my quality of life.*
>
> –60-year-old woman living with LGMD2A

> *I worry, …I would lose my family who help me with everything and who I depend on, and would simply not be able to live because I can't do almost anything by myself.*
>
> –26-year-old woman living with LGMD2A

> *It affects the life of my caregiver (my husband) enormously, as because of me he has to be by my side always. I am completely dependent upon him for bathing, toilet and other basic needs.*
>
> –**Akriti**, 29-year-old individual living with LGMD2A

Closely related to becoming a burden, the worries of **losing mobility/ability to walk**, **losing independence** and **losing the abilities to use arms and hands** were selected next.

> *I need input from carers and have no ability to stand, or walk independently. Thinking back to when I was 19 years old, this is the worst of my fears.*
>
> –**Andrew**, 41-year-old man living with LGMD2A

> *Will I get a typical college experience? Will I be able to be independent? Will I be able to drive? Will this disease take my ability to walk? Will the cure or treatment be here in time for me? I hope and pray that all these questions will be answered as a yes for me and everyone affected by this disease. I hope for a new treatment now. Sometimes, later it becomes never and we don't have time on our side.*
>
> –**Brooklyn**, 15-year-old female living with LGMD2A

One woman worried about not having a normal life, a life like other people her age. *Not being independent. Not having all the wonderful experiences that young people have. Traveling, dancing, doing sports, meeting new people, walking long distances.*

–Submitted by a parent of a 19-year-old daughter living with LGMD2A

> *My daughter was diagnosed at age 7 and is now 16. We no longer can watch her run, walk, or stand up on her own. She needs our help transferring from her wheelchair to her bed. I am most concerned about loss of strength in her arms as it will impact her independence even further.*
>
> –**Emily**, mother of a 16-year-old daughter living with LGMD2A

Additional worries selected in the polls by individuals living with LGMD2A (in descending order): **developing or worsening pulmonary and respiratory issues**; **being placed in a nursing home or other care facility**; **losing social connections**; **developing or worsening cardiac and heart issues**; **dying prematurely**; **coping with pain**.

A 61-year-old woman described her biggest worry. *Aging with LGMD and being placed in a facility for long term care if/when my husband can no longer care for my physical needs.*

–61-year-old woman living with LGMD2A

Worries not represented in the polls include worries about **falling**, **worries about passing LGMD to their offspring**, and worries about not being able to have children.

> *If I fall, it's going to be really terrible. And I'm so tall (6'7") that it's a long fall. … What I'm worried about is just this instability in the last even couple weeks. I'm starting to feel more unstable even if I'm not going to fall. I feel like I'm going to fall because of those little muscles around all the areas, hip, stuff doing that.*
>
> –**Eric**, 33-year-old man living with LGMD2A

> *I worry that there will never be a cure. That one day, I will fall really badly and hurt myself to where I break/fracture something badly and it will make things worse. Also, if one day I decide to have children, I'm afraid that the gene for LGMD will be transferred to them.*
>
> –21-year-old woman living with LGMD2A

Session 2i:
Living with LGMD2i — Symptoms, health effects and impacts on daily life

Individuals with LGMD2i and their caregivers used online polling to answer questions related to their symptoms, health effects and impacts on daily life. The outcomes of the poll results are summarized below and illustrated with patient comments. The full poll results are included in **Appendix 8**.

Impaired mobility has a significant impact on individuals living with LGMD2i, followed by fatigue, social/emotional concerns, and difficulty using hands and arms.

Poll results are shown in **Appendix 8, Q1**.

Impaired mobility (trouble walking, standing, transferring) includes challenges with stairs, and standing from a sitting position. Similar to other LGMD subtypes, impaired mobility and challenges keeping up with their peers was often one of the first LGMD2i symptoms.

> *"My son, Joshua, is 34 years old. He was diagnosed at age 12. He has been non-ambulatory for the last 5 years. He has been a heart failure patient, due to cardiomyopathy since age 20, due LGMD2i. His lung function is limited as well, due to LGMD2i."*
>
> –**Cindy**, mother of 34-year-old son living with LGMD2i

> *"Even mundane things such as walking stairs, rising from chairs, or running to be on time, are hard."*
>
> –32-year-old man living with LGMD2i

> *"The symptom that most drastically affects my life, all day everyday, is the struggle to get up from a seated position. I am unable to get up from many chairs, including many toilets. This severely limits my ability to go out and about as I never know if I will be able to go to the bathroom. I can't sit down at many of my friends' homes because I won't be able to get up from their furniture if it is too low. It is also extremely difficult to travel by plane because I really struggle to get up from the seat."*
>
> –**Kristen**, woman living with LGMD2i

A 63-year-old woman living with LGMD2i described her mobility concerns, *"Going up stairs, walking up an incline, standing up from the toilet, chair or car seat."*

–63-year-old woman living with LGMD2i

Many individuals with LGMD2i experience falls, which often results in them requiring higher levels of care.

> *"I am trying to keep as active as possibly without injury. I have fractured my pelvis twice, nose, shoulder, ankle, and most recently my sacrum. After the sacrum fracture I was not able to regain the ability I have to walk safely inside my home, or shower independently. As hard as these things are I see a future of continued loss where this reality feels like the good old days. I am constantly worrying about making sure I am pushing myself to maintain function but not getting injured."*
>
> –**Julie**, woman living with LGMD2i

> *A related symptom that makes life really hard is the frequent falls and inability to get up from the ground. I live in constant fear of a fall when I am outside my home. The instability and poor balance that result from the weakened muscles, means that if I stumble just a little, I cannot catch myself and I will fall.*
>
> —**Kristen**, woman living with LGMD2i

Jane experienced two major life-changing accidents, a fall from her horse which resulted in a broken pelvis and broken back, and a fall in her bathroom which resulted in a broken arm.

> *It's been nine months and I am still in pain daily and am not expected to make a full recovery for at least a year. Before I broke my arm, I could transfer off my raised toilet seat independently, but that small act of independence has been taken away. I'm working daily to regain not only the strength but the range of motion I need to accomplish this necessary task.*
>
> —**Jane**, 26-year-old woman living with LGMD2i

Fatigue/muscle weakness is the second most troublesome symptom for those living with LGMD2i.

> *Fatigue seems to rule my life and is very unpredictable. I can not predict how i will feel from day to day or even hour to hour. Emotionally this brings feelings of complete failure and worthlessness. I cannot commit to anyone to do even small tasks because I just don't know how I will feel to do anything at any given moment.*
>
> —**Beth**, woman living with LGMD2i

> *On my worse days my fatigue is my biggest complaint. I struggle with 'the more I do, the more tired I feel' the overwhelming fatigue I feel makes it hard to commit to something.*
>
> —**Michele**, woman living with LGDM2i

> *They struggle with energy levels and have to regulate their days, or they won't be able to complete everything they would like to.*
>
> —**Julia** and **Marcus**, parents of three daughters with LGMD2i

Social/emotional concerns (isolation, depression, anxiety) is the third most selected impacted LGMD2i symptom. Some described grief, having to overcome stigma and trying to pass as "able-bodied."

> *The grief cycle of LGMD is cruel. Each loss is heavy. We constantly make adjustments only to wonder how long this adjustment will last before the next one comes.*
>
> —**Julie**, woman living with LGMD2i

> *My condition has progressed to the point that I am always at risk of falling and being unable to get up on my own, which causes me tremendous fear and anxiety. I have had some very bad falls that required complete strangers to assist me, which was extremely embarrassing.*
>
> —**Dan**, 57-year-old man living with LGMD2i

> *Some of the daily struggles that I deal with, … is the grief and loss that people go through as they lose each one of these parts of their being. Just like most people, I started with the loss of being able to go upstairs. And then it progressed to constant falling, embarrassment and simultaneously trying to pass as being able-bodied throughout society and trying to keep a job.*
>
> —**Cindy**, 55-year-old woman living with LGMD2i

> *Mentally, it is constantly a struggle as my body keeps going through new levels of decline, and I have to go through constant mental shifts as I decline to a new normal. Sometimes I really struggle because I don't see anything in the near future that will help, and I'm getting older and declining constantly.*
>
> —**Pam**, 52-year-old woman living with LGMD2i

> *The disease robs our abilities and we never know when we are going to lose something else. I live in a hyperawareness that contributes to my fatigue. I can no longer care for myself, lift my arms, hug my children when they need comforting, it's affected my marriage both emotionally and physically. My children live in fear not knowing if I'm going to be here to attend their graduations, their weddings, meet my grandchildren, they don't know when they won't have a mom anymore.*
>
> —**Lacy**, 49-year-old living with LGMD2i

Difficulty using hands or arms was the fourth most impactful symptom for those living with LGMD2i. The results of the second poll question indicated that 20% experience difficulties with activities involving lower extremities and core and 80% of individuals experience difficulties with both upper extremities and lower extremities and core, shown **Appendix 8, Q2**.

> *Though, I do have minimal weakness in my arms, it hasn't yet affected my ability to use a utensil, type on a computer, bathe myself, or take care of hygiene matters.*
>
> —**Kathryn**, 49-year-old woman living with LGMD2i

> *Combing, washing and styling hair can cause arm and shoulder pain. Our middle daughter has very long hair.*
>
> —**Julia** and **Marcus**, parents of three daughters with LGMD2i

A woman living with LGMD2i described her most troubling symptoms. *Loss of the ability to breathe independently, loss of mobility due to the loss of strength, loss of upper arm function.*

—35-year-old woman living with LGMD2i

> *Over the last few years we could no longer reach to the sky. We can feed ourselves and brush our own hair by leaning on the kitchen table. But eventually, even this became too difficult.*
>
> —**Cyanne**, 31-year-old twin living with LGMD2i

Other symptoms with significant impacts but selected by fewer living with LGMD2i include (in descending order): **poor sleep**; **urinary/bowel issues including (incontinence, constipation, UTI and rhabdomyolysis)**; **pulmonary (breathing) issues**; **pain**; **cardiac (heart) issues**; **curvature of the spine (lordosis or scoliosis)** or **scapular winging**; **contractures (permanent muscle tightening)**; **speech and/or swallowing difficulties** and other. These are illustrated with selected patient quotes below.

> *As an individual living with limb-girdle, I have the potential to deal with breathing difficulties and cardiomyopathy as the disease progresses. In some cases, death is a result. I deal with breathing-related issues already, which is a cause of great concern.*
>
> —**Kathryn**, 49-year-old woman living with LGMD2i

> *I have pulmonary and heart failure. I use a Bipap at night and a sip and puff during the day. I take medications trying to stabilize my heart.*
>
> —**Lacy**, 49-year-old living with LGMD2i

> *He has been a heart failure patient, due to cardiomyopathy since age 20, due LGMD2i. His lung function is limited as well, due to LGMD2i. While it is so very sad, devastating and heartbreaking to lose skeletal muscle, one can still exist. Heart failure and limited lung function is a whole set of very scary and dire complications, with little to no recourse from the medical standpoint other than some blood pressure drugs to allow the heart muscle to not have to work so hard, thereby hopefully slowing down progression of muscle cells being turned into non-functioning scar tissue/fatty cells.*
>
> —**Cindy**, mother of a 34-year-old son living with LGMD2i

> *I've learned to live with always being sore or some part of my body hurting.*
>
> —**Pam**, 52-year-old woman living with LGMD2i

> *Over the past two years, Sammy has had to have two surgeries due to contractures that have developed over the years. She was unable to have her feet flat on the ground resulting in toe walking, which caused more tripping and stumbling.*
>
> —**Kelly**, caregiver for 14-year-old daughter living with LGMD2i

Most individuals living with LGMD2i are dependent on caregivers or family members for activities of daily living.

When asked to select all daily living activities upon which they were dependent on a caregiver, individuals with LGMD2i selected an average of 3.5 response options. Over 70 percent of individuals living with LGMD2i require assistance with **household chores**, and almost two-thirds require assistance with **bed mobility (getting in/out of bed, rolling over)**. Not one of the poll respondents indicated that they are fully independent, and many commented on how important their caregivers are for them. Poll results are shown in **Appendix 8, Q3**.

> *Not being able to get out of bed, not being able to get in and out of the shower, not being able to get myself dressed, not being able to make my breakfast. Afraid of losing my independence.*
>
> —Parent/guardian/caregiver of a 27-year-old man living with LGMD2i (diagnosed at 19 years)

> *The three symptoms of LGMD that affect me the most are inability to walk/climb stairs, rising from a seated position, and getting in/out of and turning in bed.*
>
> —**Karen**, 60-year-old woman living with LGMD2i

> *A lot of people don't realise how much I depend on my support workers or how much they help me live a fulfilling life. … It is hard living with this condition, having an intellectual mind, but having your body fail you. It makes you feel sad, annoyed, frustrated and even lonely at times.*
>
> —**Cyanne**, 31-year-old twin living with LGMD2i

> *Another thing my caregiver/husband does for me every day is provide emotional support and encouragement.*
>
> —60-year-old woman living with LGMD2i

Individuals with LGMD2i also require assistance with **going to the bathroom**, **transportation**, **meal preparation**, **dressing**, **bathing**, and **eating**. Some of their challenges are described below, including the emotional toll of relying on others.

> *I require assistance with dressing, meal prep, driving and all transfers. Thankfully, I have a great support system, but it doesn't eliminate the emotional toll it takes to have to rely on someone for something most people take for granted, such as standing up or bending down to pick something up off the floor.*
>
> —**Jane**, 26-year-old woman living with LGMD2i

> *Through primary school, my sister and I used a hoist to be able to use the toilet. As we had support workers, they have a no lift policy, meaning they had to use a hoist. This meant instead of taking five minutes to go to the toilet, it took half hour. That is a lot for a kid in primary school. Who had to go twice a day. It meant I missed out on a lot of school and friends/social time, even through high school.*
>
> —**Cyanne**, 31-year-old twin living with LGMD2i

> *One of the biggest issues is the loss of independence and having to rely on others for simple everyday tasks-especially bathroom needs.*
>
> —**Pam**, 52-year-old woman living with LGMD2i

Going out, socializing, traveling and walking are the everyday activities most severely impacted by LGMD2i.

Poll respondents were asked to select the top three everyday activities that they could not do at all or as fully as they would like because of LGMD. **Going out**, **socializing** and **traveling** were at the top of the list, closely followed by **walking**. Poll results are shown in **Appendix 8, Q4**. Individuals living with LGMD2i often described how stairs are a real problem.

> *Unfortunately, many of my friends' homes are no longer accessible to me due to stairs or other impediments, so more and more, I find myself having to decline invitations to social gatherings. I also find restaurants to be a source of great stress, as I am no longer able to politely and gracefully feed myself and am very self-conscious about it. It's not uncommon for me to drop a fork or spill a drink or otherwise cause some kind of embarrassing commotion while dining in public.*
>
> —**Dan**, 57-year-old man living with LGMD2i

Dan added, *"I no longer travel by air. ...Some of my worst falls have been in airports, where the chaos of travel once resulted in me getting knocked down face first onto the moving sidewalk, leaving my face with the scars to show for it."*

—**Dan**, 57-year-old man living with LGMD2i

Joshua described the biggest impacts of his disease. *"Transportation, getting around, socializing with people from those limitations. … Being chair-bound, you have to have specialized vans to get around. When those break down, it's not like a buddy can just roll up and give you a ride because you've got a [heavy] chair that you also have to transport."*

—**Joshua**, 34-year-old man living with LGMD2i

"I can't walk on the beach, I can't get out of the chair at the movie theater, can't access lake or ocean water because I lose my balance/footing on uneven material. I can't enjoy the snow because I'm afraid of falling on the ice."

—Submitted by a parent/guardian/caregiver of a 27-year-old man living with LGMD2i

"It's becoming harder to visit family and my kids because they live in places where all homes have stairs to enter."

—**Pam**, 52-year-old woman living with LGMD2i

Other everyday activities impacted by LGMD2i that were selected in the polls (in descending order): **exercising** or **participating in sports**, **personal hygiene (bathing, toileting, dressing)**, **being intimate with a spouse or partner**, **attending school or working**, **performing household chores**, **driving a motor vehicle**, **meal preparation** and **childcare**. A theme mentioned often was how LGMD2i impacts time spent with family.

