

# **Limb-Girdle Muscular Dystrophy Externally-Led Patient Focused Drug Development Meeting**

September 23, 2022

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James Valentine, JD, MHS (00:00:00):

Jennifer Levy, PhD (00:16:23):

Good morning. My name is James Valentine, and welcome to the externally led patient-focused drug development meeting on limb-girdle muscular dystrophy subtypes 2A, 2C, 2D, 2E, 2F and 2I. I'm here in the studio with my co-host Jen Levy from Coalition to Coalition to Cure Calpain 3.

(00:16:44):

Thank you James. I'm the scientific director for Coalition to Cure Calpain 3. I'm so excited to be a part of this important day for the LGMD community. I'm looking forward to hearing all of your voices throughout the day. But before we get started, I'm going to pass it back to James to introduce one of our partners.

James Valentine, JD, MHS (00:17:01):

Thank you, Jen. Jen and I are coming to you live from the Washington, D.C. Metropolitan Area, actually not too far from where the U.S. Food and Drug Administration's headquarters are located. At this point, it's my pleasure to introduce one of our meeting partners, Kathryn Bryant-Knudson, who's the founder and president of The Speak Foundation, and would be providing some welcoming remarks. Kathryn?

Kathryn Bryant Knudson (00:17:28):

Thank you, James. Welcome everyone to the externally LED patient-focused drug development meeting on limb-girdle muscular dystrophy subtypes 2A, 2C, 2D, 2E, 2F and 2I. I'm Kathryn Bryant-Knudson, living with LGMD 2I, and I'm the founder of The Speak Foundation. It's been my pleasure to plan this meeting alongside the leaders of five other nonprofit organizations that make up the LGMD Coalition. They are Coalition to Cure Calpain 3, the CureLGMD2I Foundation, the Kurt and Peter Foundation, the LGMD2D Foundation, and the McColl Lockwood Laboratory.

(00:18:27):

Our collective mission is to seek patient and caregiver perspectives on how 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. As you will hear and see today, many living with LGMD are severely affected and some have lost their lives.

(00:18:59):

Limb-girdle muscular dystrophy affects multiple body systems. There are no FDA approved treatments for any form of limb-girdle muscular dystrophy. We urgently and desperately need better treatments for people living with LGMD. This meeting will focus on a subset of LGMD types, and we hope that there will be future EL-PFDD meetings to address other subtypes. While listening and learning today, try to imagine what our lives are like. We hope and expect this meeting will encourage future research and successful new product development for people living with LGMD. We urgently need options. We would also like to see more interest in research for the rare forms of LGMD in the future. Thank you so much to the U.S. Food and Drug Administration for giving us permission to hold this meeting and for attending. We are incredibly grateful for this opportunity to share our experiences with you.

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(00:20:13):

Thank you also to our generous supporters who financially sponsored this meeting, including Sarepta Therapeutics, AskBio, Edgewise, ML Bio Solutions and Vita Therapeutics. We are also pleased to have in attendance representatives from advocacy and professional organizations, drug companies, federal agencies and universities from across the world.

(00:20:47):

To the people with LGMD and your loved ones who are participating, this meeting is for you. We encourage you to call or write in during the program and we ask that you participate in the remote polling. We want to hear as many perspectives as possible. Understand that we'll do our best to get all your comments. Please only use your first name and no other identifying information. The comments that we cannot get to on the air will be just as important though because they will be collected and could be published in the Voice of the Patient report that we will do after this meeting. Let's get started. To begin today's meeting, I am thrilled to introduce Dr. Wilson Bryan. Dr. Bryan is the director of the Office of Tissues and Advanced Therapy in the Center for Biologics Evaluation and Research, otherwise known as CBER at the FDA. Dr. Bryan will provide some opening comments from the FDA perspective. Dr. Bryan, over to you.

Wilson Bryan, MD (00:21:59):

Good morning. Thank you for that kind introduction. I am here today along with colleagues from the FDA Center for Drug Evaluation and Research and Center for Biologics Evaluation and Research. I appreciate the opportunity to say a few words on behalf of the FDA. Throughout the 1990s, I worked in several neuromuscular clinics at a medical school in Dallas, Texas. During those years, I remember seeing many adult and pediatric patients with limb-girdle muscular dystrophy. Some of those patients had severe disability while others were only mildly affected.

(00:22:48):

But in those days, my colleagues and I were unable to distinguish the different forms of limb-girdle dystrophy. I stopped seeing patients a little over 10 years ago, so it's been quite a while since I saw a patient with limb-girdle dystrophy. I know that things have changed. In the late '90s and early 2000s, the Human Genome Project mapped virtually all of the genes in the human body. Now, the many different types of limb-girdle dystrophy can be distinguished from each other, and we are beginning to fully grasp the pathophysiology and natural history of each of these disorders.

(00:23:40):

In spite of this scientific progress, I suspect that what I might hear today from Dr. Matthews and from the patients is that patients continue to struggle to get an accurate diagnosis. I'm sure that there remains uncertainty about the rate of progression and the prognosis for each individual patient. That reminds us that getting a diagnosis is not enough. We need treatments. These treatments could be innovative devices or new life's changing drugs.

(00:24:26):

I work in the part of the FDA that regulates gene therapies, so I am particularly excited about the possibility of developing separate gene therapies for each form of limb-girdle dystrophy. What we'll learn at this meeting will help us in the development of those treatments, particularly what we hear will

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help the FDA 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.

(00:25:14):

Also, this meeting's Voice of the Patient report will become a reference document for our review staff as we consider new applications. Therefore, I would like to thank the LGMD Coalition for organizing this meeting. I would also like to thank Sarepta Therapeutics, AskBio, Edgewise Therapeutics, ML Bio Solutions and Vita Therapeutics for sponsoring this patient-focused drug development meeting, and more importantly, for the work that they are doing to develop new treatments for limb-girdle dystrophy.

(00:26:02):

Drug development is not easy. It requires many years of scientific research and a commitment of substantial resources in the effort to make life better for patients. All of us owe you a debt for that commitment and effort. I also want to thank you, the patients and caregivers, whom we will hear from today. My understanding is that today's meeting focuses on limb-girdle dystrophy types 2A, 2C, 2D, 2E, 2F and 2I. As we learn more about each of these disorders, we understand that while these disorders may have some common features, no two forms of limb-girdle dystrophy are exactly alike.

(00:27:03):

In the same way, no two people with any specific type of limb-girdle dystrophy are exactly alike. So while it is important that we hear the voice of the limb-girdle community, it is even more critical that we hear the many individual voices of the members of this community, discussing the full range of challenges that you are facing. Those of us at the FDA need for each of you to continue to speak up, and we will continue to listen. Back to you in the studio.

Jennifer Levy, PhD (00:27:46):

Thank you, Dr. Bryan. Now I'd like to introduce Dr. Katherine Matthews who will be providing a clinical overview of LGMD. Dr. Matthews is professor of pediatrics and neurology and director of the neuromuscular program at the University of Iowa, Carver College of Medicine. Dr. Matthews, take it away.

Katherine Mathews, MD (00:28:07):

Hello, I'm Kathy Matthews and I'm at the University Iowa. I've been asked to do a very high level introduction to limb-girdle muscular dystrophy before we get into the meat of this meeting, listening to the patient and caregiver stories. So I do have a number of disclosures. I'm involved in clinical trial work and I have funding from NIH, CDC and Friedreich Ataxia Association.

(00:28:35):

So what is limb-girdle muscular dystrophy? So it was a category that was first proposed in 1954 and has been used over time to include a wide range of diseases. Because of this wide range of diseases that it was included, in 2017, our colleagues in Europe convened a workshop and tried to refine the definition. So the current 2017 definition of limb-girdle muscular dystrophy is a genetic disorder that presents with proximal muscle weakness as shown in the little image there.

(00:29:13):

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It causes progressive weakness due to a loss of muscle fibers, and we can detect that loss of muscle fibers by measuring creatine kinase or CK which is elevated in the blood. The genetics of limb-girdle muscular dystrophy is somewhat complex. A recent study found almost 170 genes associated with proximal muscle weakness, and there are at least 30 genes cause limb-girdle muscular dystrophy as defined by that 2017 criteria. One gene can be associated with multiple phenotypes and some genes can cause either dominant or recessive limb-girdle, so it is complicated.

(00:29:56):

Here is an overview of the different forms, subtypes of limb-girdle muscular dystrophy that meet the definition from the 2017 workshop. So in addition to changing the diagnostic criteria, they also changed the way we number the diseases. In this talk, I'm going to refer to both the old way and the new way, and shown here is the new nomenclature where R refers to a recessive disease and D refers to a dominant disease.

(00:30:34):

So the prevalence numbers for limb-girdle are somewhat variable, based on both the definition that I already referred to and to the existence of founder mutations where one geographical population will have a very high rate of one kind of limb-girdle muscular dystrophy. There's also variability in how limb-girdle is diagnosed for the purposes of epidemiology. But at a very high level, we can look at how common limb-girdle muscular dystrophy is relative to other kinds of muscular dystrophy.

(00:31:12):

So MD STARnet uses chart reviews from six geographic areas in the United States, and at a very high level again, reported how many times these each form of muscular dystrophy was found in the chart. So of approximately 1,700 people, about 250 had a diagnosis of limb-girdle muscular dystrophy recorded in the chart, and this was about 15% of the six kinds of muscular dystrophy reported in this study.

(00:31:44):

We can then drill down to look at within the population of limb-girdle muscular dystrophy how common are each of those subtypes that we talked about. I've shown here the distribution from one study, but really the patterns are similar across many studies of epidemiology. First of all, the recessive limb-girdle muscular dystrophies are far more common than those that are dominant. So the recessive muscular dystrophies require that you have one abnormal copy of the gene from your mother and the second abnormal copy of the gene from your father.

(00:32:20):

Among all the limb-girdles, mutations in Calpain 3 and dysferlin are the most common causes of limb-girdle. Then they're followed by mutations in FKRP, the sarcoglycanopathies as a group. So FKRP, the sarcoglycanopathies, there's one and Calpain, and ANO5. In this session, we're going to focus on Calpain, FKRP and the sarcoglycanopathies.

(00:32:55):

So clinicians have spent a lot of time trying to figure out how when a patient presents, they could predict which gene was the most likely cause for that person's limb-girdle muscular dystrophy. The bottom line, we couldn't do it very well because of the amount of clinical overlap. So really to identify the specific limb-girdle subtype requires genetic testing panels, which are pretty readily available today.

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(00:33:25):

Across the board, the common ways that limb-girdle presents are proximal muscle weakness being the most common. So patients may say they can't run anymore, they have trouble climbing stairs, they need to use the railing, they have trouble getting up from chairs, trouble getting into the car. If they're children, can't keep up with peers in gym class. They may notice increased falling. A second common presentation is what's called elevated liver function tests. So a primary care doctor might do a broad panel to assess health because of some unrelated problem, find abnormalities in these and...

Katherine Mathews, MD (00:34:00):

... of some unrelated problem find abnormalities in these enzymes that come from either the muscle or the liver, AST and ALT. And then, those ultimately are found to be from the muscle have elevated CK and end up with a neurologist, and we make the diagnosis. And then, muscle pain can also be a reason that brings people to the doctor.

(00:34:25):

If we look briefly at the specific subtypes mutations in Calpain 3 cause limb-girdle 2A/R1. It is a calcium dependent protease, which is an enzyme. The people who have this form of muscular dystrophy have onset of weakness, either in childhood through early adulthood. They have high CK, which is now required for the definition, and they may have prominence of the shoulder blades. The heart is typically not involved in this form of muscular dystrophy.

(00:34:58):

I'm going to introduce the sarcoglycanopathies and the dystroglycanopathies together, because they both affect this dystrophin glycoprotein complex. This is inside the cell, outside the cell, and this is the muscle cell membrane. This complex attaches the inside of the cell to the fibrous tissue outside the cell and provides stability to that muscle cell membrane. If you disrupt the complex, that muscle cell membrane is prone to breakdown and you get muscular dystrophy. We can't tell this group of disorders apart from Duchenne and Becker. Up here, I've shown you the types of muscular dystrophy that we're going to be talking about that affect this complex.

(00:35:49):

The sarcoglycanopathies are structural proteins that go through the membrane. They're shown here. Here are the four diseases that are included in the sarcoglycanopathies. They typically have weakness with onset in childhood, often have muscle hypertrophy, so the calves might look very large even though the child has weakness around the hips. The heart and the respiratory muscles are typically involved with one exception shown here.

(00:36:17):

The dystroglycanopathies are a little bit different because while beta-dystroglycanopathy goes through the membrane, like the sarcoglycans do, alpha-dystroglycan is outside the membrane, and alpha-dystroglycan has lots of sugar groups. There are about 30 genes that are required to put those sugar groups onto alpha-dystroglycan. And the dystroglycanopathies are caused by abnormalities of those 20 genes. I'm sorry, I think I said 30. 20 genes that are required for those sugar groups being put on properly.

(00:36:53):

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The most common, shown in this pie graph here, is LGMD 2I/R9, FKR-related, which counts for at least 60% of cases. The onset of weakness in LGMD 2I/R9 is highly variable, from early childhood into mid adulthood. Respiratory and heart involvement are common.

(00:37:18):

When we go back to thinking about the limb-girdles as a group, they have progressive weakness so that people may need to use a wheelchair when they're teens or sometime earlier mid adulthood. Some people walk into later adulthood. Pain is relatively common in adulthood. About 30% patients are on prescription medicines in adulthood. Respiratory muscle weakness may require things like BiPAP to support breathing. If it involves the heart, you may have shortened life expectancy as shown in this graph that shows the probability of developing abnormal heart function in LGMD 2I.

(00:38:03):

There's a critical need to develop treatments to prevent or slow skeletal muscle weakness, breathing muscle weakness, and heart muscle weakness. We have some positive things going for us. An engaged and motivated patient population as shown by the participation here. An increasingly deep understanding of the pathophysiology, which I've sort of talked about earlier. There's overlap with other types of muscular dystrophy, and we have a lot of experience on research with Duchenne muscular dystrophy. We can learn from some of that experience in planning trials for limb-girdle muscular dystrophy. We have natural history data for many of the subtypes of limb-girdle muscular dystrophy in humans. And then, we have animal models available for most of the subtypes, which is critical for testing new potential treatments.

(00:38:58):

There are some challenges, probably the main challenge is that limb-girdle muscular dystrophies are rare as a group. When you think about each specific subtype, each gene abnormality, it's even more rare. It's probable that there are some patients who aren't followed by large neuromuscular clinics, and so may not be easily available, findable for doing clinical trials. Historically, there's been incomplete genetic diagnosis of patients, but I think that's changing as genetic testing has become more easily available. I've already alluded to the genetic and pathophysiologic complexity of these groups. There are many genes, there are different subgroups, and there's no single treatment that is going to treat all limb-girdle muscular dystrophy.

(00:39:49):

We do have things in the treatment pipeline, and I divide these into those that are specific to a type and those that are not specific to the specific gene or subtype. The gene nonspecific things, we can try to increase muscle strength or decrease muscle breakdown at a level past the level of the gene. And then, the subtype specific treatments, there's one that is in early trials now that is to try to push a defective enzyme to work harder in LGMD 2I. There's also gene replacement. This is happening across genetic diseases, or gene editing to try to decrease the impact of specific mutations in a gene. It's likely that any given individual may need more than one treatment over their lifetime, so there's a lot of room to develop range of treatments to get the best possible outcomes in this group of diseases. So, limb-girdle muscular dystrophy is a group of genetically distinct muscular dystrophy with overlapping features. We are lacking specific disease-modifying treatments, and care currently is largely supportive. With that, I thank you for your attention, and I will turn the meeting back over to the organizers. Thank you.

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Jennifer Levy, PhD (00:41:28):

Thank you, Dr. Matthews. Now, I'd like to welcome our moderator for today's meeting, James Valentine, who has been working with us over the past several months as he's helped us plan this meeting. James has worked the last 14 years as a champion for the patient voice. James previously worked at the FDA where he was a patient liaison, helping to incorporate the patient perspective into medical product review. There, he helped develop and launch the patient focus drug development initiative. In private practice, James has worked with many patient organizations to ensure their community's voices were heard by decision makers. Relevant to today's meeting, James has been involved in helping plan and moderating three quarters of the over 60 externally-led PFDD meetings. So, we're in good hands with James.

James Valentine, JD, MHS (00:42:13):

Yes. Well, thank you so much, Jen. It's such a pleasure to have been able to work with the LGMD coalition to help organize this meeting, and now spend this day with the community, hearing your voices. Now that we have heard a clinical overview from a disease expert, we get to finally turn to the core of today's meeting, which is to hear from you, people living with LGMD subtype 2A, 2C, 2D, 2E, and 2F, and 2I, as well as their direct caregivers and family members. As we've heard, patient-focused drug development is a more systematic way of gathering patient perspectives on their condition and on available treatments.