"I used to be involved (at least present) in most family activities: helping coach a little-league team, attending outdoor activities, playing catch, exploring a new place while traveling, throwing the frisbee or other backyard games. Now I can't walk in grass, sand nor on any inclined slope. My necessity to prevent falls now overrides my ability to be with [my family] in many activities, or requires we change plans or not participate in some activities. Now I must plan every step and action before we get to a new place. Google maps has become my friend to help me pre-navigate new scenarios. On good days we successfully navigate a new experience in a new place together. My bad days include me often being alone by choice or necessity while those I want to be with are doing something fun together, I'm no longer able to join in."

—**John**, 45-year-old man living with LGMD2i

"Towards the end of seventh or eighth grade, I couldn't do stairs at all anymore. And in the school I went to, every single class I had was upstairs, so they had to completely rearrange how everything worked just for me. And even then, it was still a little funky as to how everything worked, but things like that had to be done, I guess."

—**Jared**, man living with LGMD2i

> *It wasn't long after being diagnosed that my career and life path took a very different turn. I was running an architectural millwork firm and putting in very long hours and the physical challenges of the job began to be too much. My life seemed to be a constant cycle of work and sleep. Eventually, when I was no longer able to keep up with the demands of my job and for the first time in my life, I got fired. This hit me quite hard and I began to realize the severe impact that my health was having on my life and my emotional wellbeing.*
>
> –**Dan**, 57-year-old man living with LGMD2i

> *I know that my little girl would love for me to be able to get on the floor and play with her, go outside, run, jump and play with her but I can't.*
>
> –**Dianna**, woman living with LGMD2i

> *I feel at a loss and sad a lot because of all the things I can't help my kids do, or won't be able to do with them like even be the volunteer mom at a class field trip because the school bus stairs are too big and I can't get on them, I never know what to expect and if in the middle of something I will end up letting people down because I'm not able to do things. I have to give a lot of trust to people I do not know in so many ways. The sadness and stress, worry and toll it takes is high and knowing we just have to deal makes it seem like we can never get ahead.*
>
> –**Stephanie**, woman living with LGMD2i and parent of a child living with LGMD2i

Other LGMD2i impacts that were described include **financial impacts** and **having to give up dreams of having children**.

Dan described how the cost of tests were expensive, in addition to everything else. *These tests were not covered under my health insurance and were quite expensive and only added to the financial difficulties I was experiencing. Eventually, I had to sell my home and apply for social security disability insurance.*

–**Dan**, 57-year-old man living with LGMD2i

> *I feel like this disease is such a huge burden for my family. We have had to give up so many dreams, including having children. Having a potential treatment on the horizon gives me and my family hope for the future.*
>
> –**Kathryn**, 49-year-old woman living with LGMD2i

Losing their independence is the biggest worry for individuals living with LGMD2i.

Other top worries, each selected by half of individuals living with LGMD2i include becoming a **burden (physically, financially, emotionally)**, **losing mobility/ability to walk**, and **developing or worsening pulmonary and respiratory issues**. Next top worries are **being placed in a nursing home or other care facility**, **losing social connections**, **losing abilities to use arms and hands**, and **dying prematurely**. Poll results are in **Appendix 8, Q 5**.

> *Living with LGMD is all consuming. One of the many concerns is the high costs of home adaptations, DME, accessible vehicles, copays are huge, ongoing obstacles that cause stress. It also is very stressful thinking about and planning for future needs. Having a treatment that would stop progression of this disease, would alleviate some of that anxiety.*
>
> –**Karen**, 60-year-old woman living with LGMD2i

> *I lost the ability to arise from the floor in 2016 and the thought of losing my ability to walk terrifies me.*
>
> –**Dan**, 57-year-old man living with LGMD2i

> *Worries: being on ventilation 24/7, another femur break, heart failure, early death, loss of independence, need to go into a facility for care at a young age.*
>
> –54-year-old woman living with LGMD2i

> *I'm constantly wondering, what condition will I be at next year, and how much more isolating will it be.*
>
> –**Pam**, 52-year-old woman living with LGMD2i

> *[I worry about] future degenerative losses or losses of what little I can still do independently.*
>
> –37-year-old woman living with LGMD2i

Additional worries include fears that they will lose a caregiver, that their children will also be afflicted with LGMD, and that they will be too old when a treatment is available.

> *My husband is my caregiver. He is 15 years older than I am and it is a constant fear that something will happen to him.*
>
> –**Lacy**, 49-year-old woman living with LGMD2i

> *I am concerned that my children may also suffer from a 'late onset diagnosis' when they are older.*
>
> –**Lindsay**, 65-year-old man living with LGMD2i

> *[I worry] that I will be too old when the treatment is available.*
>
> –64-year-old man living with LGMD2i

A 35-year-old woman living with LGMD2i worries, *That I might die soon because of my respiratory and cardiac involvement!.*

Session 3:
Current Approaches to Managing LGMD

Individuals with LGMD subtypes 2C, 2D, 2E, 2F, 2A and 2i and their caregivers came together for session 3. They used online polling to answer questions related to their current approaches to managing LGMD. Full poll results are included in **Appendix 9** and described below with patient comments.

There are no FDA-approved therapies to address LGMD subtypes 2C, 2D, 2E 2F, 2A or 2i.

This massive unmet treatment need was emphasized throughout the meeting.

> *"When I was diagnosed, the only recommendation was palliative care, management of symptoms and assistance with durable medical equipment. … Currently, there are no approved treatments that significantly slow, or stop any form of LGMD. It feels like, I'm in a desperate situation, because this is an urgent, unmet need."*
>
> –**Kathryn**, 49-year-old woman living with LGMD2i

> *"It occurs to me that most of the 'treatments' being talked about are not really treatments but symptom control or "dealing with" the weakness. A real treatment would at the very least, stop the progression. Current treatments at best, slow progression."*
>
> –**Martha**, woman living with LGMD2A

> Beatrice's son, *"does motor physiotherapy twice a week. He does respiratory physiotherapy twice a day with a cough machine, as well as occupational therapy and equine therapy."* Beatrice says, *"these treatments only help slow down the worsening. He's also taking steroids, but that causes eating difficulties and problems with his bones."*
>
> –**Beatrice**, mother of a son living with LGMD2E

> *"The progressive nature of it leaves me feeling terrified about what my future holds, as I live alone and must face these challenges on my own. Any treatment or drug therapy that would even slow the progression of my condition would be considered a very major victory in my book."*
>
> –**Dan**, 57-year-old man living with LGMD2i

To help manage their symptoms, individuals living with LGMD primarily take **dietary and herbal supplements** and **over-the-counter medications (acetaminophen, ibuprofen)**. Although OTC pain medications are efficacious, there is not yet published scientific evidence to demonstrate that dietary and herbal supplements have a therapeutic value for LGMD. However, with no other treatment options, this is one of the only avenues that individuals living with LGMD have to help their symptoms. Poll respondents selected an average of 1.9 responses each. Poll results are shown in **Appendix 9, Q1**.

> *"On my own I have taken supplements. I cannot say any have worked."*
>
> –42-year-old woman living with LGMD2C

> *We supplement with vitamin D, iron, creatine. Just anything that could potentially help him in any way, we're really trying. It's discouraging when you see the disease continue to take hold, but he's a strong little guy, he's doing a good job.*
>
> —**Faran**, mother of a nine-year-old son living with LGMD2D

> *Vitamin D, multivitamins, good diet, stretching, activity-based exercise like swimming, positive focus on abilities.*
>
> —Parent/guardian/caregiver of an 11-year-old daughter living with LGMD2E

> *Aleve as needed for pain.*
>
> —60-year-old woman living with LGMD2A

> *I take D-ribose and I think that it helps a little bit.*
>
> —63-year-old woman living with LGMD2i

> *The only daily management I use is assistive devices and OTC pain killers as needed.*
>
> —37-year-old woman living with LGMD2i

The third most frequently selected response option was **not currently using any medication**. These include those who received a late diagnosis, or who are still early in their disease pathway.

> Paul wasn't diagnosed until his late 30s and received no therapy. *All these symptoms were attributed to difficulties during my birth and I received no therapies, or medical care, aside from the Achilles tendon surgery [in my teens], until I was in my early 30s.*
>
> —**Paul**, 65-year-old man living with LGMD2C

> *I have never received treatments. I have always been told there was nothing to do. Only have had the routine examinations to observe progression.*
>
> —42-year-old woman living with LGMD2C

> *[Our son] can do normal activity at school and does not need physical, or occupational therapy at this time. However, as years pass and the longer it takes for treatment options to become available, I could see how we may treat his symptoms differently.*
>
> —**Rachel**, mother of a five-year-old son living with LGMD2D

> *I didn't have any experience [with treatment] other than keeping my spirits high and being active.*
>
> —50-year-old man living with LGMD2D

Other medications selected in the polls include (in descending order): **medications for anxiety and depression**, **prescription pain medications**, **recreational marijuana**, **cannabidiol (CBD) products**, **investigational drugs (expanded access and clinical trials)** and **steroids**.

Paul requires pain medications when he is moved. *"It's quite painful to be placed in the Hoyer and to sit in my wheelchair. I take all pain medications on these occasions."*

—**Paul**, 65-year-old man living with LGMD2C

"I feel the real effect only from pain pills."

—46-year-old woman living with LGMD2A

"I have used PT primarily for pain management and see a pain specialist. I have had injections in my hips and nerve ablation to my lumbar area which has been life changing."

—**Angela**, woman living with LGMD2A

"I take baclofen for severe muscle spasms in my back. I often use a heating pad or ThermaCare patches for my back. I have a TENS unit for my back. I use OTC drugs for bursitis in my shoulders and hips. I have had cortisone shots as well."

—49-year-old woman living with LGMD2A

"When I was 14, I began taking corticosteroids. My doctor thought this would help me maintain my muscle tone. Let me be very clear. Being on steroids is not a cure, nor is it a viable treatment for this disease. However, my parents weighed the risks versus the benefits of being on steroids and at the time, saw it as our only option."

—**Jane**, 26-year-old woman living with LGMD2i

"I use TENS, ice, heat, Tylenol, and CBD to ward off debilitating chronic thoracic back pain."

—**Karen**, 60-year-old woman living with LGMD2i

Many individuals living with LGMD have participated in **clinical trials** or have tried **investigational drugs**. They described how much time, energy and sometimes travel are required to participate. Sometimes trials are halted early, and with all investigational medications, the outcomes can be uncertain.

"In 1999, I became the first person in the world to do gene therapy with Dr. Jerry Mendell for any form of muscular dystrophy. … In my trial, we jumped from the mouse model to the human. I would consider participating in either a drug trial or another gene therapy trial to stop my disease. … I've already risked my life by doing gene therapy using AAV [adeno-associated viral vectors], and would consider doing non-viral gene therapy."

—**Donavon**, 59-year-old man living with LGMD2D

"Would I participate in a trial? Talk to me about risk benefit. My body is already so broken, it would need to have serious upside, with almost no downside."

—**Patrick**, 49-year-old man living with LGMD2E

> *In 2006, I was very fortunate to be involved in a large multi-site trial for a drug called MYO-029. I was on the cusp of losing the ability to walk. At the time, it felt like the scientific community was coming to my rescue at the perfect time. Sadly, the trial was halted midway through phase two, due to a safety concern. Since then, no other trials have been relevant for my condition.*
>
> —**Andrew**, 41-year-old man living with LGMD2A

> *In 2015, I was among 20 patients enrolled in the very first clinical trial for LGMD2i/R9, which involved the myostatin inhibiting drug domagrozumab. The trial lasted 36 months and required me to travel from Denver to Baltimore 29 times during that period. Naturally, I became very emotionally invested in the prospect of finding something to help my condition, so when the trial was discontinued, I was once again, devastated.*
>
> —**Dan**, 57-year-old man living with LGMD2i

> *As wonderful as it is to be included in a trial, … Sammy has had to miss many days of school over the past two years in order to make the long trip to the clinic, which is a four-hour drive from home. The days in the clinic are long and exhausting, not to mention the multiple blood draws and the pain of several muscle biopsies. We know that this is what it takes to move science forward, so Sammy takes it on like a champ, but that's not to say it isn't overwhelming at times.*
>
> —**Kelly**, mother of a 14-year-old daughter living with LGMD2i

> *Having a treatment like gene therapy, would ideally address the symptoms I mentioned, that [my son] currently experiences and the symptoms he fortunately hasn't had to experience yet. It would help significantly slow down the progression of this disease to maintain, or help build current muscle strength, by giving his entire body the Alpha-sarcoglycan protein that's missing. We want to prevent him from having trouble walking, becoming non-ambulatory, or even worse, having this disease progress to severe cardiac, or pulmonary issues. An effective treatment would help prevent some of the worst LGMD symptoms from my son. And it will allow for him to run as long as his little legs wanted, without having to worry about them hurting, that he'd trip and fall, or that he needs to drink an excessive amount of water, because he's being too active.*
>
> —**Rachel**, mother of a five-year-old son living with LGMD2D

Other medications not included in the polls but described in the comments include **cardiac medications**, **blood pressure medications**, **sleep medications**, **diuretics** and **other edema supports**.

> *I'm also taking various heart medications and blood pressure medicines.*
>
> —**Paul**, 65-year-old man living with LGMD2C

> *I've dilated cardiomyopathy, has gotten worse, especially in the last three years. I went from no medication to three daily medications to try to treat that. And that seems to be the biggest change for me." These medications are beneficial for Jared. "I can get through the day without being as tired or I can sleep definitely more soundly during the night. It definitely increased energy quite a bit.*
>
> —**Jared**, man living with LGMD2i

> *There is no medicine or treatment, but I take meds for heart issues. I try and keep my stress low, stay as active as possible, without further damaging my muscle, eat healthy, attempt to keep my weight down.*
>
> —54-year-old woman living with LGMD2i

> *I take medications at night that help me relax and sleep.*
>
> —**Angela**, woman living with LGMD2A

> *I deal with lower extremity edema. I've been wearing custom compression stockings for years, take daily diuretics, and use sequential compression pumps.*
>
> —**Carol**, 61-year-old woman living with LGMD2A

Beyond medications and supplements, the top approaches to manage LGMD symptoms are mobility aids, modified home environments, and physiotherapy/exercise

Individuals living with LGMD used online polling to select the many non-medical approaches that they used to manage their symptoms. Each respondent selected an average of 3.8 approaches to help manage their symptoms. The results are shown in **Appendix 9, Q2** and summarized below.

Mobility aids (canes, walkers, scooters and wheelchairs) were the top approach, selected by 70% of individuals living with LGMD, both inside and outside their homes. Many living with LGMD first use canes, then transition to walkers, to regular wheelchairs and finally to motorized wheelchairs as their disease progress. Some require sit-to-stand devices and power wheelchairs to help them stand. Some also use mopeds, scooters, and all-terrain wheelchairs to get around and to protect them from falling. One individual tried using exoskeleton suits for walking.

> *I progressed to using a cane, then a scooter, and then starting about four years ago now, I started using a wheelchair.*
>
> —**Cindy**, 55-year-old woman living with LGMD2i

> *Clearly mobility devices are, I think for many people, the difference between being homebound completely or being able to be out in the world, whether that be school or a job. Outside of [mobility aids], I would say most of the treatments or therapies are extremely mild in the sense of whether they're potentially effective and just general.*
>
> —**Jordan**, 36-year-old man living with LGMD2A

> *I used a walker for three months, but ultimately found that, to go any distance, I had to use a wheelchair to get around outside the house. … In 2007, I began using motorized scooters that eventually progressed to a power wheelchair.*
>
> —**Paul**, 65-year-old man living with LGMD2C

"[Mobility] is what he's most affected by and we've seen that change over the years as things have progressed." Recently Michele's son has started to use a power chair, *"which gives him more maneuverability and takes the fatigue off of those muscles and being able to use it throughout the day. … It has certainly helped for him to be able to go to school and access his classrooms quickly without the fear of falling or any injuries. So that has certainly given him more independence."*

–**Michele**, caregiver of a 15-year-old son with LGMD2D

"Presently I am using a Sit & Stand device to get up from sofa seat, dining table chair, to get out or get into car seat, to get up from movie theatre seats."

–**Prakasa**, 32-year-old man living with LGMD2D

"Now, I am using the wheelchair almost for everything but not in home or in my job (small spaces that I know very well)."