(00:42:54):

As we heard from FDA's Dr. Bryan, your input can help inform the agency's understanding of LGMD to inform drug development and review. While FDA's held many of its own patient-focused drug development meetings, today marks the 64th externally-led patient-focused drug development meeting. With over 7,000 known rare conditions, that really makes this a unique and important opportunity for this community.

(00:43:23):

Today's meeting is interactive, so let me tell you a bit about what we'll be asking of you and how today's meeting will be organized. First, starting in the morning, we're going to have a pair of sessions where we'll be exploring the patient and caregiver experience of living with LGMD and its impacts on your daily life. Then in a third session, we'll come back after a break in the afternoon to explore the various approaches to treatment, including participating in clinical trials. We'll also, in that session, be asking for your preferences for future treatments for your LGMD.

(00:43:58):

What will these different discussions look like? Well, today, we'll primarily be using three different methods or ways to bring your voices into the conversation. We'll be starting each of our sessions by hearing from panels, made up of both patients and caregivers of individuals with LGMD. These panelists will set a good foundation for our broader discussion, and they were selected to reflect a range of different experiences with the various LGMD subtypes that we'll be covering today. But we recognize that a panel of even a handful of patients and caregivers can't fully reflect the range of experiences, which is why we'll build on those panel discussions through a live audience discussion that I'll be facilitating with all of our patients and caregivers that are tuned in today.

(00:44:45):

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I'll be asking questions and inviting you to state your name and your subtype of LGMD, and provide a comment on these various topics. This can be done in one of two ways. We'll be inviting you to dial in by phone and share your comments and talk with us live, as well as to submit written comments, which can be done on the web form that's under the livestream on the webpage today. You'll also see that we'll be having a Zoom panel of patients and caregivers who will also be adding their thoughts and experiences throughout the program.

(00:45:19):

The third way we'll be bringing your voices into the conversation are through some remote polling questions. We'll be inviting patients and caregivers only to use their phone to respond or doing so on the web. In fact, we want to take a moment here just to go ahead and get you on this system now. So that way, in a few moments, when we get to our first set of polling questions, you'll already be there, and this is a page you can keep up throughout the day today. New questions will automatically arrive there.

(00:45:48):

At this point, I want to invite you to take out your phone, open up a web browser, or if you're following along on your computer, you can open a new tab in your web browser. Go to [www.PollEV.com/LGMD](http://www.PollEV.com/LGMD). Again, feel free to go there now, [www.PollEV.com/LGMD](http://www.PollEV.com/LGMD), and we'll be getting to polling very soon. These polling questions will broaden the discussion to everyone, give us a sense of the different experiences in our audience today, as well as aid in our discussion, as we want you to help explain your choices, why you made certain selections of the different response options. And, again, we'll invite you to call in and write in to help us understand those.

(00:46:35):

I want to mention that there'll also be an opportunity to provide written comments for 30 days after this meeting. Perhaps you'll think of something else that you weren't able to share during the live meeting today. Maybe you weren't able to share everything that you wanted, or perhaps you're watching this video on demand right after the meeting, and you would like to provide your comments. We invite you to do so, again, for the next 30 days after this meeting. All of today's input and that written input will be summarized in what's called a voice of the patient report, a summary of today's proceedings, which will be provided both to the Food and Drug Administration, as well as made publicly available for researchers and drug developers to access.

(00:47:21):

One more thing before we get to our first set of polling questions is I want to cover some ground rules for today's meeting. We encourage individuals with LGMD and their caregivers to contribute to the dialogue through polling, phone, and written comments. The discussion today is limited to patients, family members, and other direct caregivers with LGMD subtypes 2A, 2C, 2D, 2E, 2F, and 2I only. We understand that there may be some of you from the LGMD community living with other subtypes that are on today, and we welcome you to tune in, but we do ask that you refrain from answering questions. It is the hope of your community's leaders that there will be opportunities to have your voices heard in future meetings.

(00:48:06):



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I'd also like to note that our colleagues from the Food and Drug Administration, from drug development companies, as well as clinicians and researchers are here, and they are here to listen only as well. Views expressed today will be inherently impersonal, and the discussion may at times get emotional. And so, respect for one another is paramount. To that end, we ask that you please do try to be focused and concise in your comments, so that way, we can hear as many voices as possible. Without further ado, let's get into our first set of polling questions, which will give us a sense of who we have in our live audience today. Again, please go to [PolLEV.com/LGMD](https://PolLEV.com/LGMD), and you can do that on your phone browser, on a web browser tab on your computer. Let's go ahead and get into our first polling question.

(00:48:59):

Here, we want to know have you, and again, this is open to the patients and caregivers of the different LGMD subtypes we're covering today. We ask that you select all that apply. Are you an individual living with LGMD, one of these subtypes? Or are you a parent or caregiver of an individual with LGMD? We understand that you may be both a patient and a caregiver, in which case you can select both options. I will mention that because we are allowing individuals to select more than one option, we're seeing a percentage of total responses, not a percentage of people that select one of these individual responses.

(00:49:47):

I know this is a simple question, yet we want to spend a few moments here just to make sure all of you have an opportunity to get into this polling system. As I mentioned, we'll be going to these polling questions throughout the day. We've got a few more to follow in this first set, but we want to make sure we can track your responses throughout the whole program, and we'll be able to also share those responses in our voice of the patient report.

(00:50:18):

It looks like about two-thirds of our responses are indicating that we have quite a few individuals living with LGMD that have joined us today, but it's also great to see that we also have a large contingency of parents and caregivers. For those of you that may be both, we certainly want to hear from both of your perspectives as someone living with the condition, as well as someone who cares for someone else living with the condition. Just to make sure it's clear, if you are a parent or a caregiver and you yourself are not living with LGMD, we want to hear your voices too.

(00:50:57):

We're going to do our second polling question. Here, we want to know where you, or your loved one who is living with LGMD lives. The options are: A, in the US Northeast; B, in the US Mid-Atlantic; C, in the US Midwest; D, in the US South; E, in the US Mountain region; F, in the US West Coast; G, Canada; H, Central or South America; I, Europe or the UK; J, Asia; K, Africa; L, Australia or New Zealand; or M, some other country or region that's not otherwise listed in this question. Again, we want to know where all of our patients and our caregivers today, where you live. We'll give you a few moments here for everybody to get in their responses.

(00:51:53):

Right off the bat, I'm so pleased to see that every single one of these is being selected. That means we've got a good representation from not only all across the US, the different regions of the United States, but really from around the world. For those of you who are joining us from outside of the United States, we want to welcome you and invite you to participate fully in this meeting. This truly is an open

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meeting, and we welcome you regardless of where you live. I do see we do have good representation across the US with some of the regions, most well represented being the Midwest, Northeast, South, and West. We also have a large contingency from Europe and UK, but again, we're seeing participation from all around the world.

(00:52:42):

If we go to our next polling question. Here, we want to know what is your age, or if you're a caregiver, what is the age of your loved one who's living with LGMD. This is the age of the person with LGMD. The options are: A, younger than five years of age; B, between five and 11 years of age; C, between 12 and 17 years; D, 18 to 29 years; E, 30 to 39 years; F, 40 to 49 years; G, 50 to 59 years; or H, 60 years of age or older.

(00:53:22):

As you'll see, all of our questions moving forward are asked in terms of their wording to the patient, person living with LGMD. So for caregivers, you'll be answering all of our questions thinking of and on behalf of the person with LGMD that you care for.

(00:53:43):

Again, great to see a great range of ages of individuals living with LGMD represented today. It looks like our slightly largest group is the 30 to 39 year age range, followed close behind those in the just younger age range of 18 to 29, and just older age range of 40 to 49. But we're really seeing actually quite a nice bell curve here, and glad to see that we do have representation both in our youngest age ranges, in those various pediatric age ranges, as well as those who are in our oldest age range of age 60 or older. We want to hear and learn about what LGMD looks like and your treatments across the lifespan. So, we encourage everyone to participate.

(00:54:33):

We go to our next polling question. Here, we want to know how do you, or your loved one with LGMD identify. A, male; B, female; C, gender variant or non-conforming; or D, if you prefer not to answer. Again, this is answering either as the patient, for yourself, or as the caregiver answer this on behalf of your loved one with LGMD.

(00:55:09):

We'll give you just a few more moments here to get in your responses. We see that they're still coming in. I'll just say that it's moving around a little bit, but we're seeing pretty much a near split between people with LGMD that identify as male and identify as female. We are not seeing anyone reporting that they're gender variant or non-conforming, or prefer not to answer.

(00:55:44):

All right. If we can go to our next polling. Appreciate you guys bearing with us through these questions. It's just so helpful for us to know who we have in our audience. Now, we want to know how long ago were you diagnosed with LGMD, or if you're a caregiver, your loved one. How long ago were they diagnosed with LGMD? The options are: A, within the past five years; B, between five and 10 years ago; C, more than 10 years ago; or D, if you're not sure when you or your loved one was diagnosed with LGMD.

(00:56:25):

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While responses are coming in, I'll just say that for those of you that have been recently diagnosed, certainly we heard from Dr. Wilson Bryan from the FDA, very interested in your experiences, not only since diagnosis but what was your experience leading up to diagnosis. Have you been living with symptoms and health effects of LGMD for some time prior to actually getting a diagnosis? So, we're very interested to hear, again, about the full range of experiences of living with LGMD. It looks like about two-thirds of our audience is reporting that they were diagnosed more than 10 years ago, but we do have good representation for those that were diagnosed more recently, both between five and 10, as well as within the past five years. It looks like a small fraction of our audience is not sure of when they were diagnosed.

(00:57:21):

If we go to our last polling question for this first set of questions to help us understand our audience. Here, we'd like for you to identify which genetically confirmed diagnosis of LGMD that you have, or that your loved one has. The options here are: A, for 2A; B, for 2C; C, for 2D; D, for 2E; E, for 2F; F, for 2I; G, if you have a genetically confirmed subtype that's not listed above; H, genetic testing that was inconclusive; I, if you're not sure; or J, if you never had genetic testing, saliva or blood test to confirm your LGMD diagnosis.

(00:58:22):

All right. We'll give you a few more moments here to get your responses in so we can understand who we have in our audience today. We heard a little bit about not only the rarity of LGMD overall, but some of the differences in prevalence amongst some of the different subtypes. I see we're seeing that played out a little bit here in our responses. It looks like our largest contingency from the community are those living with 2A or their caregivers, followed by 2I. We do have good amount of representation from subtypes 2C, 2D, and 2E. No one, at least at this point, reporting that they are living with 2F. We do see some of those other responses being selected by a few. Just as a reminder for today's meeting, we are focused on those who are living with and have that diagnosis of one of those six subtypes.

(00:59:27):

I want to thank you all for participating in these polling questions, again, just to really give us a good sense of who we have in our audience with us today. Now, we get to our first topic for today, which is really to understand what it is to live with LGMD, and hear from you about those experiences. So, if we can pull up our first set of discussion questions, these are going to apply to both our first and second sessions, but we'd like to focus in our first session on the experiences of those living with sarcoglycanopathies, which again are the LGMD subtypes 2C, 2D, 2E, and 2F. We'll focus on this group for about an hour, and then, we'll cover these similar topics for those living with LGMD subtypes 2A and 2I. So, if you're living or a caregiver of someone with 2A or 2I, just hold on. You can go get a cup of coffee and join us back in about an hour, and we'll be asking for your input.

(01:00:28):

In this session, we want to really understand, again, what it is to live with LGMD. And so, we want to know, of all of the different symptoms and health effects that you experienced as a result of LGMD, which maybe one to three of those have the most significant impact on you or your loved one's life? We want to know what that kind of looks like, and if there's any variability in your experience with those symptoms, whether that's day-to-day, week-to-week, month-to-month, or over the course of years.

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Perhaps, one way to think about that is how does LGMD affect you or your loved one on best days versus on worst days.

(01:01:08):

We also want to know how you or your loved one's symptoms and ability to cope have changed over time. And knowing that there are so many different symptoms and health effects that are a result of LGMD, we not only want to know what those are, but also how they impact activities in your daily life. So, we'll be asking you to share with us those specific activities that are important to you or your loved one, that you or they cannot do either at all, or as fully as you would like because of LGMD.

(01:01:37):

Finally, we know that while there's so much that you have already experienced and you're currently experienced, we also know that you're thinking about your lives in the future living with LGMD. So, we want to know about your fears and your worries for the future. To get us started on these topics, we have a panel of your peers who will be sharing their perspectives on these issues and will serve as a foundation for our discussion. We have Rania, Kurt, and Peter, Donovan, and Elizabeth. Rania, take it away.

Rania M (01:02:11):

My earliest memory, I was different than other kids my age, was when I was eight years old, and my teacher confirmed my mom's maternal instinct that something was wrong. I would use my arms and legs to get off the floor. I had more of a waddle to my walk. I got tired faster, and I needed help to climb the school bus steps to go on our field trip. These symptoms were all things my mom had noticed. However, she didn't want to face reality, and thought maybe every kid had their own uniqueness. After months of countless doctor's appointments and a muscle biopsy to confirm, at nine years old, I knew I had a disease that I would live with forever.

(01:02:52):

Hello, my name is Rania. I am 35 years old, and I was diagnosed with limb-girdle muscular dystrophy 2E. Living with limb-girdle muscular dystrophy means that every aspect of my life is planned. Sometimes A, B, C and D may follow. I was 12 years old when I got my first power wheelchair. I was falling more frequently when walking, and I can no longer get up on my own or do things independently. 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.

(01:03:42):

After my surgery was when 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. This was the start of planning my day-to-day. 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. My dad then drops me off at work. The only free time my parents have to attend to their needs are during my working hours.

(01:04:32):

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During my work day, 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. 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. During lunch, my coworkers help me heat up my food and cut up large pieces of food. Being an adult with limb-girdle muscular dystrophy left me with no choice but to be comfortable asking other adults and sometimes strangers for help with everyday task a young child might need assistance with.

(01:05:14):

After my work day, 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. If my parents need to leave for longer than an hour, I ask other relatives or friends in advance to stop by and stay with me. It makes my heart heavy seeing the physical decline in my aging parents, while they're trying to maintain the stamina and physical strength needed to be a full-time caregiver, 24 hours a day, for a physically disabled adult that needs 100% total assistance.

(01:05:51):

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. It means I cannot plan for the long term, but only for the foreseeable short term I need to manage to meet my basic needs. Every day is a challenge living with limb-girdle muscular dystrophy. Some challenges are predictable and others are thrown in like curve balls. Living with limb-girdle muscular dystrophy has made me a realist and a planner. I dream of the day where I can live in a world where I can be an idealist and can experience spontaneity without dependency. Thank you.

Kurt F. (01:06:56):

Hi, my name's Kurt [inaudible 01:06:58]. I'm 16 years old, and I live in the San Francisco Bay Area with limb-girdle muscular dystrophy type 2C. LGMD 2C. My mom, who is a doctor, suspected that something was wrong when I was three and was still not jumping. That led our family done a long diagnosis process. First, suspecting Duchenne, and finally arriving at LGMD 2C after a muscle biopsy.

Peter F. (01:07:20):

Hi, I'm Peter. Kurt's 14-year-old brother. Being younger than Kurt and with less obvious symptoms at an early age, my parents hoped I did not have LGMD 2C. Following Kurt's diagnosis however, I tested positive for LGMD 2C when I was two.

Kurt F. (01:07:35):

When I was a little kid, the main symptoms of LGMD that I noticed were a general lack of stamina and strength. I found it hard to keep up with my classmates. This was particularly difficult at a young age when team sports and physical games on the playground are the main means of connection. I still find ways to connect, but my physical disability made it harder.

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Peter F. (01:07:54):

The first symptoms I remember were tightness in my ankles and getting tired faster than other kids. This made being popular and accepted in school challenging, because young kids are not understanding of it.

Kurt and Peter F. (01:08:00):

Be popular and accepted in school, challenging because young kids are not understanding of physical differences. In elementary school, I could not play basketball with my friends and had to do activities that did not require running. By same time, stress could have got worse in elementary school. 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. A good tip for LGMD2C patients is not to pick the cello as an instrument. And by fifth grade, stairs became very difficult, and I was using the elevator. I also couldn't climb playground equipment. I got my first mobility device in fifth grade that I used for a school outdoor education trip.

(01:08:48):

My symptoms have progressed more slowly than Peter's. I just finished my sophomore year of high school, and I have not used a wheelchair at school. Although, I did use a wheelchair for the first time this year on a class trip.