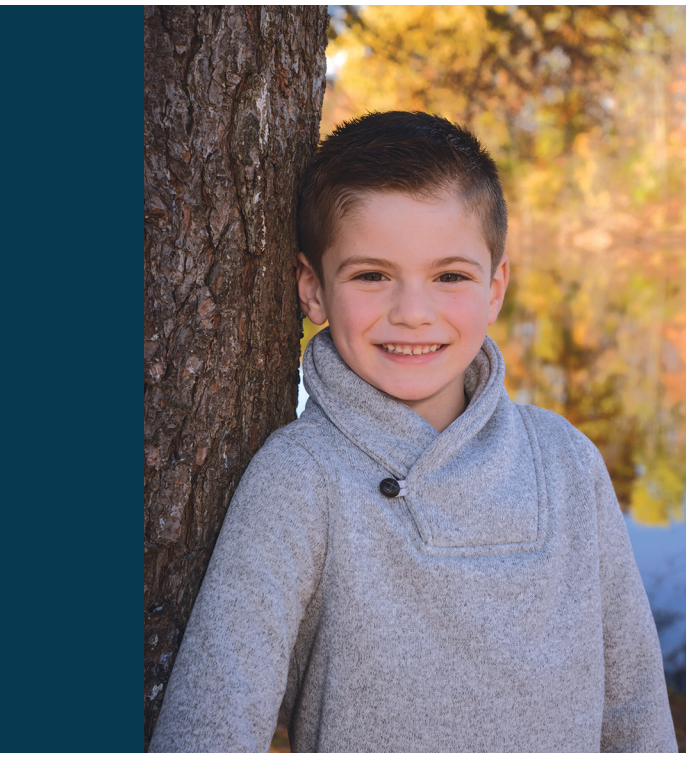
–**Carles**, individual living with LGMD2E

"There's mobility scooters and things like that, but I live in a very small one-bedroom apartment and it's just not big enough for that type of equipment."

–**Tomie**, 50-year-old woman living with LGMD2F

"I began using a moped to get around campus outside. Being on my moped not only helped me get around but protected me from getting knocked down if someone accidentally bumped me. Currently, I use a walker inside my house and my manual wheelchair when I leave the house or feel tired."

–**Jane**, 26-year-old woman living with LGMD2i



Downsides of mobility aids: wheelchairs cannot navigate all environments or surfaces (i.e. sandy beaches), and are not suitable for small living spaces. Exoskeleton suits are quite crude as they are still in early developmental stages. Many individuals living with LGMD have to spend much of their time in a wheelchair in later stages of the disease.

One-third of individuals living with LGMD rely on a modified home environment as well as adaptive devices and technologies. They described lifts and tracks to help with transfers, roll-in showers and shower chairs, lowered counters, railings, no stairs, ramps, smart lights, and many adaptations for sleep. Many also described modified or adapted school and work environments, modified vehicles including a customized lift to put a scooter in the trunk, and adaptive technologies.

> *I use a Hoyer Lift and an electric wheelchair when I need to leave the house for my appointments. I also have an adjustable air bed, which has been of great importance to my overall comfort, since I'm in it all the time. I am put in my wheelchair for a few hours, twice a week to be showered.*
>
> —**Paul**, 65-year-old man living with LGMD2C

> *When I went to the wheelchair, I had to get a different house that would be accessible, remodel the house, buy a handicapped van, pay for 25% of my wheelchair and significant cost for a SureHands lift. These are major financial expenses that aren't always a one-time thing.*
>
> —**Donavon**, 59-year-old man living with LGMD2D

> *I spent about $9,000 on a ceiling track, lifted toilet and a bunch of bathroom modifications, and I still need a full-time caregiver around, when I need to empty my bowels.*
>
> —**Patrick**, 49-year-old man living with LGMD2E

> *I use a desktop computer but with great difficulty due to the weakness in my hands. I rely on voice-to-text or eye gaze technology and a speaker phone whenever I can.* Carol sleeps in an adjustable bed or in her power wheelchair and requires *multiple pillows for positioning, a six-and-a-half-pound weight on my left hip to stabilize the joint, and a satin pillowcase for head mobility.*
>
> —**Carol**, 61-year-old woman living with LGMD2A

> *Currently, I'm wheelchair-bound. I have been full time for about three years. And the hardest thing is just trying to adapt from a certain level of weakness to the next. What equipment is needed now? How do people assist me now? Because it constantly is changing. And that can be really hard to have to explain to people that aren't experiencing these issues.*
>
> —**Jared**, man living with LGMD2i

> *I have home modifications like a ramp toilet with moveable arms, shower seat. I wear loose clothing. I use satin sheets and satin-type night clothes to help rolling over through the night. Everything I need to access such as cupboards, fridge, freezer are all within my reach.*
>
> —42 year old woman living with LGMD2A

> *The local fire department was becoming all too familiar with coming out and picking me up off the floor, so I now have a lift in my home that I can use independently to get up on my own.*
>
> —**Dan**, 57-year-old man living with LGMD2i

> *I use a recliner to sleep instead of a bed because the lift can't get at me on the bed, whereas the lift can come straight on at me on the recliner. And then to bathe, you have to tear out your tub and put in a roll-in shower, and all your sinks, you have to come in and tear out your cabinets and put in wheelchair-accessible countertops, so there's a lot of daily accommodations you have to do.*
>
> —**Josh**, a 34-year-old man living with LGMD2i

> *Three years ago, our family built a new home to accommodate Sammy as she was no longer able to independently make a full flight of stairs to get to her room. She now has single floor living, which keeps her independent throughout the day.*
>
> —**Kelly**, mother of a 14-year-old daughter living with LGMD2i

Cost is a clear downside of all these required modifications and adaptions. Sometimes essential adaptations, including elevators, break down. Home modifications are hard because anticipating someone's needs in the future is challenging as the disease progresses.

> *The future for us is always changing with our muscles progressively getting weaker. It's hard to plan for future events or life because what will our physical ability look like. I could design for my abilities today but what about in a year or in 5 years? It is hard to know what I will need in the near future.*
>
> —**Edith**, woman living with LGDM2i

Physical or occupational therapy and exercise are used by many living with LGMD to stay as healthy as possible. Many use water/aquatherapy for exercise, so these are included here. Many commented about wanting to stay in the best condition possible to prepare them for future potential treatments.

> *Upon my release from the hospital [for multiple abdominal surgeries, due to a poor outcome of appendicitis in 2005], I had three months of at-home physical therapy to regain my ability to walk.*
>
> —**Paul**, 65-year-old man living with LGMD2C

> *Balneotherapy with an arnica oil massage and a magnesium salt bath are the best for the symptoms.*
>
> —Parent of a young daughter living with LGMD2C

> *We see a physical therapist every week. She does a variety of stretches and some muscle strengthening moves with him. This has helped a lot.*
>
> —Parent of a 9-year-old son living with LGMD2D

> *The physical therapist has been working with him on certain strength exercises and his hips, and also assisting with him walking upstairs, just really basic life necessities, really. They did notice a bit of an improvement in the strength in his hips at his last appointment, which was really exciting.* During the physiotherapy, *a big focus is heel striking when he walks. That's a big thing, it helps prevent him from tripping. … Being able to stabilize his body when he is playing tag with his friends or running around, having proper heel strikes when he's walking makes a big impact on his ability to stay upright and not injure himself.*
>
> —**Faran**, mother of a nine-year-old son living with LGMD2D

> *We are doing our best to fight this disease, swimming pool, exercise, stretching, breathing exercises, splints at night. We take care of food and rest, but no matter what we do, the disease progresses very quickly.*
>
> —Parent of a 14-year-old son living with LGMD2E

> *I have checkups and doctor visits every other year. I take medication for heart failure. I do physical therapy twice a week and respiratory gymnastics four times a week. I try to feed myself properly. Physiotherapy relieves my pain and I hope it avoids joint tension long enough.*
>
> —Woman living with LGMD2E

> *I get out of my house everyday and try to remain active. I have found it to be very beneficial, less fatigue and improved strength. I try to move for at least six hours. This was versus a sedentary lifestyle that caused dramatic muscle fatigue and cramping.*
>
> —26-year-old woman living with LGMD2A

> *The physical therapy is important just for trying to maintain day-to-day mobility. …Sometimes even very tiny things can make a huge difference in someone's life. So even if it's just being able to obviously reach the controller of the wheelchair or be able to twist around in bed or something like that. Also, anything to do with transferring is probably the main one. So being able to, even if you're not able to walk, how difficult it is to be able to get in and out of the wheelchair is a huge element of daily quality of life. So those are, I think, areas whether it be strength or flexibility, are important.*
>
> —**Jordan**, 36-year-old man living with LGMD2A

> *I began attending physical therapy, my first form of treatment, twice a week around age seven and continue to do so today. I've been seeing my current therapist for over 10 years. We have an amazing relationship and I'm so grateful for everything he has helped me accomplish and maintain.*
>
> —**Jane**, 26-year-old woman living with LGMD2i

> *Sammy's early years were only mildly challenged as she was able to participate in softball, gymnastics, dancing, horseback riding, and swimming. However, she's no stranger to physical therapy and has had consistent therapy services since she turned one year old.*
>
> —**Kelly**, mother of a 14-year-old daughter living with LGMD2i

> *Physical therapy is an underrated treatment. It helps me tremendously.*
>
> —46-year-old man living with LGMD2i

While exercise and physiotherapy help to maintain mobility and strength, the LGMD still rapidly progresses. Individuals living with LGMD described the need for well-trained physiotherapists who are knowledgeable about the diseases. Many individuals particularly described how aquatherapy and swimming are not always accessible for them.

> *I used to like swimming, but there are too many problems from moving to dressing and undressing, to the cold water not being suitable for my muscles.*
>
> —Individual living with LGMD2E

> *It is challenging, to have the right equipment, access to a pool. There are limitations of my energy reserves, if I ever do it. It's not independent activity, and I started in the hospital setting, but there's obviously limited number of sessions available. I've now moved on to using a private pool with carers.*
>
> –**Andrew**, 41-year-old man living with LGMD2A

> *Tried aquatherapy but was unable to safely get out of the chair lift.*
>
> –27-year-old man living with LGMD2i

Other options selected in the polls include **diet modifications**; **complementary/alternative therapies (chiropractor, acupuncture, massage)**; **ventilation devices (BiPAP, tracheotomy, cough assist)**; **counseling or therapy; braces, kinesio tape, etc.**; **urinary incontinence devices (pads, catheters, Botox)**; **surgery (scapular fixation, heel cord elongation)**. A small number of individuals (7%) stated that they are not doing anything to manage symptoms.
Many mentioned using their diet to maintain a reasonable weight (particularly people with LGMD2A).

> *I am careful with my diet, so is not to gain too much weight or encourage other health problems.*
>
> –42-year-old woman living with LGMD2A

> *I generally no longer eat sugar/sweeteners or flours of any kind in order to reduce inflammation and cut down on my pain. I follow this diet also to keep my weight from getting too high. I used it to lose 50 pounds and maintain that weight loss when I stick to the plan.*
>
> –49-year-old woman living with LGMD2A

Complementary/alternative therapies (chiropractor, acupuncture, massage) were used by some.

> *Chiropractor treatment helped with my scoliosis and balance, hip pain. Husband uses a massage roller on my hips, I use kinesio tape everywhere. I have soft orthotics for my feet and legs. I swam and worked out at the YMCA for years but it's too draining now but I greatly encourage it.*
>
> –**Karen**, 62-year-old woman living with LGMD2A

> *Michelle sees both a chiropractor and a massage therapist, however doesn't have an expectation that this will cure her disease. "I definitely notice the difference. …He doesn't force anything. It's a very gentle approach. And massage therapy is another one that I utilized. And especially when my muscles are sore or tired or tight.*
>
> –**Michelle**, woman living with LGMD2i

Many require **ventilation devices** to breathe.

> *In the last two years, specifically, I've needed my ventilator more throughout the day and almost 24/7. I can no longer go more than a few hours before my heart races and my headache begins as CO_2 retention increases. … I lack the strength to breathe without a ventilator.*
>
> –**Elizabeth**, 42-year-old woman living with LGMD2C

> *I began using a CPAP machine, which had no beneficial effect on my diaphragm. Since 2012, I've been using a trilogy ventilator and currently, use it 24 hours a day. This has helped noticeably, reduce the decline in my diaphragm's capability for the last two years. The ventilator is easy to use and portable enough to hang from my wheelchair when I'm away from home.*
>
> —**Paul**, 65-year-old man living with LGMD2C

> *I use a bi-pap at night and I have a non-invasive ventilator (sip and puff) attached to my wheelchair during the day time. I also use a cough assist and function device to assist with coughing. …I am fortunate enough to be able to use a non-invasive sip and puff ventilator instead of a tracheostomy, however, I still struggle emotionally and physically.*
>
> —**Kelly**, woman living with LGMD2D

> *LGMD2A affects my breathing. Due to the weakness of my diaphragm, I rely on a ventilator during the night to breathe and use a cough-stimulating device. Decreased pulmonary functions have also weakened my voice volume.*
>
> —**Carol**, 61-year-old woman living with LGMD2A

Counseling/therapy and meditation and mindfulness approaches were mentioned by a number of individuals living with LGMD. They discussed the mental health support they receive to deal with a progressive disease and with the anxiety caused by severe side effects. Some mentioned support groups and the power of maintaining a positive attitude.

> *I started seeing a therapist, because the weight of the progression of my disease was getting heavier and heavier, knowing that losing mobility and finally being paralytic was in my future. With my therapist's help, I realized I was an alcoholic and started attending a 12-step program. I also started getting help for the fear as well. It was a great paradigm shift for me. I no longer dreaded the outcome of my disease and began to seek assistive ways to live.*
>
> —**Paul**, 65-year-old man living with LGMD2C

> *I have done yoga breathing and meditation for the last 25 years. Daily commitment to the breathing has really helped to keep my muscles going. Meditation to manage anxiety.*
>
> —**Erik**, 45-year-old living with LGMD2E

> *There is a lot of stigma with this disease and it does weigh on our minds and gives us anxiety and sometimes depression. And we feel like burdens and all those things, I know that we all feel all those things. And I've tried to incorporate mindfulness and meditation and just closing my eyes and listening to videos, whether it's an app or whatever, just to self help myself.*
>
> —**Anita**, 61-year-old woman living with LGMD2i

> *My mom is a relentless warrior, who will stop at nothing to live her life to the fullest. My father and I envy her amazing attitude and endless smiles. She keeps us going, she keeps us strong, she keeps us happy and not the other way around.*
>
> —**Nick**, caregiver of his mother living with LGMD2i

Braces, kinesio tape, and other physical supports including splints and standing frames are used by many living with LGMD. Many described the downsides of splints, including pressure sores and discomfort or sweating which can interfere with sleep. Others described using a standing frame to stretch and to breathe.

> *For about 10 years growing up, I wore removable night splints that kept my ankles at 90 degrees while I slept. This would keep my hamstrings loose, the doctors said. They were made of fiberglass. They didn't tell me that they would make my legs sweat. They didn't tell me that I would develop sores on my ankles, or other parts of my legs from the thigh down, due to skin irritation so bad, that it stopped me from sleeping most nights.*
>
> —**Patrick**, 49-year-old man living with LGMD2E

> *I have a brace to help slow the contractures I am getting in my ankles. I have a new brace that attaches to my chair to help me sit upright/support my trunk. I have and use the tilt feature on my power chair for helping to alleviate horrible pain under my ribs (from not being able to support my trunk any longer), my back, hips and neck.*
>
> —49-year-old woman living with LGMD2A

Urinary incontinence devices and strategies, including pads, catheters, Botox are required by some living with LGMD. Several spoke of having a catheter placed to reduce the number of transfers to the toilet.

> *I elected to have a suprapubic catheter placed to reduce the number of transfers each time to the toilet.*
>
> —**Elizabeth**, 42-year-old woman living with LGMD2C

Surgery, including scapular fixation, heel cord elongation, can be used to address some of the LGMD-related symptoms. The downsides are numbness, pain, inconvenience, and a great deal of time spent in the hospital.

> *I was born with short Achilles tendons. And therefore, had to walk on my toes, until I had corrective surgery at the age of 15.*
>
> —**Paul**, 65-year-old man living with LGMD2C

> *Until the age of 16, I could still walk or transfer with assistance, until I had spinal fusion surgery to correct the 50 degree curve in my spine. The scoliosis was indirectly a symptom of limb-girdle muscular dystrophy due to being a full-time wheelchair user and poor sitting posture due to my muscles weakening.*
>
> —**Rania**, 35-year-old woman living with LGMD2E

> *In the fall of 2020, she underwent a bilateral heel cord lengthening procedure. During her recovery, she had to wear casts on both legs for six weeks and endured serial casting while recovering from the surgery to increase her ankle flection. Then just last summer, she had to have a major spinal fusion surgery due to severe scoliosis. She was hospitalized for three weeks and basically had to learn an entire new way of walking and compensating for her weakness. It was a long and painful recovery and she still is having numbness along her back as well as rib pain from having to cut into five of her ribs to make the correction.*
>
> —**Kelly**, mother of a 14-year-old daughter living with LGMD2i

Treatment approaches are not very effective, are costly, are unavailable or inaccessible.