(01:08:59):

One of the most significant events for me was realizing by the end of fifth grade that I would need to use a wheelchair full-time in middle school because walking was too difficult. 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.

(01:09:21):

My best days are when I'm cooking. Towards the end of elementary school, I became obsessed with cooking. I applied to Master Chef Junior and made it to the top 40 out of thousands of candidates. My interest in cooking hasn't gone away. In fact, if it were not for muscular dystrophy, I'd probably be working in a restaurant kitchen every free moment I have. My worst days with LGMD2C are when, because of physical or accessibility barriers, I can't participate in the things I enjoy, like cooking, or when I'm unable to do what my friends are doing.

(01:09:49):

As a teenager, living with LGMD2C, my best days of sleeping in and playing video games with my friends. On those days, the disease does not impact me too much, although I still need help getting out of bed and with personal care tasks. My worst days with LGMD2C are days in which I do a lot of physical activity, including getting in and out of my wheelchair multiple times and walking short distances or standing for a period of time.

(01:10:13):

The symptoms of LGMD2C that affect me the most are fatigue, arm and leg weakness, and back pain. This year, I've started using a wheelchair some of the time, which has been a big change. If I could change one thing about my disability, it would be having more stamina when walking places.

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(01:10:28):

Some of the challenges I face include avoiding using the restroom when I'm not home, including at school, because I know I would need help. I also 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. 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.

(01:11:09):

Because of LGMD2C. I know that I'll never be able to cook professionally, both because of the long hours, heavy lifting, and general physical stamina that is required in a professional kitchen, and the knowledge that unless there's a treatment of some kind, my disability will continue to deteriorate. This is something that has been difficult for me to grapple with. Even since middle school, cooking along with other daily tasks have gotten harder as my symptoms of LGMD progress.

(01:11:35):

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.

(01:11:49):

Like Peter, 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. And, 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. Thank you all for listening to our story.

Donavon D (01:12:15):

Hello, my name is Donovan and I'm from Andover, Kansas. I was diagnosed with limb-girdle muscular dystrophy 2D 44 years ago. At the time I was diagnosed, four of my siblings were also diagnosed with limb-girdle muscular dystrophy 2D. Later, two of my nieces were diagnosed with limb-girdle muscular dystrophy 2I. My family was devastated. My parents had tremendous guilt for years. Even though neither one of them were affected with the disease, with my type of dystrophy, both parents had to be a carrier. 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 that was causing my gait, but actually it was my muscular dystrophy. When I was in my late twenties to early thirties, it began harder for me to walk and stand up.

(01:13:22):

I went to the wheelchair at the age of 42. I worked as an air traffic control specialist for 20 years till the start of 2012. 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. During the day I rely on my battery powered wheelchair. Once I get in the wheelchair in the morning, I'm in it till it's time to go to bed. My

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wife dresses me and helps me throughout the day. My wife is unable to work outside the home because she's my caretaker.

(01:14:04):

Muscular dystrophy has taken my ability to drive, taken my ability to breathe on my own at night. So I use the Trilogy machine for helping me breathe to give my lung muscles a rest, so I would be stronger during the day. However, in last six months or so, I've had to start using my machine during the day. 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 wire 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. As my sister Jolene said, "Every day, my muscular dystrophy causes adjustments for things we do or don't do."

(01:15:04):

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. 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 2014, my sister Drew was the first person in the world to undergo a gene therapy using vascular delivery, again with Dr. Mendell. In my trial, we jumped from the mouse model to the human. I would consider to participate in either a drug trial or another gene therapy trial to stop my disease. 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.

(01:16:05):

This would change my quality of life by strengthen the muscles around my lungs and diaphragm. I've already risked my life by doing gene therapy using AAV, and would consider doing non-viral gene therapy. I've lost two sisters, Monica and Mary. Both died from respiratory failure. My sister, Jolene has very little lung capacity, as she's on a Trilogy machine most of the time. My lung capacity's down to 32%. If I die because of respiratory failure, I know that's a terrible death. In closing, I'd like to thank you for allowing me to share my family's story. I urge the FDA to use as much flexibility as possible in considering data from small trials in this area because of the need is great even if it's hard to do trials in this rare disease. My family members and friends are dying while we keep waiting for new treatments to be approved.

Elizabeth F (01:17:10):

My name is Elizabeth, and I have a limb girdle muscular dystrophy 2C. I apologize if my voice is muffled due to [inaudible 01:17:18] ventilation. My first symptoms started to appear when I was seven years old in 1987. I was in second grade and quite active, as kids are at that age, but I began to fatigue quickly during physical activity. I had trouble climbing stairs, I fell easily, my calf muscles were large, and I began to toe walk. My gym teacher noticed the way I was getting up after a fall, and he called my parents. This led to a conversation at parent teacher conferences, where they all noticed my struggles. A muscle biopsy at the local MDA clinic confirmed LGMD. I didn't have a full diagnosis of my subtype until adulthood when DNA testing became widely available.

(01:18:04):



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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. By age 10, I started utilizing my first mobility device on being in a wheelchair. I was able to still walk at this time, but I tired very easily. Long distance walking was a struggle, and running was not possible, and my muscles constantly felt sore. By age 12, I transitioned to a motorized scooter. I was never strong enough to be able to push my manual wheelchair, and I was seeking more autonomy. At the time, I primarily used my wheelchair during school days because I would often fall with the slightest touch, and I could no longer sit myself up if I leaned forward.

(01:19:04):

By age 15, I was no longer able to walk, and I used my wheelchair a hundred percent of the time. I transitioned to my first power wheelchair during this time too. I was able to still stand with assistance, but walking was not possible. This was the time I began needing assistance making transfers to and from the toilet, dressing myself showering, and grooming. My parents took on this daily role to physically assist me. Also, my arms began to weaken during this time, and I would often need to prop them up against a table to raise my hands to my face to brush my teeth and to eat. From ages 15 to 25, I had the slowest decline in symptoms. I graduated from high school and college, and during my college years, I chose to live in the dorms on campus, and I hired non-family aid care for the first time. During this 10 year period, it felt like I had plateaued, but my symptoms just progressed very slowly.

(01:20:12):

From ages 25 to 35, I was working full time with few accommodations beyond a very free access, but 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. I was placed on oxygen at night, which is not advisable with my diagnosis. My headaches and foginess only worsened. Once I found a pulmonologist familiar with neuromuscular disease, he placed me on noninvasive ventilation, mostly at nights to assist with proper ventilation. I immediately had more energy, and I slept better than before. During these years, I was also referred to a cardiologist that determined I have a low injection fraction of the left ventricle.

(01:21:09):

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. I now use adaptive technology to type, and during this time, I lost the ability to raise my arms. Even when propped at the table, I can no longer feed myself independently. In the last two years, specifically, I've needed by 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 CO2 retention increases. Additionally this year, I elected to have a suprapubic catheter placed to reduce the number of transfers each time to the toilet. 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. I lack the strength to breathe without a ventilator, and I fear I'll ultimately die from respiratory or heart failure. I don't know exactly what will entail, but I'm still hopeful. Thanks.

James Valentine, JD, MHS (01:22:35):

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Wow. Thank you so much, Elizabeth, and to all of our panelists for being so brave to share first with us today and help us understand your experiences and what you're living with as a result of the sarcoglycanopathy subtypes of LGMD. We're now at the point in the program where it's our first opportunity to welcome all of you who are in the live audience and provide you that opportunity to share your voices live on the program, here first focused on the sarcoglycanopathies and what it is that all of you are living with. To get us started on this topic and thinking about the ranges of issues and what you're experiencing, we are going to start with a couple of polling questions. So, for all of you who are living with a Sarcoglycanopathy or a caregiver of someone, we ask that you go ahead and pull out your phone, go to that webpage, go to that tab that you opened up earlier, and go to [www.PollEV.com/LGMD](http://www.PollEV.com/LGMD). Again, [PollEV.com/LGMD](http://PollEV.com/LGMD).

(01:23:42):

And, we have some polling questions here throughout the session we'll go to for our sarcoglycanopathy segment of the community. So, here we want to know of all the LGMD symptoms that you have experienced, which have had the most significant impact on your daily life? And, you can select up to three. The options are A. Cardiac or heart issues, B. Contractures, C. Curvature of the spine or scapular winging, D. Difficulty using hands or arms, E. Fatigue, F. Impaired mobility, G. Pain, H. Poor sleep, I. Pulmonary or breathing issues, J. Social or emotional concerns, things like isolation, depression, and or anxiety, K. Speech and or swallowing difficulties, L. Urinary or bowel issues, or M. Some other symptom or health effect of your LGMD that you would rate as one of the top three that have had the most significant impact on your daily life.