Individuals living with LGMD used online polling to indicate how well their current regimen controlled their symptoms overall and to identify the biggest downsides of their treatments. The results of the two polls are shown in **Appendix 9, Q3** and **Q4**. Many treatment downsides were already mentioned in the previous sections. Some additional patient comments are included below.

Treatments are not very effective. The results of the two polls were consistent; 79% of poll respondents indicated that their treatments only control their symptoms either "very little" or "somewhat."

> *I hope that a treatment of some kind will become available because, currently, we have nothing. At every doctor's appointment, we get told to do the same stretches and exercises, which we follow religiously, but for the most part, they don't change anything. We both notice worsening symptoms. Both Peter and I just want something, anything, so we'll be able to pursue our dreams and live life like everybody else.*
>
> —**Kurt**, 16-year-old male living with LGMD2C

> *We do stretches every day, exercise, proper nutrition, rest. The drugs used do not help in any way.*
>
> —Parent/guardian/caregiver of 14-year-old son living with LGMD2E

> *We are doing our best to fight the disease. Swimming pool, exercise, stretching, breathing exercises, splints at night. We take care of food and rest. But no matter what we do, the disease progresses and very quickly.*
>
> —Parent/guardian/caregiver of 14-year-old son living with LGMD2E

> *As far as I know, there are no real treatments. I've tried physical therapy, but the knowledge is limited and the results lacking.*
>
> —32-year-old man living with LGMD2i

> *I am hearing ambulatory patients talk about alternative treatments like physical therapy, chiropractic, supplements, and I think it shows how traumatizing this disease is. We do not want the cruel reality of what this disease takes from us. There is no treatment and I have personally spent so much money and energy trying anything and everything. I now use a wheelchair full time with a cruel reality that harder days are coming and only so much is within my control.*
>
> —**Julie**, woman living with LGMD2i

Limited availability or accessibility of treatment can be due to the general lack of accruing clinical trials, trained individuals, distance, cost, or building accessibility.

> *Unfortunately, the most significant downside for us is there are no trials, or commercial treatments available today for my son. After years of research and trials by dedicated doctors and researchers, there's still not an approved treatment that my son can have to change the progression of this disease. We would learn about and be willing to try whatever we could, if it were available.*
>
> —**Rachel**, mother of a five-year-old son living with LGMD2D

> *My biggest challenges have been finding providers that are knowledgeable about LGMD, access to patient studies as the travel is not always re-imbursed and difficult to arrange or doesn't allow for a companion to go with me without expenses. For many years a big challenge was finding an accurate diagnosis.*
>
> —**Angela**, woman living with LGMD2A

> *The things that currently help me the most are my caregivers, my Hoyer Lift and electric wheelchair, and my ventilator. I wish I had better access to durable medical equipment. These pieces of equipment are very expensive, which limits access to them.*
>
> —**Paul**, 65-year-old man living with LGMD2C

> *My insurance doesn't cover chiropractic or massage, very little physical therapy if I were to go.*
>
> —**Michelle**, woman living with LGMD2i

> *One of the biggest things that I see besides cost and not necessarily monetary cost, but the cost of, 'Yes, I'd like to go to the YMCA and use their pool.' But just the toll on my body getting just from my car to inside or there may even be accessibility issues. One step, one small step can make a big difference. And this is even when I've participated in clinical trials, that the accessibility of the buildings that you go into, the accessibility of doctor's offices, can also be an issue.*
>
> —**Lisa**, 57-year-old woman living with LGMD2i

Other downsides selected in the polls, include: **requires too much effort and/or time commitment**; **I am not using any treatments**; **negative side effects**; **numbers of pills/medications needed per day**. Again, many of these were discussed in the previous sections describing the different medications and treatments. Steroid side effects generated a number of comments.

> *I couldn't sleep and the steroids gave me chronic stomach pain and stomach issues, which I still deal with daily despite having been off steroids for seven years. I gained weight and suffered cushingoid effects. My metabolism is still not correct for someone of my age. I've osteopenia and had to give myself a daily injection for two years to combat this side effect. I also had to have a double cataract surgery and now wear readers at age 26.*
>
> —**Jane**, 26-year-old woman living with LGMD2i

> *Prednisone resulted in a long-term diagnosis of anxiety. "After just a few days on prednisone, Sammy suffered from headaches, stomach aches and a racing heart and sleepless nights.*
>
> —**Kelly**, mother of a 14-year-old daughter living with LGMD2i

Individuals living with LGMD are impatient for a cure. They want a treatment that will help regain strength and/or muscle function, followed by a treatment to slow or stop the loss of muscle function

They used online polling to select their top choice for what would represent a meaningful benefit in a future treatment. This is shown in **Appendix 9, Q5** and illustrated with patient quotes below.

Individuals living with LGMD would like treatments to help them **regain strength and/or muscle function** and **slow or stop the loss of muscle function**. The patient comments about these treatments are so similar that they are grouped together. Some individuals would just improve their strength or muscle function to their last plateau before their latest regression. Some were specific about wanting to maintain the existing function in their upper extremities.

> *"As I look into the future, my biggest hope is that a treatment will become available that will slow the progression of the disease and perhaps allow me to start rebuilding some physical abilities, such as reaching for things with my arms and standing up."*
>
> —**Peter**, 14-year-old male living with LGMD2C

> *"I think just slowing the progression of muscle deterioration would certainly be beneficial. That's one of the main things that we look for. Is it safe? Is it effective? Then, we're on board."* Michele would like to preserve her son's ability to walk, *"And also the upper limbs being able to raise arms up and turn over in bed and kind of preserving those activities of daily living."*
>
> —**Michele**, parent of a 15-year-old son with LGMD2D

> *"I don't care if I'll never walk again, but stopping the progression would be enough. Slowing the progression would be enough at this point. Meanwhile, while I wait, I can't lift my arms to scratch my face. I can't wipe my own butt and I really can't go anywhere by myself, unacceptable. Forty years of having muscular dystrophy is enough, I'm done. Actually, I was done 30 years ago, but here I sit."*
>
> —**Patrick**, 49-year-old man living with LGMD2E

> *"I can deal with not walking but loss of upper extremity strength is the worst. It would be great if I could improve my upper extremity strength...even just a little."*
>
> —61-year-old woman living with LGMD2A

> *"If I could stop declining and stay where I'm at, that would be huge. I'm slowly getting worse every day. If I could stay where I am and maintain this quality of life, I would be happy."*
>
> —54-year-old woman living with LGMD2i

> *"I would love to regain some of my lost muscle strength and function. However, I would also be thrilled to simply stop the progression of the disease. Stopping the progression of this disease would be a huge success. The fear of things getting worse, and increased disability from this disease is intense. Having the ability to stop the disease from causing more muscle weakness would allow patients living with the disease to maintain whatever level of independence we have now and spare us from suffering further disability and further limitations. Please know that hitting the pause button is a major victory."*
>
> —**Kristen**, woman living with LGMD2i

Other meaningful benefits selected in the polls include **preserving respiratory and lung function**, **preserving cardiac function**, **lessening pain or fatigue**.

> *"LGMD affects his heart and he is already taking heart medications. So, most importantly, I would want to improve his cardiac function, but obviously slowing or stopping the progression and helping his muscles is a close second. But the heart function of course is number one because it's his heart. If you stopped or slowed the progression of the disease in the other muscles, it would also help slow the progression of the cardiac function as well."*
>
> –**Tiffany**, mother of a 15-year-old son living with LGMD2C

> *"I would love to be able to walk again and have a normal life, but success could also be defined as being able to breathe without a machine. This would change my quality of life by strengthening the muscles around my lungs and diaphragm. ...My lung capacity's down to 32%. If I die because of respiratory failure, I know that's a terrible death."*
>
> –**Donavon**, 59-year-old man living with LGMD2D

> *"I would like treatment that would not make the disease worse, especially breathing."*
>
> –Individual living with LGMD2E

> A meaningful benefit would be *"to stop the disease progression and to gain vital lung capacity!"*
>
> –35-year-old woman living with LGMD2i

> *"I just want to slow the disease down, so that my breathing muscles and my heart muscle allow me to live for 30 years more. …A treatment that would slow progression, would mean that I may not have to use a ventilator one day. …The fear of my heart and lungs greatly overcomes any concern about walking."*
>
> –**Kathryn**, 49-year-old woman living with LGMD2i

Additional LGMD clinical trial endpoint recommendations

Many individuals living with LGMD are very keen to participate in clinical trials. Although this was not a defined meeting discussion topic, many individuals with LGMD made clinical trial suggestions during the September 23, 2022, EL-PFDD meeting.

Consider clinical trial designs without a placebo control arm or a shorter placebo duration. Individuals living with LGMD are hoping that participation in natural history studies will remove the future requirement for placebo control arms in the future. Alternately, some recommended that the duration of the placebo arm of trials to be shortened so that patients receive the active drug sooner.

> *"We ask that the FDA reconsider and direct the placebo period in clinical trials … for this ultra-rare disease, LGMD2i, be eliminated or reduced to a minimum, months, not years. The long placebo period would appear to be unnecessary for an investigational drug for an ultra-rare disease. Our concern is that within months a patient can become non-ambulatory with no way to reverse the loss."*
>
> –**Stephen**, parent of two daughters living with LGMD2i

> *"When I think about trials, I don't wish to participate in any placebo control trial, but I would if that was the only option available. But, having to wait more time for a potential treatment while I continue to progress, is something that really bothers me. I feel like I already have enough burden to deal with already."*
>
> –**Kathryn**, 49-year-old woman living with LGMD2i

> *"We are very concerned with clinical trial designs for ultra-rare diseases such as LGMD2i/R9 that include long placebo periods. … An anticipated trial design of a 3-year placebo destroys any sense of hope a patient with this ultra-rare disease holds onto as they physically struggle to get out of bed in the morning."*
>
> –**Stephen**, parent of two daughters living with LGMD2i

> *"My daughter is in a clinical trial that seems to be working with a drug that is safe. She did not receive the placebo but we have concerns for patients who continue to deteriorate who have to take a placebo for an extended period of time. If a drug has proven to be safe it's inhumane to require patients to continue on a placebo and deteriorate when they could benefit by taking the drug."*
>
> –**Luther**, father of a young woman living with LGMD2i

> *"Participation in a clinical trial is always voluntary and a patient can withdraw at any time. Are you going to stay in a trial for 3 years once you realize you are on the placebo?"*
>
> –**Stephen**, parent of two daughters living with LGMD2i

Consider clinical trial designs that require only very few patients. This is especially important for the very rare LGMD subtypes, where it is difficult to enroll enough patients of each subtype to fulfill normal clinical trial enrollment targets.

> *I urge the FDA to use as much flexibility as possible in considering data from small trials in this area because the need is great even if it's hard to do trials in this rare disease.*
>
> –**Donavon**, 59-year-old man living with LGMD2D

> *My concern is that some subtypes of LGMD are so rare, it's difficult to find patients with strict inclusion criteria.*
>
> –**Kathryn**, 49-year-old woman living with LGMD2i

Clinical trial endpoints need to consider outcome measures other than just walking. Individuals living with LGMD suggested evaluating treatments by improvements in upper arm strength or changes in respiratory function. This would also increase the number of patients who were eligible for clinical trials, and would allow patients with more advanced disease to try potentially disease-modifying therapies.

> Including respiratory improvement as a clinical trial outcome measurement means that individuals with respiratory impairment would not be excluded. *I do believe that being able to walk is extremely important and should be measured; but being able to help somebody breathe better should be a target. To me, breathing is actually more important than walking for older patients.*
>
> –**Donavon**, 59-year-old man living with LGMD2D

> *I feel very frustrated when I'm in a clinical trial and things that matter to me are ignored.* Kathryn described how she would like a treatment to help maintain the strength in her upper arms and her diaphragm and would like those measures incorporated as appropriate endpoints. *I sometimes feel that trials focus on walking measures, getting up out of chairs and going up steps. I feel like more progressed patients are left out, due to the clinical trial design. I would like for stakeholders to understand what success would look like for me and others.*
>
> –**Kathryn**, 49-year-old woman living with LGMD2i

Consider the variability within the separate LGMD subtypes and endpoints that could be measured over a longer period of time.

> *I also feel that my form of LGMD is so slowly progressing, that it would be super challenging to track it over several years. But, also in my particular form, there are patients with a heterozygous mutation that progress super-fast. With this wide variability within just one subtype, there needs to be a special consideration.*
>
> —**Kathryn**, 49-year-old woman living with LGMD2i

Lesson the burden of clinical trials for patients. During the meeting many parents described how intensive the clinical trial procedures were for their children.

> *We also need to keep in mind, there are people who have lives outside of our research environment. So, we need to minimize disruption in our everyday lives. Please lessen the burden, we are tired, we're exhausted, and we need every help we can possibly get.*
>
> —**Kathryn**, 49-year-old woman living with LGMD2i

Some requested clinical trials to be conducted in different countries from around the world.

> *My final hope is that one day Australian patients can be included in formal trials. Surely it isn't that difficult this day and age.*
>
> —**Lindsay**, 65-year-old man living with LGMD2i

Finally, individuals living with LGMD had many requests for more research, including research into the rarer disease subtypes.

> *Our son is almost 13, he has so many questions that unfortunately we, his parents, or his doctors can't answer. He reads online all the progress and steps being taken for other types of MD, but we need more focus on LGMD.*
>
> —**Nikki**, parent of a son with LGMD2C

> *There have been promising developments for other forms of LGMD. …We would love to see more exploration of the cross-functionality between subtypes for these treatments and more fast tracking of approvals. We are truly desperate to slow the progression of this disease to prolong our children's mobility as long as possible.*
>
> —**Faran**, mother of a nine-year-old son living with LGMD2D

> *At five years old, we've heard from his doctors, that now is an optimal time for him to have a treatment and he would be a great candidate, because of his current strength. Even a recurring treatment that provides his body what it needs, would be a blessing, while we wait for a cure to help people in need, like my son. As each day without a treatment passes, this could change. We want Jacob to be able to live his life to the fullest, without the physical and mental pain from a disease where we know that a treatment is possible.*
>
> —**Rachel**, mother of a five-year-old son living with LGMD2D

Incorporating Patient Input into a Benefit-Risk Assessment Framework

The FDA uses a Benefit-Risk Assessment Framework which includes decision factors such as the analysis of condition, current treatment options, benefit, risk, and risk management. The Framework provides an important context for drug regulatory decision-making and includes valuable information for weighing the specific benefits and risks of a particular medical product under review.

Table 1 speaks to the challenge of having a lifelong disease burden that individuals living with LGMD endure. It serves as the proposed introductory framework for the Analysis of Condition and Current Treatment Option to be adapted and incorporated in the FDA's Benefit-Risk Assessment. This may enable a more comprehensive understanding of this unique condition for key reviewers in the FDA Centers and Divisions who would be evaluating new treatments for LGMD. The data resulting from this meeting may help inform the development of LGMD-specific clinically meaningful endpoints for current and future clinical trials, as well as encourage additional researchers and industry to investigate options for treatments.

The information presented captures the perspectives of caregivers and patients living with LGMD presented at the September 23, 2022, meeting. This meeting focused specifically on LGMD subtypes 2C, 2D, 2E, 2F, 2A and 2i. It also includes information from survey responses collected prior to the meeting and comments submitted before, during, and after the meeting through the online portal.

Note that the information in this sample framework is likely to evolve over time.

	EVIDENCE AND UNCERTAINTIES	CONCLUSIONS AND REASONS
ANALYSIS OF CONDITION/IMPACTS ON ACTIVITIES OF DAILY LIVING	**LGMD affects multiple body systems.** Impaired mobility is the most impactful symptom affecting walking and balance, difficulties getting up from sitting, and challenges with stairs. Other impactful symptoms include fatigue, difficulties using hands and arms, and social/emotional challenges. For many, constant pain, urinary and bowel issues, poor sleep, muscle contractures, pulmonary and cardiac issues are a way of life. Symptoms vary from one day to the next. **All individuals with LGMD progress, but at different rates.** Individuals living with LGMD worry about their continuing progression and eventually losing all independence. Adapting to disease progression is extremely challenging and individuals living with LGMD worry about whether they will have someone who will assist them in the future.	**Many with LGMD are severely affected.** LGMD affects every aspect of life and robs individuals of their independence. Most rely heavily on their caregivers or family members for activities of daily living, and some require 24-hour care. Many described catastrophic falls, which then resulted in higher care requirements. **LGMD is stigmatizing.** Discrimination and social exclusion are part of life. Many are adversely impacted by the limitations they experience compared to their peers. Some try to hide their disability from others. Anxiety and depression are common, and feelings of grief and loss are constant as symptoms progress.
CURRENT TREATMENT OPTIONS/PROSPECTS FOR FUTURE TREATMENTS	**There are currently no FDA approved treatments for any form of LGMD.** There is no way to stop their disease from progressing. **Treatment approaches are palliative only and do not change the course of the disease.** Approaches include dietary supplements, medications to help manage different symptoms, a wide range of mobility aids, extensive home and vehicle modifications, physical therapy and exercise.	**People living with LGMD urgently and desperately need better treatments.** Short of a cure, most would like a treatment that would help regain strength and/or muscle function, followed by a treatment to slow or stop the loss of muscle function, not only to maintain mobility but to support cardiac and pulmonary functions. **Individuals living with LGMD want to participate in clinical trials.** Clinical endpoints need to address each LGMD subtype and an individuals' disease course.

See the Voice of the Patient report for a more detailed narrative.

TABLE 1: LGMD subtypes 2C, 2D, 2E, 2F, 2A, 2i Benefit-Risk Table

Appendix 1: Meeting Agenda

Externally-Led Patient Focused Drug Development Meeting for September 23, 2022

10:00 AM — **Welcome**
Kathryn Bryant Knudsen
Founder of the Speak Foundation and individual living with LGMD2i

10:10 AM — **FDA Speaker**
Wilson Bryan, MD, OTAT, CBER

10:15 AM — **LGMD Clinical Overview**
Katherine Mathews, MD
Professor of Pediatrics & Neurology, University of Iowa

10:30 AM — **Introduction & Meeting Overview**
James Valentine, JD, MHS, Associate, Hyman, Phelps, & McNamara
Jennifer Levy, PhD, Scientific Director, Coalition to Cure Calpain 3

10:35 AM — **Demographic polling**
All 6 subtypes

10:40 AM — **Session 1: Living with Sarcoglycanopathies (LGMD2C, 2D, 2E, 2F) – symptoms, health effects, and impacts on daily life**
Pre-recorded panelists, Zoom discussion starters (live), patient/caregiver audience remote polling and moderated audience discussion

11:40 AM — **Session 2: Living with LGMD2A and LGMD2i – symptoms, health effects, and impacts on daily life**
Pre-recorded panelists, Zoom discussion starters (live), patient/caregiver audience remote polling and moderated audience discussion

12:40 PM — **Lunch**

1:20 PM — **Session 3: Current and Future Treatments (all six subtypes)**
Pre-recorded panelists, Zoom discussion starters (live), patient/caregiver audience remote polling and moderated audience discussion

2:50 PM — **Closing Remarks & Next Steps**
Charlotte Drew, MD
Co-Founder, Kurt+Peter Foundation and caregiver of two sons living with LGMD2C

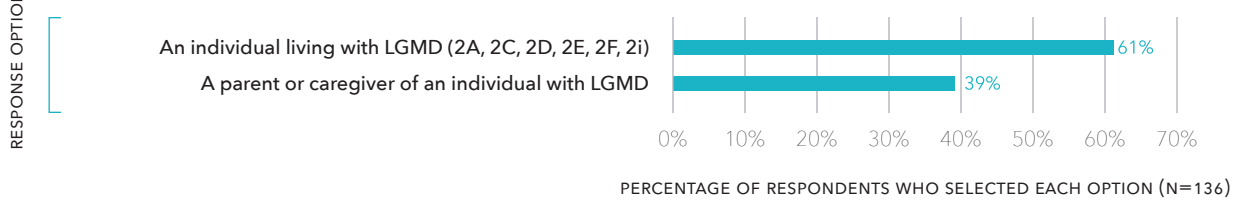
3:00 PM — **Adjournment**

Appendix 2: Meeting Demographics

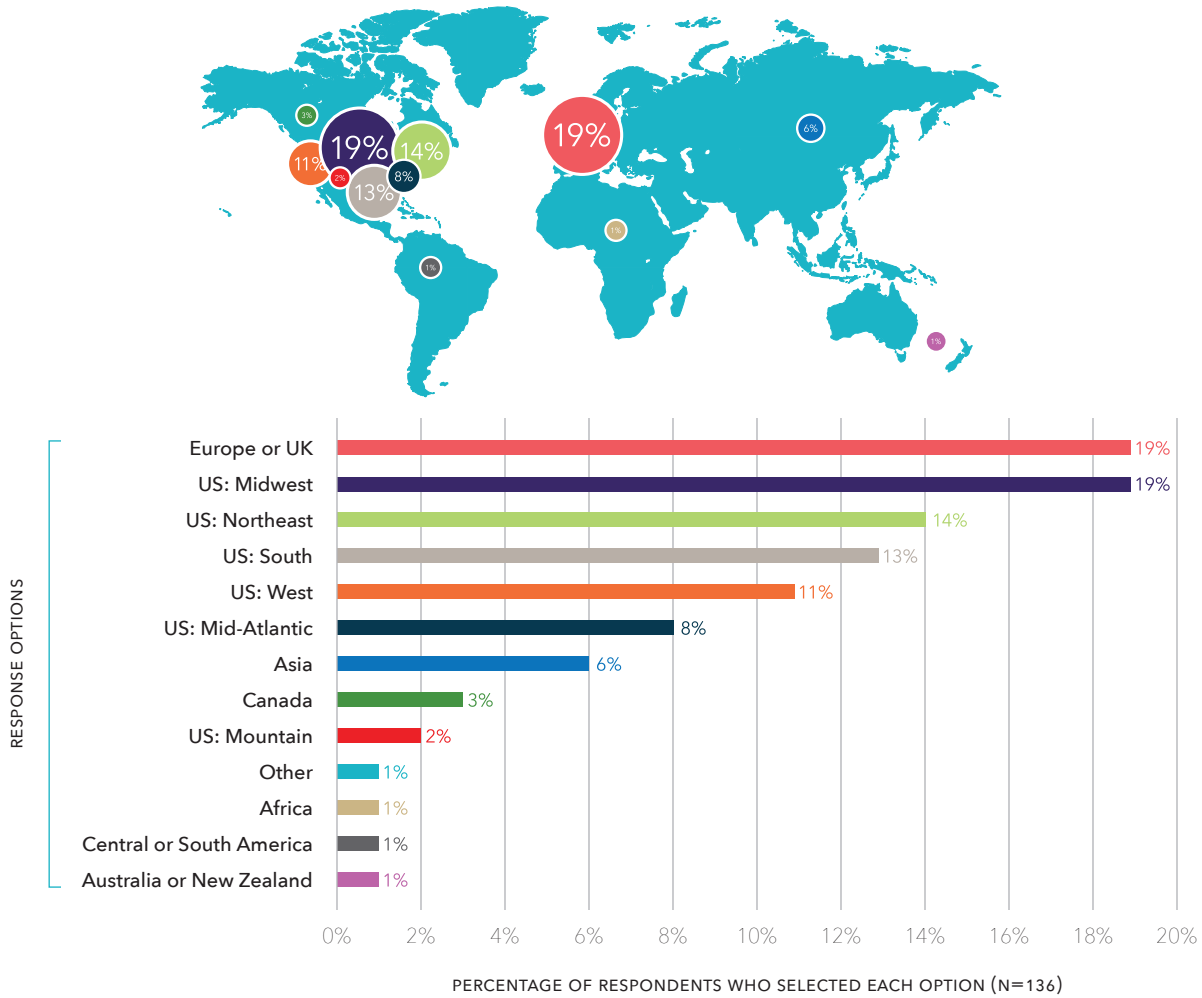
The graphs below include all attendees who chose to participate in online voting. Parents and caregivers were asked to answer the questions on behalf of the individual living with LGMD. The number of affected individuals and caregivers who responded to each polling question is shown below the X axis (N=x).

While the response rates for these polling questions is not considered scientific data, it provides a snapshot of those who participated in the LGMD EL-PFDD meeting and is intended to complement the patient comments made during and after the meeting.

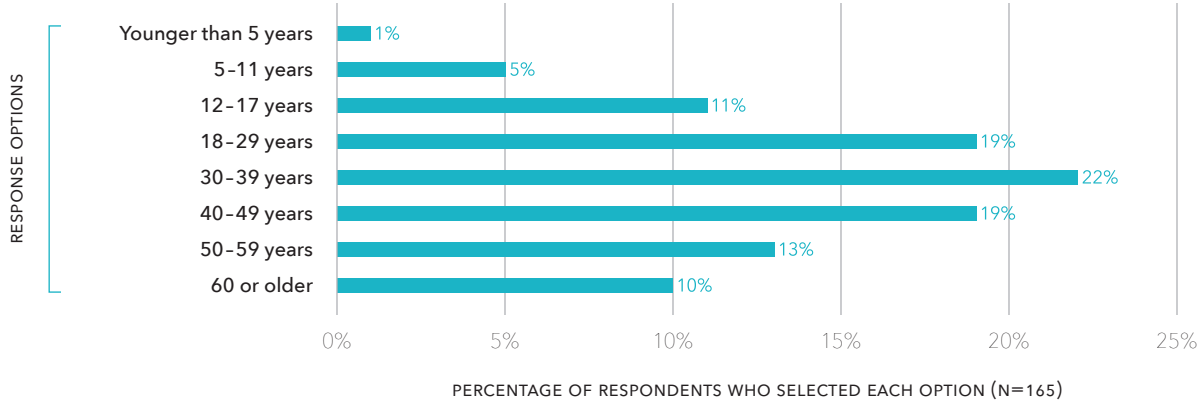
1 Are you? (Select ALL that apply):



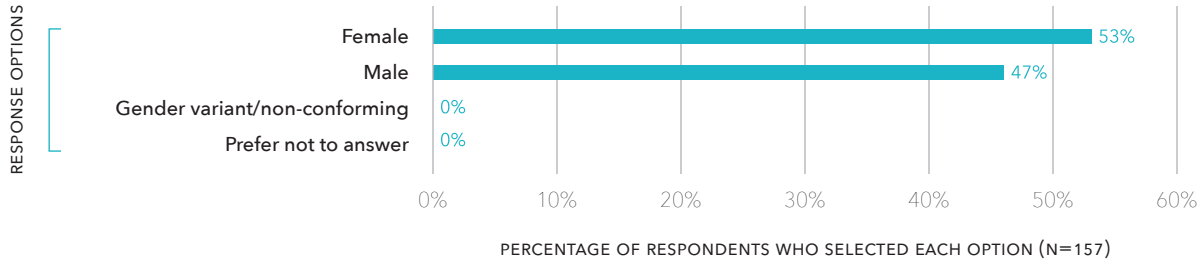
2 Where do you live?



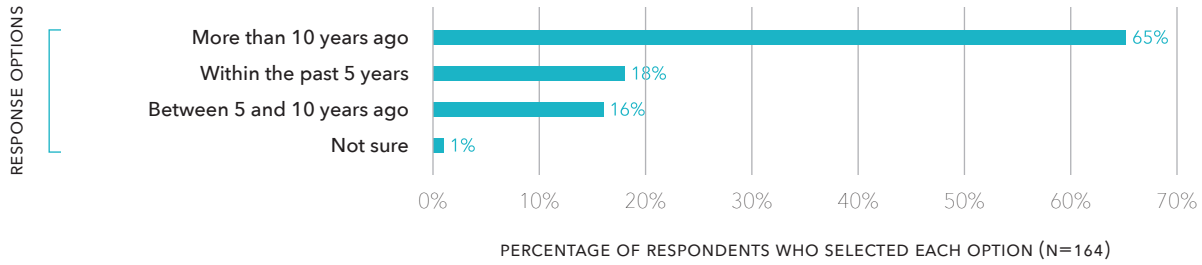
3 What is your age?