(01:24:53):

And so, as you're making these selections, I want you to be thinking about why it is you're choosing these as your top three that have the most significant impact on your life. What came to mind for you? And, we hope that you'll call in and write in to share those experiences. As it stands, it looks like, and again, these are percentages of responses, not percentages of people who have selected a single response, but it does look like, perhaps, the top ranked symptom that's most significantly impacting daily life is the impaired mobility. After that, we're seeing fatigue and difficulty using hands in arms and, perhaps, fourth after that is the social and emotional concerns.

(01:25:34):

However, what really stands out to me is that each and every single one of these symptoms is in some, and in many cases, many people's top three most significant symptoms in terms of impacts in daily life. So, we want to hear about all of these different symptoms, what this actually looks like. And, if you're one of those people that selected other, and we weren't able to include your top impact in this question, we want to hear what it is that is your impact.

(01:26:05):

So, we go to our second polling question. So, we want you to be thinking about those range of different symptoms and health effects and think about as a result of those, which one of the following statements are true? And you can select one, that A. You have difficulty with activities that involve upper extremities, B. You have difficulty with activities that involve lower extremities and your core, C. You have difficulty with activities involving both. So, both upper extremities and lower extremities and core, or D. If you do not have difficulties with activities. So, please select which applies to you or your loved one living with a sarcoglycanopathy subtype of LGMD.

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(01:26:58):

All right. So, as some final results are still trickling in here, we're seeing that by far, the most common experience in our audience today is that people are experiencing difficulty, both with activities of upper extremities and lower extremities and core. However, we do have about a fifth of our audience living with sarcoglycanopathies that are having difficulty only with activities involving lower extremities and core, no one reporting difficulties only with upper extremities, and a small fractions reporting that they're not having any difficulties at all. And so, of course, we want to hear about these ranges of experiences, and I want to encourage you all to think about and consider calling in. In fact, this is our first opportunity to really hear from you. So, if you would like to call in, you can dial in at any point at +1 703-844- 3231. Again, the phone number to call in, share your experiences of living with LGMD at +1 703-844-3231.

(01:28:13):

When you call in, we'll make sure to get you into our caller queue. That way we can bring you into the live discussion. You can also, throughout the program, submit written comments. There's a little comment box that you'll see under the live stream. And so, please submit those comments, and we'll be reading and sharing some of those throughout the program as well. So, while you're doing that, I want to welcome our Zoom panel for this session, some of your peers who will be sharing some of their experiences living with LGMD, and I'd like to, let's just get right into it. Maybe, we can start with you, Makayla. As you're thinking about the different symptoms and health effects, we've had a big list of those on that first polling question, what symptoms, one or two symptoms, have the most significant impact in your life?

Makayla C. (01:29:06):

I think the most symptoms I have, I deal with pain and lack of sleep. I think those are the ones that I deal with the most.

James Valentine, JD, MHS (01:29:17):

Sure and Makayla, can you tell us a little bit about your experience with LGMD, what subtype you have?

Makayla C. (01:29:24):

So I have limb-girdle type 2E, and I was diagnosed three years ago.

James Valentine, JD, MHS (01:29:30):

Okay. Thank you. So, as you were thinking, you just mentioned pain and lack of sleep. How long have you been experiencing both of those symptoms? You mentioned you have a fairly recent diagnosis of LGMD. Did you have those symptoms well before, or is that also more recent?

Makayla C. (01:29:52):

So, I had the symptoms before, and I went through a bunch of testing and stuff. And then finally, genetic testing decided that I did have the limb-girdle muscular dystrophy.

James Valentine, JD, MHS (01:30:04):

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And, can you remember or tell us how long ago maybe it was that you first started having pain? How did you notice that? What did...

Makayla C. (01:30:12):

I think I was 12 when I started to notice the pain and stuff. And then, later on down the road, I did start noticing weakness and stuff like that.

James Valentine, JD, MHS (01:30:23):

And the pain, where do you have your pain? Is it kind of like a dull pain, a sharp pain? Can you maybe describe that a little bit for us in a little bit more detail?

Makayla C. (01:30:34):

So, I feel like the pain I have is more achy type feeling. And then with activity, I think the muscle contractions start to start up. I have noticed lately my shoulders have started to contract more than my legs. Normally, it's normally just my legs.

James Valentine, JD, MHS (01:30:53):

Okay. And that pain, do you wake up in the morning and you're already in pain, or is it really something that sets in more as the day goes on, and you're kind of trying to do more activities?

Makayla C. (01:31:05):

So, I'm in constant pain all the time, and with activity, it just worsens.

James Valentine, JD, MHS (01:31:09):

It's just worsens. And, maybe one more thing for you, Makayla, just really trying to understand your experience. Do you have good days and bad days with your pain? And if so, if there is that, some of those differences from one day to the next, can you tell us maybe what a good day would look like? Even though that may still be a day that you do have constant pain versus one of those bad days?

Makayla C. (01:31:38):

I think a good day is being able to go out and do everything with my friends and family and not have to suffer with trying to keep up with them. And then, bad days are really just not being able to really do anything because of how bad the pain is.

James Valentine, JD, MHS (01:31:56):

Wow. Wow. Well, thank you so much, Makayla, for sharing that. It's so helpful to hear. Brian, I'd like to bring you into this conversation. Same question, thinking of all of the different symptoms and health effects, maybe what stands out as the top one to two most troublesome symptoms?

Bryan S. (01:32:13):

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I'm Brian. Age 12, I was diagnosed as having some form of MD. At that time, they thought it was Becker's. I'm 55 now, so 43 years of dealing with this. The one thing I didn't realize during that time is that my respiratory would be affected. Found out just in the last 90 days, lung capacity is down to 38%. I had to go on a BiPAP, and that kind of hit me out of left field. I've been able to take on every challenge. That one was crippling, to say the least.

James Valentine, JD, MHS (01:32:54):

Yeah. And, when did you first notice some of those pulmonary respiratory challenges, and have they gotten worse over time?

Bryan S. (01:33:03):

Yes, probably in 2019. Started noticing when I'd lie down, I would feel like somebody was on my chest. My diaphragm was weakening. I didn't realize that at the time, but it felt like somebody was on my chest, and I would gasp for air. Through Donavon Decker, who spoke earlier, he shared with me his path, and I went in and got checked and, lo and behold, I had lung capacity issues and needed to be on a BiPAP.

James Valentine, JD, MHS (01:33:31):

Wow. And how, maybe in your day to day life, would you gauge how well you're doing on a given day? Are there certain activities that are particularly hampered or ways that you feel that's kind of your gauge of how you're doing?

Bryan S. (01:33:54):

When I was younger, it was certainly fatigue. 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.

James Valentine, JD, MHS (01:34:14):

Sure. And when you wake up on one of those days, maybe where it is a little stronger than others, do you know that you're going to have to kind of tackle the day a little differently than on other days? How does that translate?

Bryan S. (01:34:28):

Yeah. It's kind of like landing a plane and not knowing how long your runway is. You just take what's in front of you, and you adapt, and you make changes as you go. Otherwise, your disease is defining you, not you defining how you approach it.

James Valentine, JD, MHS (01:34:45):

Yeah, absolutely. Well, thank you, Brian. And, thank you for sharing on that. I want to keep exploring this topic and bring Alexa into the discussion. I know this can be very... Every question really is personal here, and I want to know personally for you, what maybe represents that most troublesome or most burdensome symptom.

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Alexa C. (01:35:10):

Yeah. Hi. I'm Alexa, and my daughter is eight and she has LGMD2C. For her, I picked the social emotional, and really going back to what Kurt and Peter said earlier is that other kids don't really understand. And, she's just had to have this mental toughness far and above her years to understand what inclusion means and how to understand when she's excluded and how we move past that. And, the pandemic was particularly hard too, because she wasn't able to participate in school like the other kids. She has rhabdomyolysis with fevers, and so she was at a really high risk. So yeah, that's the primary issue that we deal with the most, I think.

James Valentine, JD, MHS (01:35:58):

Yeah. And so, is that really just a risk that you're trying to, therefore, prevent infections? And so, you're kind of restricting her exposures, and that's keeping her from being able to do all of those activities? It's not necessarily just, and this is me clarifying, how she's feeling, necessarily, that's limiting what she's doing?