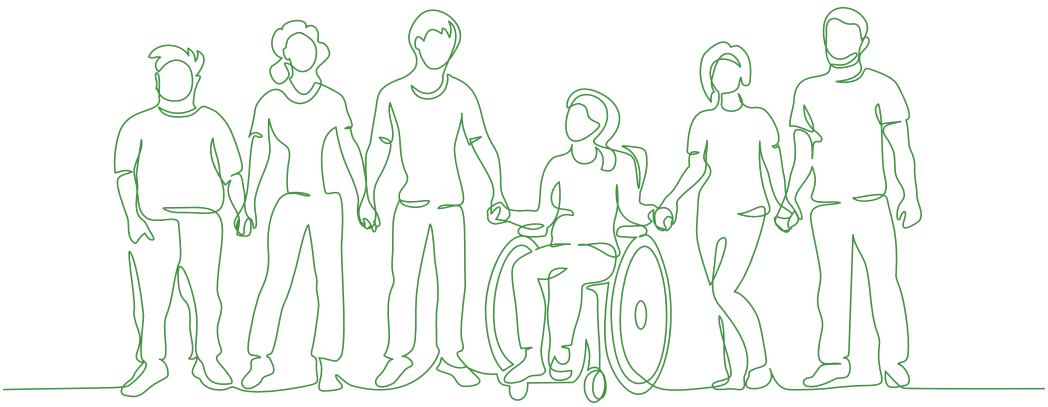


4 How do you identify?

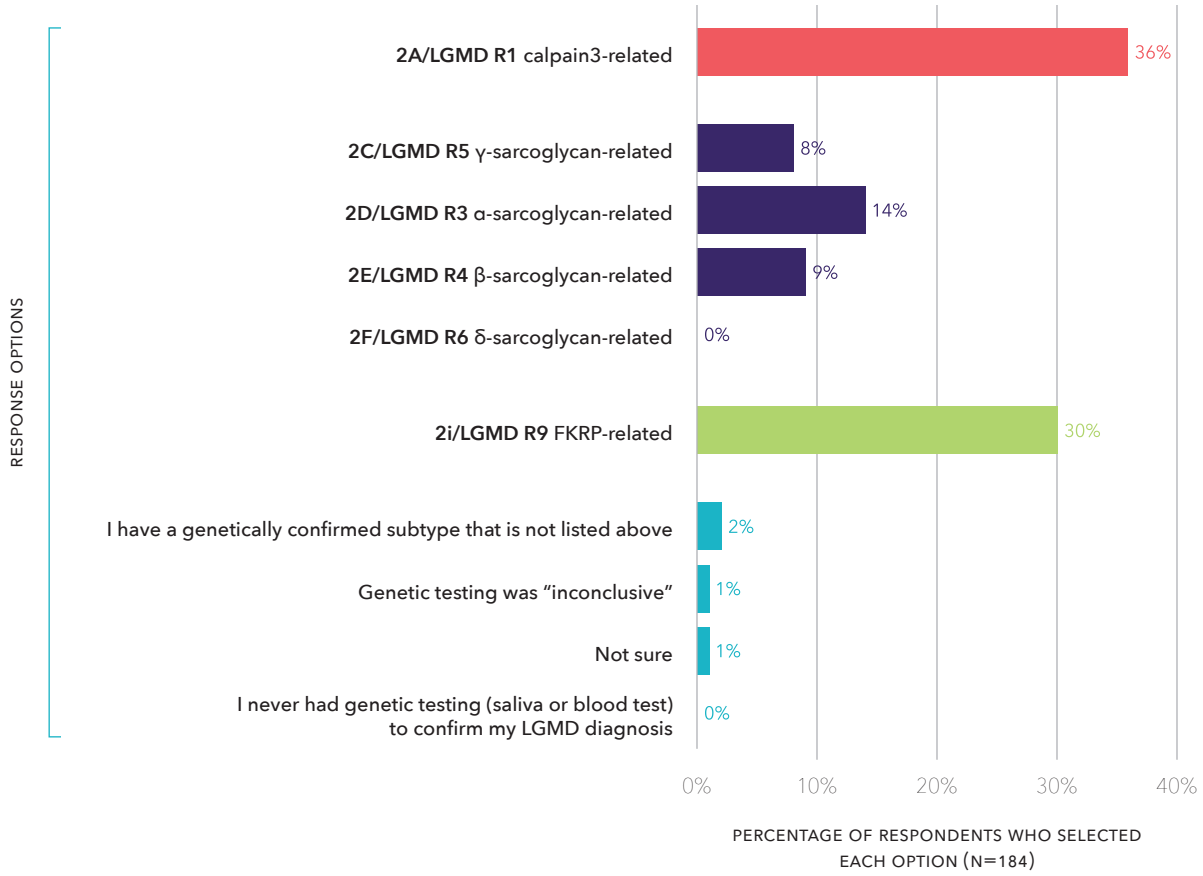


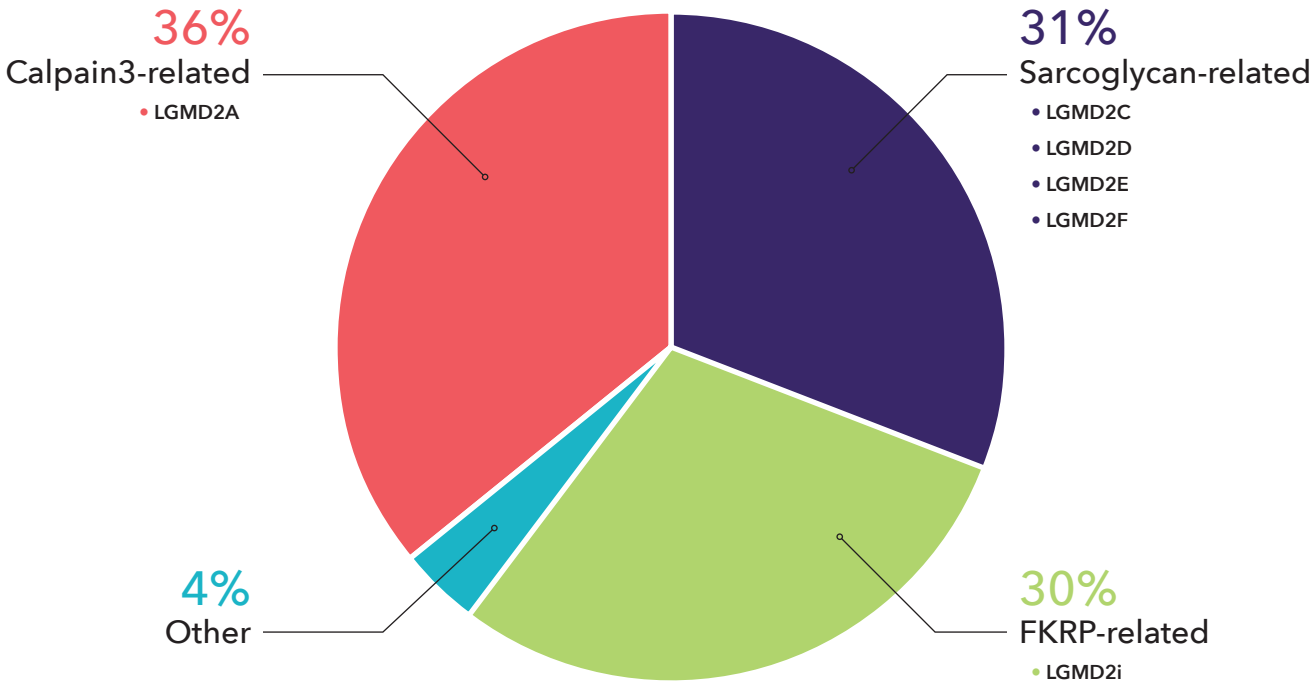
5 How long ago were you diagnosed with LGMD?





6 Which type of genetically confirmed diagnosis of LGMD do you have?





Appendix 3: Meeting Discussion Questions

Sessions 1 and 2: Symptoms and Daily Impacts

1. Of all the symptoms and health effects of LGMD, which 1-3 symptoms have the most significant impact on you or your loved one's life?

2. How does LGMD affect you or your loved one on best and on worst days?

3. How has your or your loved one's symptoms and ability to cope changed over time?

4. Are there specific activities that are important to you or your loved one that you cannot do at all or as fully as you would like because of LGMD?

5. What do you fear the most as you or your loved one gets older? What worries you most about you or your loved one's condition?

Session 2: Current & Future Approaches to LGMD Treatment

1. What are you currently doing to manage your or your loved one's LGMD symptoms?

2. How well do these treatments address the most significant symptoms and health effects of LGMD?

3. What are the most significant downsides to your or your loved one's current treatments and how do they affect daily life?

4. Short of a complete cure, what specific things would you look for in an ideal treatment for LGMD? What factors would be important in deciding whether to use a new treatment?

Appendix 4: Meeting Presenters

SESSION 1

Session 1 Pre-Recorded Panelists

- **Rania**, 35-year-old woman living with LGMD2E
- **Kurt**, 16-year-old male living with LGMD2C
- **Peter**, 14-year-old male living with LGMD2C
- **Donavon**, 59-year-old man living with LGMD2D
- **Elizabeth**, 42-year-old woman living with LGMD2C

Session 1 Zoom Discussion Starters

- **Makayla**, 17-year-old woman living with LGMD2E
- **Bryan**, 55-year-old man living with LGMD2D
- **Alexa**, mother of an eight-year-old daughter with LGMD2C
- **Tomie**, 50-year-old woman living with LGMD2F
- **Scott**, father of two male teens, age 16 and 14, living with LGMD2C

Session 1 Caller

- **Buri**, friend of an individual living with LGMD2D

SESSION 2

Session 2 Pre-Recorded Panelists

- **Jane**, 26-year-old woman living with LGMD2i
- **Dan**, 57-year-old man living with LGMD2i
- **Brooklyn**, 15-year-old female living with LGMD2A
- **Melina**, mother of a 15-year-old daughter living with LGMD2A
- **Carol**, 61-year-old woman living with LGMD2A

Session 2 Zoom Discussion Starters

- **Noni**, 55-year-old woman living with LGMD2A
- **Jessica**, mother of a nine-year-old daughter living with LGMD2A
- **Joshua**, 34-year-old man living with LGMD2i
- **Cindy**, mother of a 34-year-old son living with LGMD2i

Session 2 Callers

- **Jared**, man living with LGMD2i
- **Peter**, 24-year-old man living with LGMD2A
- **Cindy**, 55-year-old woman living with LGMD2i

SESSION 3

Session 3 Pre-Recorded Panelists

- **Sammy**, 14-year-old female living with LGMD2i
- **Kelly**, mother of a 14-year-old daughter living with LGMD2i
- **Andrew**, 41-year-old man living with LGMD2A
- **Paul**, 65-year-old man living with LGMD2C
- **Rachel**, mother of a five-year-old son living with LGMD2D
- **Patrick**, 49-year-old man living with LGMD2E
- **Kathryn**, 49-year-old woman living with LGMD2i

Session 3 Zoom Discussion Starters

- **Michele**, caregiver of 15-year-old son with LGMD2D
- **Jordan**, 36-year-old man living with LGMD2A
- **Lisa**, 57-year-old woman living with LGMD2i

Session 3 Callers

- **Anita**, 61-year-old woman living with LGMD2i
- **Faran**, mother of a nine-year-old son living with LGMD2D
- **Eric**, 33-year-old man living with LGMD2A
- **Tiffany**, mother of a 15-year-old son living with LGMD2C

Appendix 5: Session 1 – Living with Sarcoglycanopathies (LGMD2C, 2D, 2E, 2F)

Symptoms, health effects and impacts on daily life

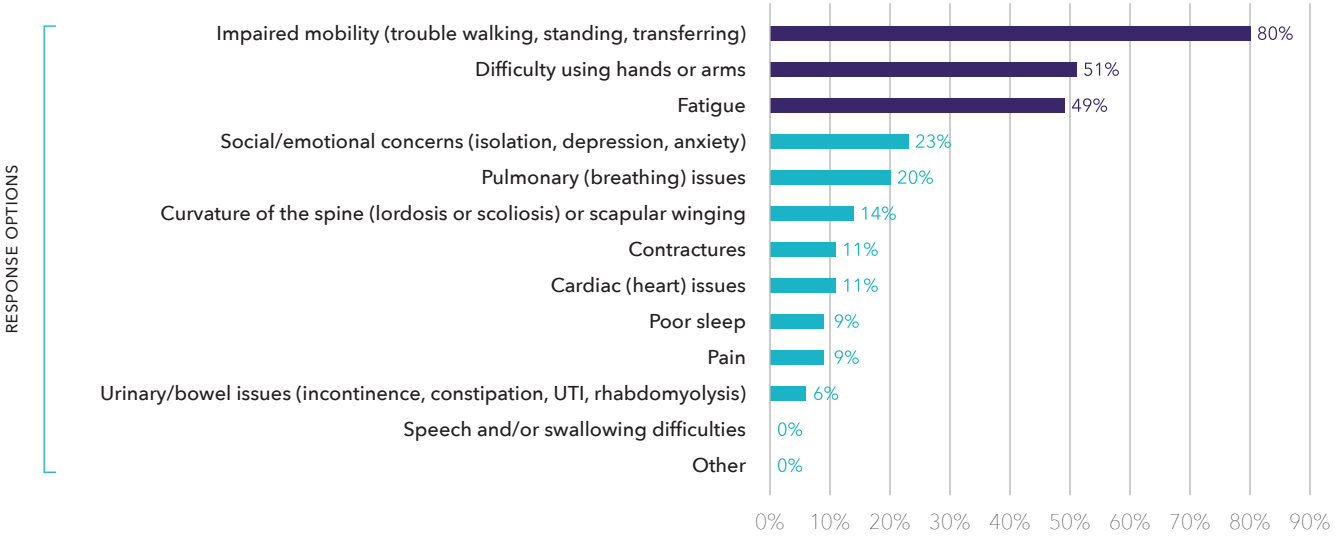
The graphs below include all attendees who chose to participate in online voting, and includes those living with LGMD subtypes 2C, 2D, or 2E or parents and caregivers who answered questions on behalf of the individual living with LGMD. The number of affected individuals and caregivers who responded to each polling question is shown below the X axis (N=x).

There were no individuals living with LGMD2F who participated in online polling.

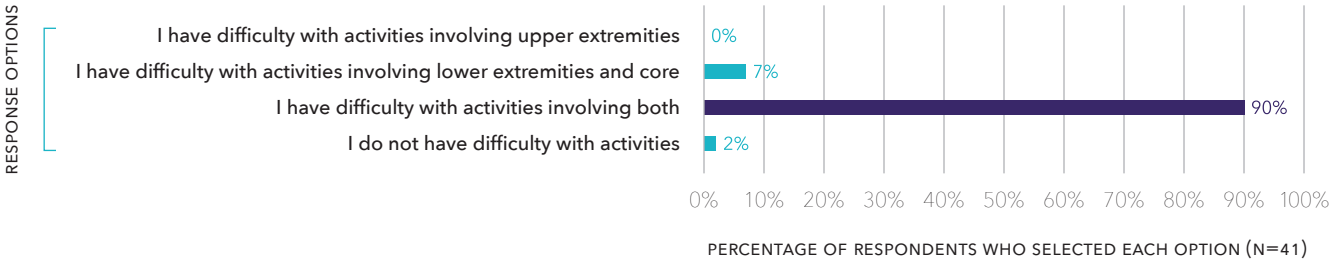
The responses for these polling questions are not considered scientific data, but are provided to present a snapshot of those who participated in the LGMD EL-PFDD meeting and is intended to complement the patient comments made during and after the meeting.

For a further breakdown of this data into specific subtypes, please see **Appendix 6**.

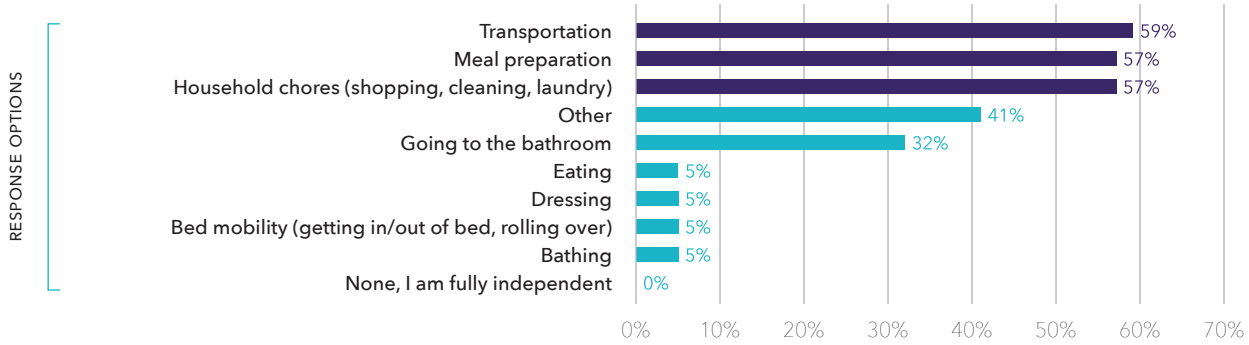
1 Of all the LGMD symptoms you have experienced, which have the most significant impact on your daily life? Select up to THREE.



2 As a result of your condition, which of the following statements are true? Select ONE.

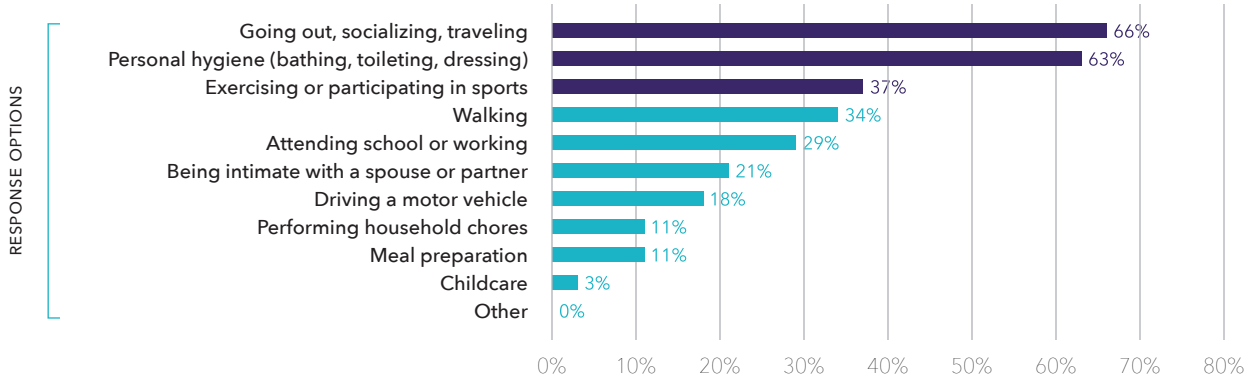


3 Which daily living activities are you dependent upon a caregiver or family member to assist you with some or all of time? Select ALL that apply.



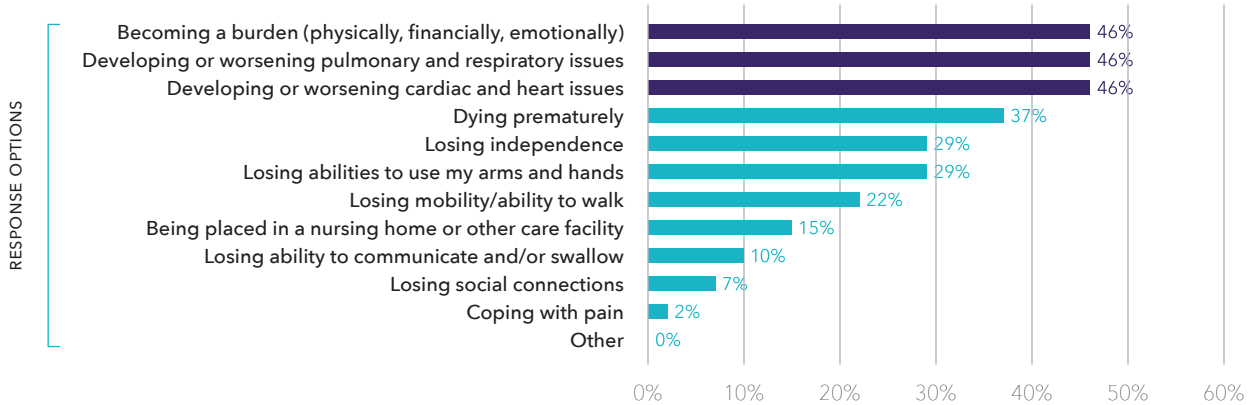
PERCENTAGE OF RESPONDENTS WHO SELECTED EACH OPTION (N=37) ▪ EACH RESPONDENT SELECTED AN AVERAGE OF 2.7 RESPONSES

4 Which everyday activities, that you cannot do at all or as fully as you would like because of your condition, are the most important to you? Select top THREE.



PERCENTAGE OF RESPONDENTS WHO SELECTED EACH OPTION (N=38)

5 What worries you most about your condition in the future? Select up to THREE.



PERCENTAGE OF RESPONDENTS WHO SELECTED EACH OPTION (N=41)

Appendix 6: Session 1 – Data Tables

Polling data from Session 1 **(Appendix 5)** was further broken down by subtype for individuals living with 2C, 2D and 2E only.

The tables below include a subtype-specific breakdown of the attendees who chose to participate in online voting, illustrated in **Appendix 5**.

A total of 15, 17 and 25 individuals living with LGMD subtypes 2C, 2D or 2E (or their representatives), participated in online polling, respectively. All individuals may not necessarily have responded to all polling questions. There were no individuals living with LGMD2F who participated in online polling.

The responses for these polling questions are not considered scientific data, but are provided to present a snapshot of those who participated in the LGMD EL-PFDD meeting and is intended to complement the patient comments made during and after the meeting.

1 Of all the LGMD symptoms you have experienced, which have the most significant impact on your daily life? Select up to THREE.

LGMD SUBTYPE RESPONSES	2C	2D	2E
Total number of responses	**41**	**34**	**31**
Unique participants from each subtype	**12**	**12**	**11**
Response options			
a. Cardiac (heart) issues	1	0	3
b. Contractures	1	1	2
c. Curvature of the spine (lordosis or scoliosis) or scapular winging	0	2	3
d. Difficulty using hands or arms	7	3	8
e. Fatigue	6	7	4
f. Impaired mobility (trouble walking, standing, transferring)	10	10	8
g. Pain	1	2	0
h. Poor sleep	4	2	1
i. Pulmonary (breathing) issues	7	3	0
j. Social/emotional concerns (isolation, depression, anxiety)	3	3	2
k. Speech and/or swallowing difficulties	0	0	0
l. Urinary/bowel issues (incontinence, constipation, UTI, rhabdomyolysis)	1	1	0
m. Other	0	0	0

2 As a result of your condition, which of the following statements are true? Select ONE.

LGMD SUBTYPE RESPONSES	2C	2D	2E
Total responses	**13**	**16**	**12**
Unique participants	**13**	**16**	**12**
Response options			
a. I have difficulty with activities involving upper extremities	0	0	0
b. I have difficulty with activities involving lower extremities and core	1	2	0
c. I have difficulty with activities involving both	12	13	12
d. I do not have difficulty with activities	0	1	0

3 Which daily living activities are you dependent upon a caregiver or family member to assist you with some or all of time? Select ALL that apply.

LGMD SUBTYPE RESPONSES	2C	2D	2E
Total responses	**88**	**63**	**79**
Unique participants	**14**	**11**	**12**
Response options			
a. Bathing	13	5	10
b. Bed mobility (getting in/out of bed, rolling over)	11	7	9
c. Dressing	12	8	10
d. Eating	2	5	4
e. Going to the bathroom	12	6	10
f. Household chores (shopping, cleaning, laundry)	12	10	11
g. Meal preparation	10	7	8
h. Transportation	11	9	10
i. Other	5	6	7
j. None, I am fully independent	0	0	0

4 Which everyday activities, that you cannot do at all or as fully as you would like because of your condition, are the most important to you? Select top THREE.

LGMD SUBTYPE RESPONSES	2C	2D	2E
Total responses	**42**	**36**	**32**
Unique participants	**14**	**13**	**11**
Response options			
a. Attending school or working	4	5	2
b. Being intimate with a spouse or partner	3	2	3
c. Childcare	0	0	1
d. Driving a motor vehicle	0	4	3
e. Exercising or participating in sports	8	3	3
f. Going out, socializing, traveling	8	8	8
g. Meal preparation	3	0	1
h. Performing household chores	0	1	3
i. Personal hygiene (bathing, toileting, dressing)	10	8	6
j. Walking	6	5	2
k. Other	0	0	0

5 What worries you most about your condition in the future? Select up to THREE.

LGMD SUBTYPE RESPONSES	2C	2D	2E
Total responses	**42**	**43**	**34**
Unique participants	**14**	**15**	**12**
Response options			
a. Becoming a burden (physically, financially, emotionally)	4	10	5
b. Being placed in a nursing home or other care facility	3	2	1
c. Coping with pain	0	0	1
d. Developing or worsening cardiac and heart issues	7	4	8
e. Developing or worsening pulmonary and respiratory issues	8	5	6
f. Dying prematurely	6	4	5
g. Losing abilities to use my arms and hands	4	5	3
h. Losing ability to communicate and/or swallow	2	2	0
i. Losing independence	3	8	1
j. Losing mobility/ability to walk	3	3	3
k. Losing social connections	2	0	1
l. Other	0	0	0

Appendix 7: Session 2A – Living with LGMD2A

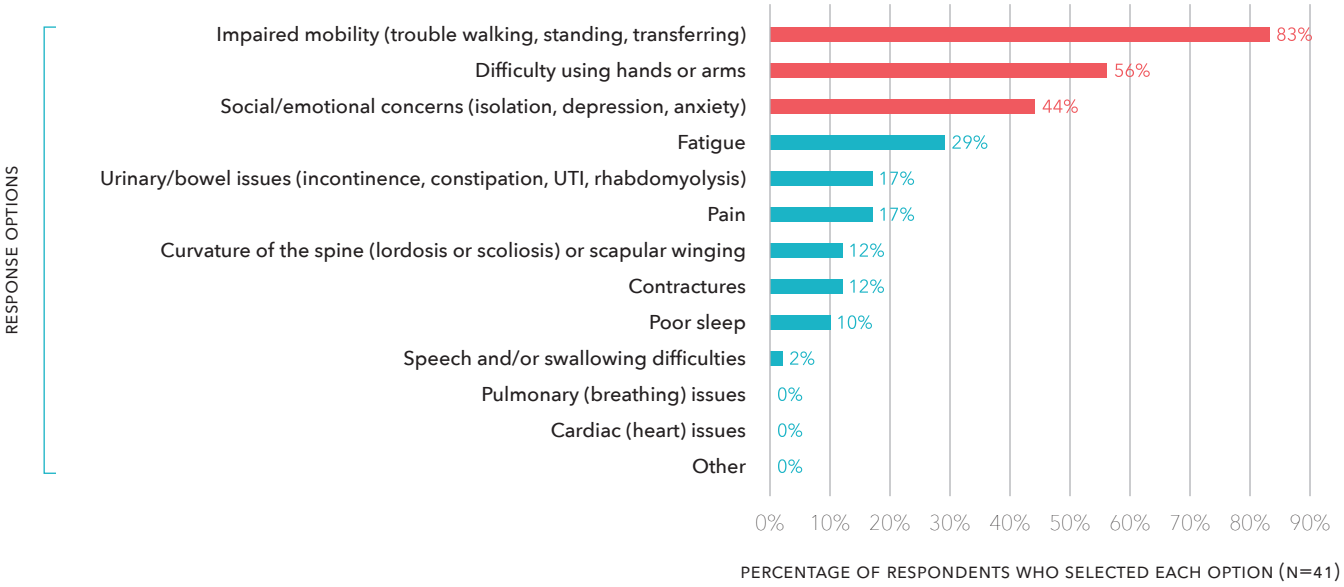
Symptoms, health effects and impacts on daily life

The graphs below include all attendees who chose to participate in online voting. Parents and caregivers were asked to answer the questions on behalf of the individual living with LGMD. The number of affected individuals and caregivers who responded to each polling question is shown below the X axis (N=x).

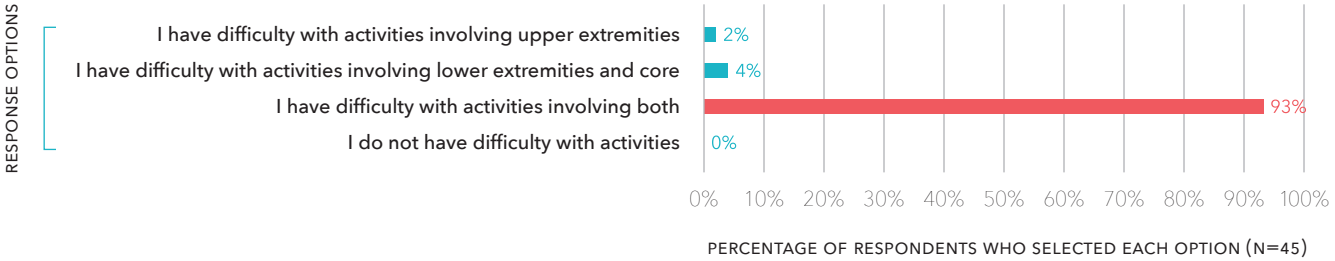
While the response rates for these polling questions is not considered scientific data, it provides a snapshot of those who participated in the LGMD EL-PFDD meeting and is intended to complement the patient comments made during and after the meeting.

Note that due to a world-wide YouTube outage during Session 2, there were fewer respondents for poll question five.

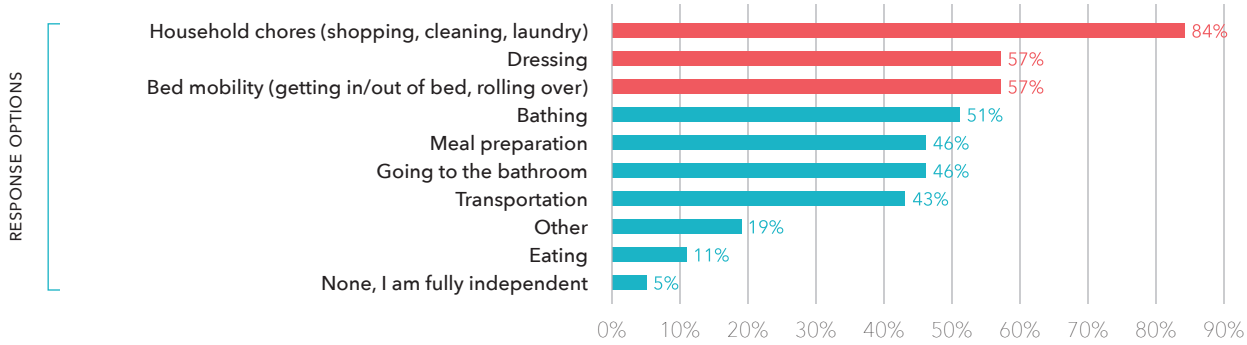
1 Of all the LGMD symptoms you have experienced, which have the most significant impact on your daily life? Select up to THREE.



2 As a result of your condition, which of the following statements are true? Select ONE.

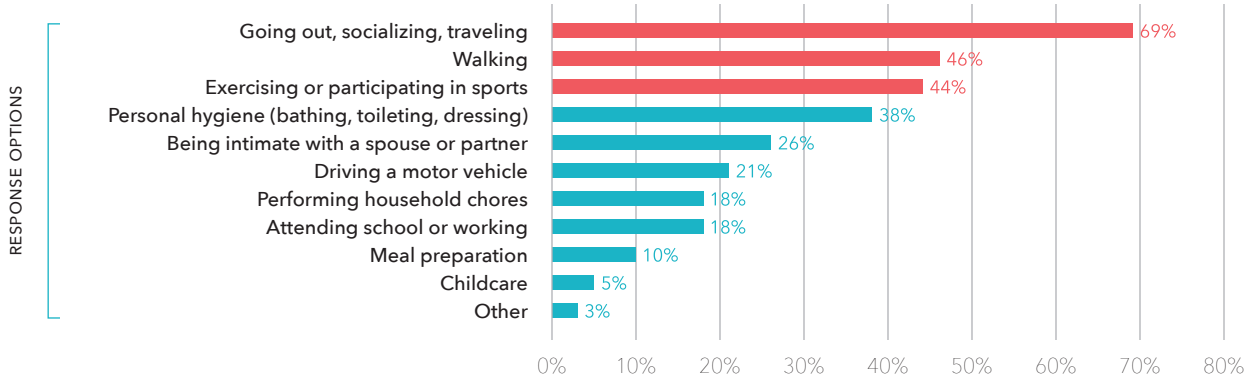


3 Which daily living activities are you dependent upon a caregiver or family member to assist you with some or all of time? Select ALL that apply.



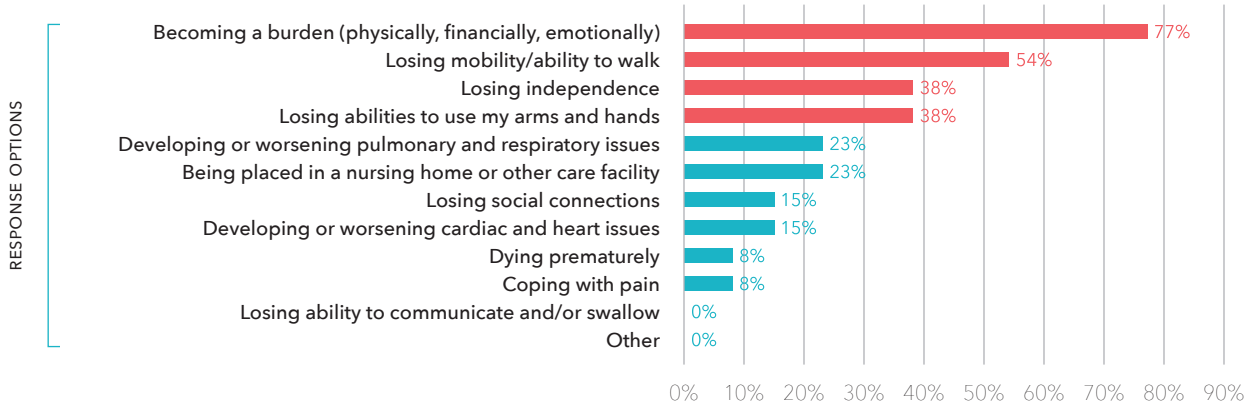
PERCENTAGE OF RESPONDENTS WHO SELECTED EACH OPTION (N=37) ▪ EACH RESPONDENT SELECTED AN AVERAGE OF 4.2 RESPONSES

4 Which everyday activities, that you cannot do at all or as fully as you would like because of your condition, are the most important to you? Select top THREE.



PERCENTAGE OF RESPONDENTS WHO SELECTED EACH OPTION (N=39)

5 What worries you most about your condition in the future? Select up to THREE.



PERCENTAGE OF RESPONDENTS WHO SELECTED EACH OPTION (N=13)

Appendix 8: Session 2i - Living with LGMD2i

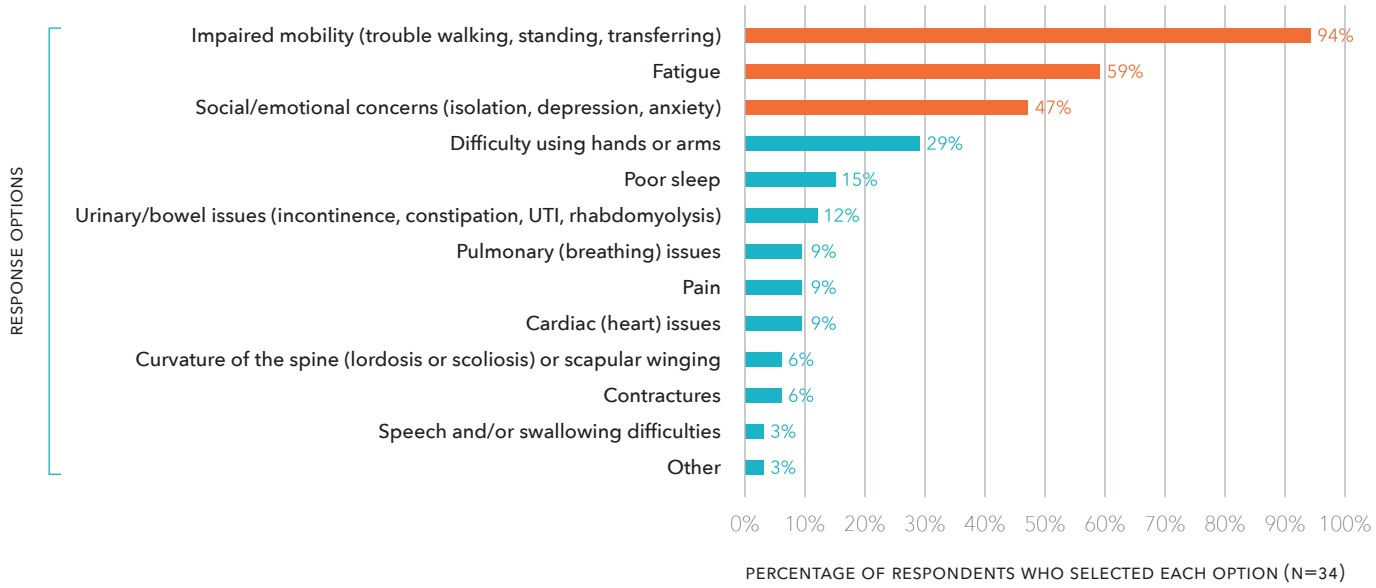
Symptoms, health effects and impacts on daily life

The graphs below include all attendees who chose to participate in online voting. Parents and caregivers were asked to answer the questions on behalf of the individual living with LGMD. The number of affected individuals and caregivers who responded to each polling question is shown below the X axis (N=x).