Alexa C. (01:36:28):

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 rhabdo, 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.

James Valentine, JD, MHS (01:37:11):

I see. I see. And, you mentioned that kind of the way that, what you picked off of the list was kind of the social and emotional. Has she kind of expressed those feelings directly, or is this more of just your observation of, maybe, her mood or what she is willing or not willing to do?

Alexa C. (01:37:35):

No. I mean, she's heartbroken all the time. She made a new friend at an activity that she does, chorus, and his mom invited her to his birthday party, and she texted me and she's like, "I want her to come to his birthday party." And then, we were really excited about it. She gets to go to a birthday party, and then she texted me. She's like, "It's at the trampoline park." And I was like, "Okay." Or, when she was four or five and she'd get invited to birthdays at the swimming pool that wouldn't allow life jackets. It is heartbreaking for her because not everybody understands inclusion or how to include their friends, especially at an age that young. And so, she's just had to develop this very, very tough mind, and I think she's too young for that. She should get to experience her childhood a little bit more.

James Valentine, JD, MHS (01:38:28):

Yeah, no, absolutely. Thank you so much for sharing that. I see that we have some written comments that are coming in, but I would like to encourage anyone that would want to share via phone to dial in at this time. That phone number again is +1 703-844-3231. Again, in this session, we're focusing on the

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sarcoglycanopathy subtypes. So, if you're living with one of those or you're a caregiver of someone living with one of those subtypes, we want to hear from you now. We'll have an opportunity a little later to hear from our other subtypes, but we do want to hear from those of you that are living with those subtypes, and so please do call in as well as continue to write in. And so, I want to go ahead and check in now with Jen. What are we seeing in terms of impacts from different symptoms and health effects?

Jennifer Levy, PhD (01:39:33):

We're getting some great comments being emailed in. The first one I'd like to read is from a 64-year-old woman with 2F, LGMD type 2F is one of the rarest subtypes. She says that the top three daily challenges for her are managing stairs, getting up from the floor or chair, and lifting her hands, and opening bottles. We also have a comment from Vanessa from the US. She says, "I have ongoing muscle weakness, especially now that it is taking away my air. The inability to take a deep breath, the inability to hold a conversation without gasping for air, the need to be hooked up to noninvasive ventilation, the need to carry such a device everywhere I go, and the need to not only use it at night, but for a portion of my day."

James Valentine, JD, MHS (01:40:23):

Wow. Yeah, so thank you for those of you who have been writing in. We'll be continuing to share those statements and hopefully we'll be hearing from you soon on the phones as well. But, I do want to kind of expand the discussion. We're continuing to understand the different symptoms and health effects of LGMD, and so we know that and have heard that that impacts activities in daily life, but I want to kind of more directly address that and ask the audience to think about, of all of the activities that are important to you, which maybe are you not able to do at all or as fully because of your LGMD? And so, to get us thinking about this as a group, we have a couple of polling questions. So, go ahead and pull out your phone. Open that browser. Go to that tab in your web browser, go to [PolLEV.com/LGMD](https://PolLEV.com/LGMD). We're going to ask and get some of your experiences around these activities in daily life.

(01:41:23):

So, our question for you here is which daily living activities are you dependent upon a caregiver or a family member to assist you with some or all of the time? Or, if you're a caregiver, which of the daily activities is the person that you care for depending upon you or others some are all of the time? And again, select all that apply. The options here are A. Bathing, B. Bed mobility, C. Dressing, D. Eating, E. Going to the bathroom, F. Household chores, G. Meal preparation, H. Transportation, I. Some other activity in daily life that you or your loved one...

James Valentine, JD, MHS (01:42:00):

... activity in daily life that you or your loved one are dependent upon a caregiver some or all of the time. Or J, none if you or your loved one are fully independent. Again, here, we want to know all of these different activities in daily life that need some assistance or maybe always need assistance with. I'll give you a few more moments. I see results are still trickling in.

(01:42:33):

It looks like there's a lot of different activities that you all are dependent upon a caregiver or family member, either some or all of the time. The top one being household chores that we're seeing, but it

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looks like most of the others are pretty high up there as well. Everything from bathing, bed mobility, dressing, going to the bathroom, meal prep and transportation. We're seeing a little bit less in terms of assistance with eating, but we are seeing some others, so we do want to hear about those other activities in life. It looks like we may have one or a few saying that they're fully independent.

(01:43:16):

We have one more question here at this time on impacts in daily life, so we can go to our next polling question. Here, we want to know which everyday activities that you cannot do at all or as fully as would you like because of your condition, are most important to you. You can select up to three. Of all of those things in life that are important to you, which of those maybe are most impacted in terms of you not being able to do them at all or as fully as you would like? The options are A, attending school or working; B, being intimate with a spouse or partner; C, caring for a child; D, driving a motor vehicle; E, exercising or participating in sports; F, going out, socializing or traveling; G, meal preparation; H, performing household chores; I, personal hygiene; J, walking; or K, some other everyday activity that's important to you that you cannot do at all or as fully that represents one of those top three activities for you. We'll give you a few more moments here. Results are still coming in.

(01:44:28):

As always with these questions, where we're seeing a percentage but respondents can select more than one. We're seeing a percentage of total results, so think of these bars as rankings. Right now, it looks like the top most important activity that's impacted is going out, socializing and traveling, followed by exercising and participating in sports, and maybe around the same level as personal hygiene and walking. However, importantly, every single one of these three things is in somebody's top three. Please, please, we want to hear from you to help understand what that looks like, which symptoms and health effects maybe are making it so you can't do this at all or as fully as you would like. We'd like to explore that with you now.

(01:45:20):

I'd like to come back to our Zoom panel here. Tomie, maybe we can start with you. Thinking about all of the activities in life that are important to you, which maybe would you rate is most important that's limited?

Tomie B. (01:45:37):

Mobility. Being able to play with my granddaughters, being able to travel. Travel is very difficult. Sorry. My name is Tomie Bunch. I'm from Cleveland, Tennessee and I have muscular dystrophy type 2F.

James Valentine, JD, MHS (01:45:55):

2F.

Tomie B. (01:45:55):

Movement is very difficult.

James Valentine, JD, MHS (01:45:57):



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Sure. Tomie, let's talk about that a little bit. Your movement, are you talking specifically about movement on your feet, walking, or also other types of movement maybe with the upper body?

Tomie B. (01:46:12):

Both. Walking is extremely difficult. There's a lot of pain involved. No stairs. I can't navigate stairs at all. Just trying to fix my hair or even brush my hair can be difficult because my arms skip out very easily. I have to lean on something to be able to do so much as wash my face. Any kind of movement is very difficult. 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.

James Valentine, JD, MHS (01:47:00):

Right. When you say that some of these activities are difficult, is it difficult just because they're painful or do you also have some weakness? What makes those types of activities difficult for you?

Tomie B. (01:47:17):

Weakness is a big problem. There is pain, yes, but I can deal with pain. But the weakness, a few steps and then I have to rest. If I do manage a couple of stairs, I have to just stop when I get two or three stairs behind me and just take a minute, and rest before I can move on. Just the walking itself is very difficult. It's hard to manage to move around my apartment. 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.

James Valentine, JD, MHS (01:48:03):

Right. How long has it been that it's been this difficult to be mobile and get around? Has it been this way for a while for you or has this been more of a recent progression in terms of how severe these mobility issues are?

Tomie B. (01:48:23):

I was diagnosed in 2005, but I had been experiencing symptoms since '99. I'm rolling up on about 23 years. I'm now 50 years old. I was 30 when I was diagnosed. It's off and on for the last 15, it has been a daily thing, but then I would have days that everything is normal and I can move around like there's nothing wrong with me. Then, I may wake up tomorrow and not be able to lift my arm.

James Valentine, JD, MHS (01:48:58):

Wow.

Tomie B. (01:48:58):

Or not be able to move my legs to get out of bed and would need assistance with that.

James Valentine, JD, MHS (01:49:04):

Wow. And how many days would you describe as being those really severe days? Maybe within a week and a month, whatever, however you would think about it.

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Tomie B. (01:49:17):

I would say out of seven days, at least five-

James Valentine, JD, MHS (01:49:22):

Wow.

Tomie B. (01:49:23):

... are challenging. The weather also affects this disease. It's changing in the Tennessee Valley over to fall so I have had a lot of pain this week. I have had some movement difficulties, especially with my arms, opening bottles and lifting gallons of milk have all been challenging.

James Valentine, JD, MHS (01:49:48):

And it's due to the cool weather.