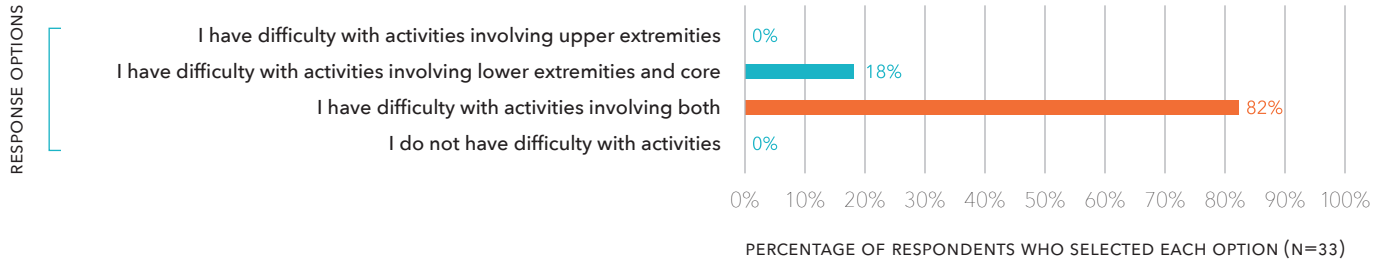
While the response rates for these polling questions is not considered scientific data, it provides a snapshot of those who participated in the LGMD EL-PFDD meeting and is intended to complement the patient comments made during and after the meeting.

Note that due to a world-wide YouTube outage during Session 2, there were fewer respondents for the fifth poll question.

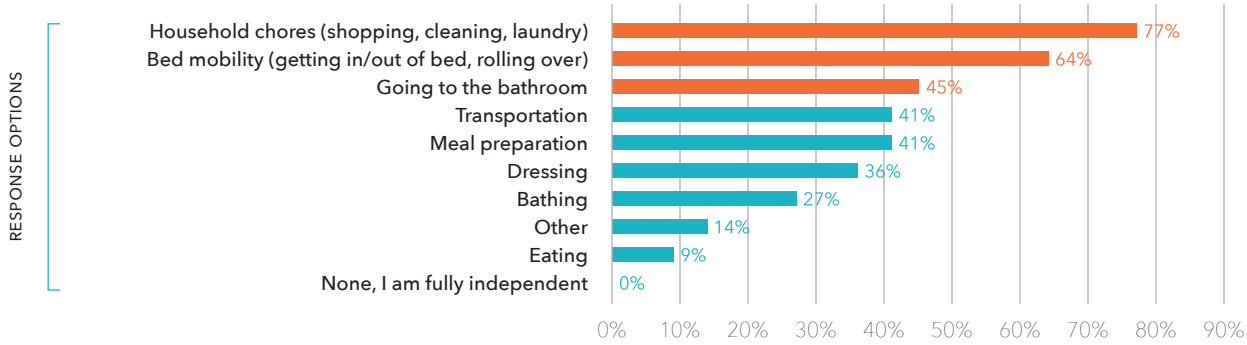
1 Of all the LGMD symptoms you have experienced, which have the most significant impact on your daily life? Select up to THREE.



2 As a result of your condition, which of the following statements are true? Select ONE.

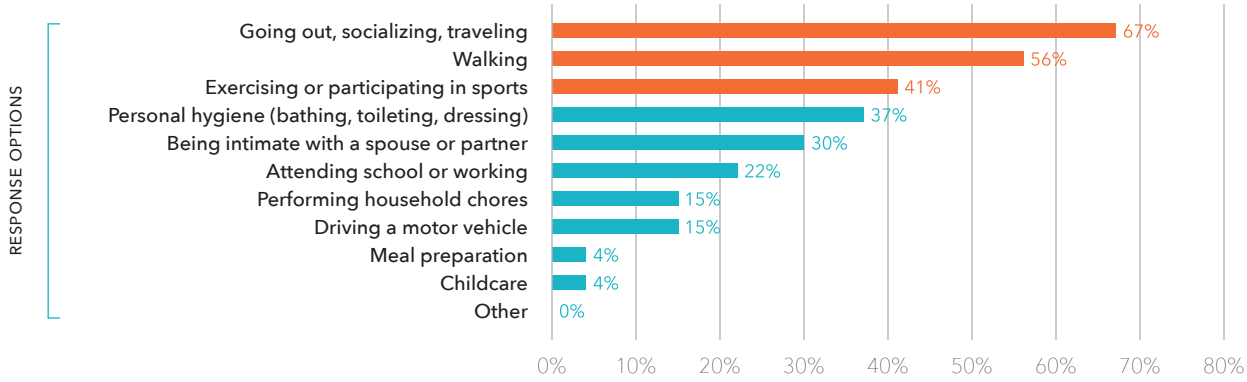


3 Which daily living activities are you dependent upon a caregiver or family member to assist you with some or all of time? Select ALL that apply.



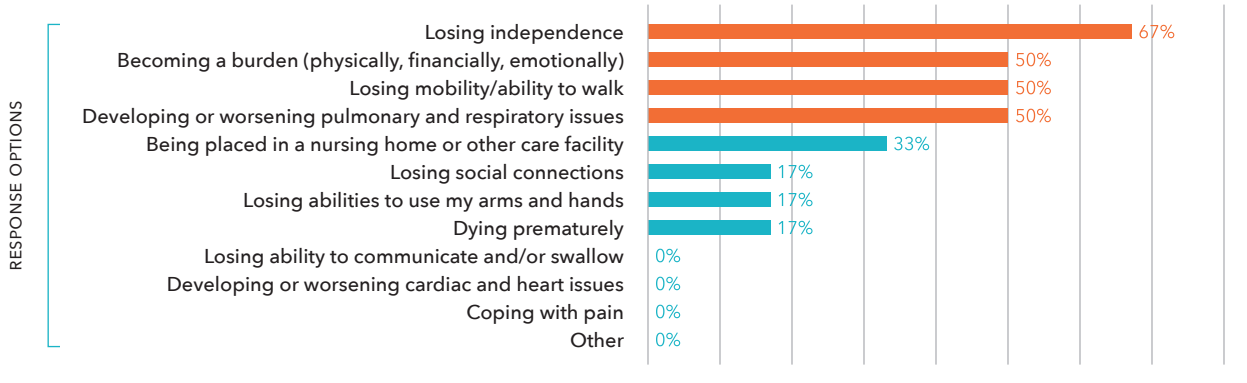
PERCENTAGE OF RESPONDENTS WHO SELECTED EACH OPTION (N=22) ▪ EACH RESPONDENT SELECTED AN AVERAGE OF 3.5 RESPONSES

4 Which everyday activities, that you cannot do at all or as fully as you would like because of your condition, are the most important to you? Select top THREE.



PERCENTAGE OF RESPONDENTS WHO SELECTED EACH OPTION (N=27)

5 What worries you most about your condition in the future? Select up to THREE.



PERCENTAGE OF RESPONDENTS WHO SELECTED EACH OPTION (N=6)

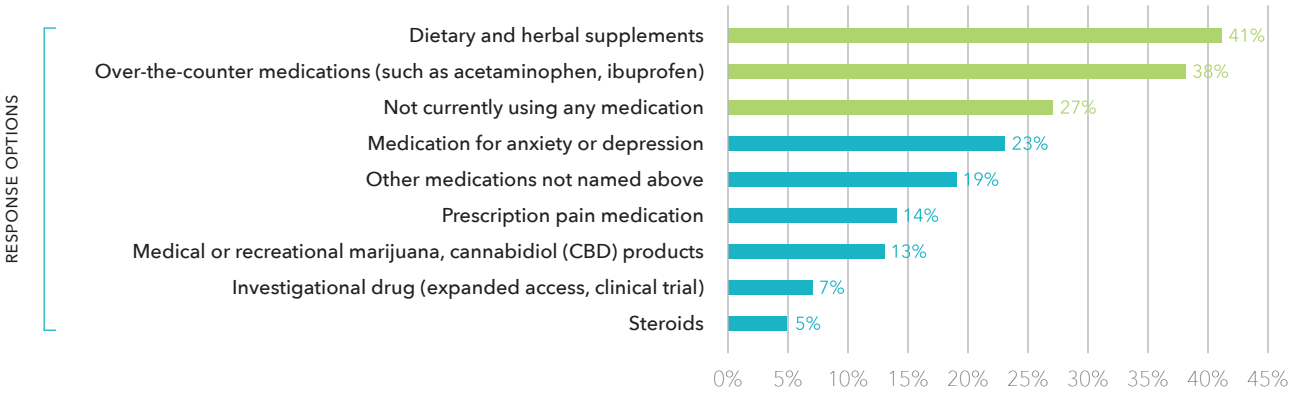
Appendix 9: Session 3 – Current and Future Treatments

All six subtypes

The graphs below include all attendees who chose to participate in online voting. Parents and caregivers were asked to answer the questions on behalf of the individual living with LGMD. The number of affected individuals and caregivers who responded to each polling question is shown below the X axis (N=x).

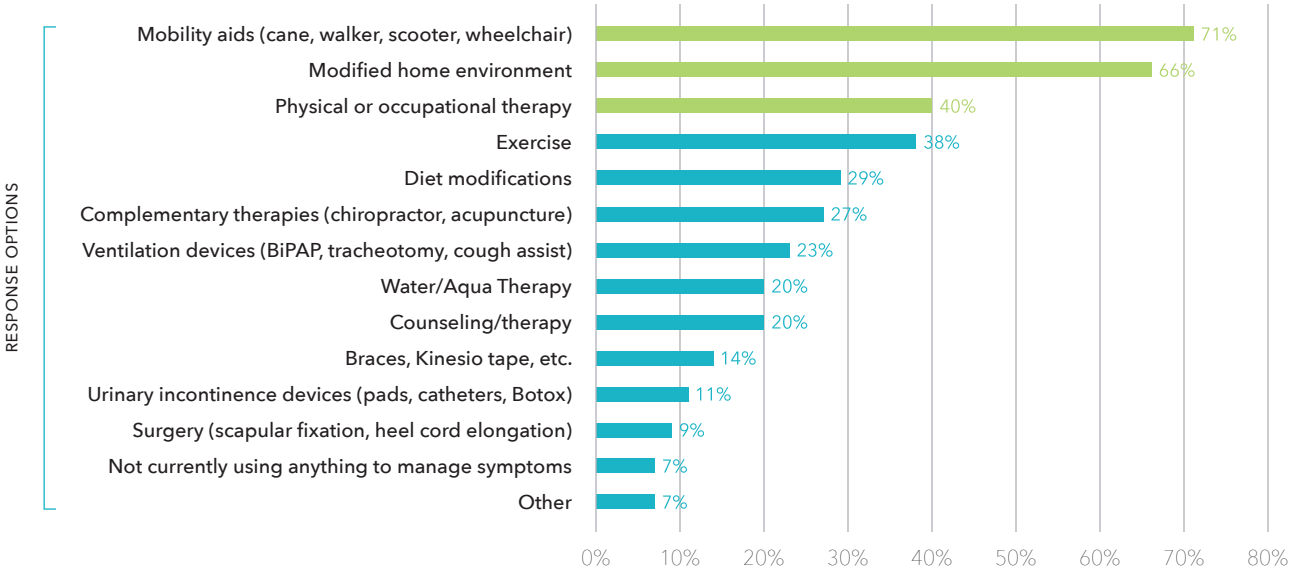
While the response rates for these polling questions is not considered scientific data, it provides a snapshot of those who participated in the LGMD EL-PFDD meeting and is intended to complement the patient comments made during and after the meeting.

1 Which of the following medications do you use to manage LGMD symptoms? Select ALL that apply.



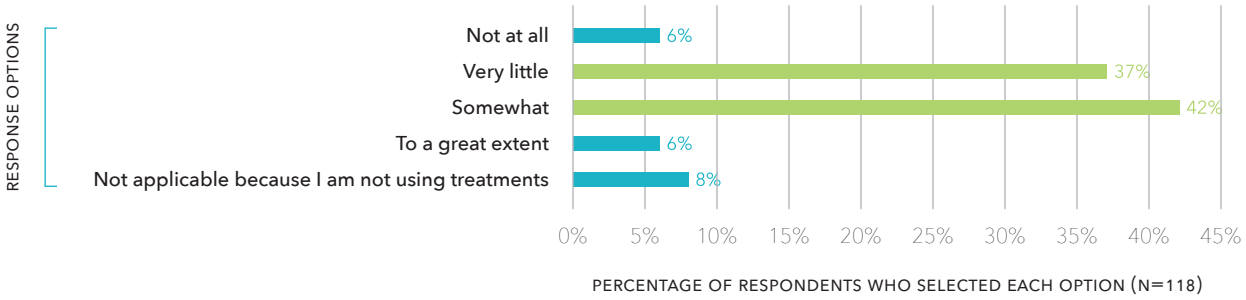
PERCENTAGE OF RESPONDENTS WHO SELECTED EACH OPTION (N=113) ▪ EACH RESPONDENT SELECTED AN AVERAGE OF 1.9 RESPONSES

2 Beyond medications and supplements, are you using any of the following to manage LGMD symptoms? Select ALL that apply.

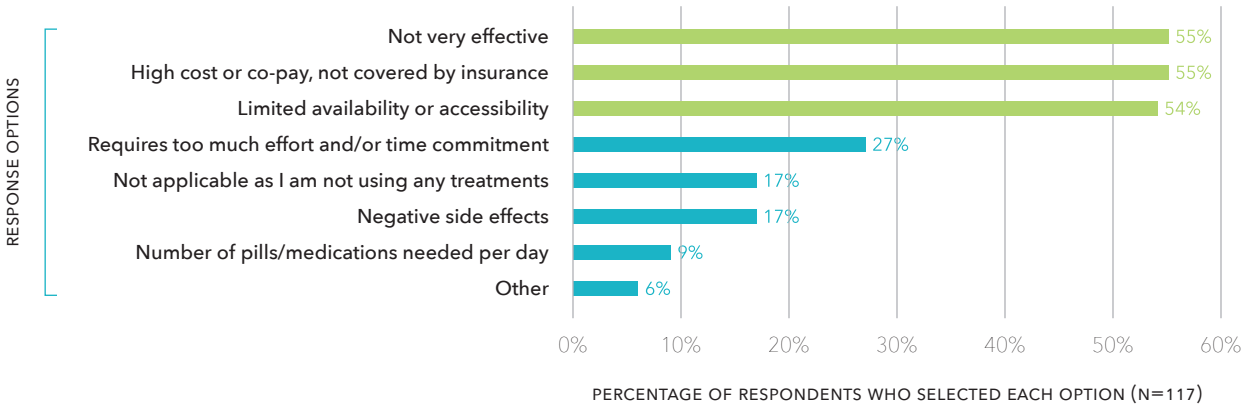


PERCENTAGE OF RESPONDENTS WHO SELECTED EACH OPTION (N=114) ▪ EACH RESPONDENT SELECTED AN AVERAGE OF 3.8 RESPONSES

3 How well does your current regimen control your symptoms overall?



4 What are the biggest drawbacks of your current approaches? Select up to THREE.



5 Short of a cure, what would represent a meaningful benefit to you in a future treatment? Select your TOP choice.