Tomie B. (01:49:50):

Because the weather.

James Valentine, JD, MHS (01:49:50):

The cool weather?

Tomie B. (01:49:51):

Yes, the coolness is coming in and the barometric pressure, of course, adjusts and every time that barometric pressure moves, my body senses that change and my symptoms increase just a little every time it changes.

James Valentine, JD, MHS (01:50:05):

Wow. Well, thank you, Tomie, so much for helping us understand that progression over time, but also just that seasonal variability, that day to day, week to week variability too. Scott, we haven't had a chance to bring you into this discussion yet. I'd like to, on this topic of activities that maybe are most impacted in daily life, what stands out to you?

Scott (01:50:29):

My name is Scott. I'm a parent of two kids with 2C who are teenagers currently. Certainly as kids, the loss of mobility is the first thing I think that really was a significant issue for our kids. But certainly all the other aspects, the social emotional that Alexa talked about, all those things are important and really key things. Our two kids have not experienced the same pain that Makayla and Tomie have talked about, fortunately. But the rapid progression of this disease is something that is really just the variability and the rapid progression are things that are really notable with the two kids that we have.

James Valentine, JD, MHS (01:51:14):

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Yeah. In terms of maybe how that then translate to daily life, that variability, does that impact what they can do? Do you and they make decisions about what they're choosing to participate in or plan for different, knowing that maybe some days maybe they can do more than others? Can you maybe tell us a little bit about that, Scott?

Scott (01:51:40):

That is absolutely true. 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. Then, if you think about it over a longer window of time, just thinking about planning for kids' activities, how they get to school or get to an event, like Alexa was talking about birthday parties, or other social events. Some days, kids really struggle to get to things, setting aside the physical barriers that may exist.

James Valentine, JD, MHS (01:52:11):

Right. Does that translate into any frustration or other emotions for them, just knowing that maybe they're able to do something certain days so they know they can do it, but then other days that they can't? Are there any maybe examples that come to mind, times you can remember with them that transpired or came out a little bit?

Scott (01:52:41):

Well, I definitely think when you can do something, such as perhaps an activity in the kitchen or the house on one day and then you're unable to do it fairly short time later because of fatigue or just muscle weakness, of course, that's extremely frustrating for anybody, but also particularly frustrating for a child or a teenager who's growing up. That's really challenging.

James Valentine, JD, MHS (01:53:05):

Yeah, absolutely. I see nodding heads from your panel too, so I think that's a shared experience there. The time that we have left, I do want to recognize that so much of what you shared is already your current experiences and we want to know also, as you're thinking about life in the future with LGMD for you and your loved ones, what maybe worries you or concerns you the most about that?

(01:53:31):

We have one more polling question for you here. Go ahead and pull out your phones, go to that browser, go to [pollev.com/lgm d](http://pollev.com/lgm d). Here we want to know what worries you the most about your condition in the future and try to select the top three of those. The options are A, becoming a burden, either physically, financially or emotionally. B, being placed in a nursing home or other care facility. C, coping with pain. D, developing or worsening cardiac or heart issues. E, developing or worsening pulmonary or respiratory issues. F, dying prematurely. G, losing abilities to use arms and hands. H, losing the ability to communicate and or swallow. I, losing independence. J, losing mobility, the ability to walk. K, losing social connections. Or L, some other worry that you have about your condition in the future. We'll give you a few more moments here to get your responses in. Thinking about, again, what are maybe your top three worries for the future living with LGMD? As it stands, it looks like perhaps becoming a burden is the top of these worries that we're seeing represented in our audience, followed

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by a cluster after that. We're seeing developing or worsening pulmonary respiratory issues. Worsening or developing cardiac and heart issues, losing independence, losing the ability to walk and mobility all being rated very highly as a top three worry for the future, as well as dying prematurely. Like we've been seeing, I think, across so many of these polling questions, we're seeing that every single one of these different worries here in this question is a top three for some number of people, and so we really want to hear about those different worries as well. First, I see that we actually do have a caller. We have [inaudible 01:56:07] India who is living or is a friend of someone living with LGMD subtype 2D and wants to share some of those experiences and perspectives. [inaudible 01:56:21] are you with us?

Buri (01:56:24):

Hello? Can you hear me?

James Valentine, JD, MHS (01:56:25):

Yes. Welcome.

(01:56:25):

Buri (01:56:27):

Yeah, thank you very much for taking me in and it's my privilege to be here, like I can talk to you all.

James Valentine, JD, MHS (01:56:32):

Yes.

Buri (01:56:35):

This is about my dearest friend. He lives in India. His name Prakash Munjuluri. He's basically from southern part of India. He was never having this kind of problem and he never knows this problem until he started graduating. When he started graduating, he was very much fine, but by the end of engineering, he could not able to walk.

James Valentine, JD, MHS (01:57:01):

Wow.

Buri (01:57:01):

That is deteriorating day by day and he's trying to reach lot of people all over the world to get treatment or to get a support, but he's unable to get some response from anyone. He's trying very hard. I'm like a closest friend of him and I wanted to tell his problems for now. His financial situation, he is also not supporting and also he needs support to even walk.

James Valentine, JD, MHS (01:57:30):

Right.

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Buri (01:57:31):

My friends, luckily they are in India and they are supporting him a lot and his family members also, but I'm here to tell his problem to all over the world and maybe he'll get some solution.

James Valentine, JD, MHS (01:57:49):

Yes. Well, I want to thank you first for sharing your friends' experiences with us and we know that this is something that is experienced around the world, so absolutely thankful for sharing that. You mentioned that it was when he was graduating, he started losing the ability to walk.

Buri (01:58:11):

Yeah. He's unable to walk.

James Valentine, JD, MHS (01:58:14):

How quickly did he?

Buri (01:58:14):

Sorry?

James Valentine, JD, MHS (01:58:18):

I was just saying over how many months or years from when he started losing the ability did it take to lose?

Buri (01:58:27):

2007, I believe, he started losing his ability when in 2007, he identified that there is a problem with him and slowly it got degraded. Now, without support, he cannot walk. He used to ride a bike, like a scooter in 2007. Now, he's unable to do that as well. [inaudible 01:58:46] and he's trying to gain some muscle strength but still it is getting worse day by day.

James Valentine, JD, MHS (01:58:55):

Right. Well, I just want to thank you so much for calling in and sharing that and adding just another... We're seeing some of these different symptoms, mobility issues impact people so differently, and so thank you for sharing that. I want to just-

Buri (01:59:14):

Yeah. A request, like a word from him. I wanted to put it here. He's ready to support himself for any kind of treatment or any medical examinations. He's open to participate, if in future, if there is any medical advancement happens.

James Valentine, JD, MHS (01:59:33):

Yes.

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Buri (01:59:33):

He is willing to do that.

James Valentine, JD, MHS (01:59:34):

Yeah. Well, thank you for sharing that as well and we will be covering in the afternoon session, preferences and thoughts about what people's needs are for treatments and willingness to even participate in clinical trials and the like. Thank you for adding that as well. To conclude our session here, I want to come back to our Zoom panel again on this topic of worries for the future. Tomie, I think you wanted to say something here. What is maybe standing out for you as a main worry or concern for the future?

Tomie B. (02:00:14):

Being a burden and actually having care other than a nursing home. I have one child and she also has limb-girdle muscular dystrophy. She has 21 and 30 years old, she went into congestive heart failure because of her diagnosis. With her children, yes, she has her husband, but that leaves mom. When you only have one child, you are limited on who's going to help care for you. I do have a relationship currently in my life and should this relationship continue, then I know I can count on that person, but there are folks out there living like me that either don't have children or only have one and what are they going to do when the time comes that they're completely incapacitated? 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.

(02:01:14):

The prospect of going into a nursing home is very scary. I worked in the medical field when I was younger. I worked in nursing homes. I've seen how they run. I'm not saying they're horrible options. Just thinking about yourself having to be in that situation is one of the most unpleasant things you will ever have to do in life, especially for folks who are under 50 years old. We're looking at kids that are these parents of these teens, they're thinking the parents are thinking, well, when I'm no longer here, who's going to care for my child?

(02:01:54):

I think all parents have that thought, but really, to know that your children have something wrong with them, there's a disease that has taken over their bodies and then you have to worry about the prospect of your child passing before you and you outlive your children, which is very unnatural. There's a lot of uncertainty about our futures that I know most of us, if not all of us, would really like to have something that says, hey, you have this disease, but here's what we can do for the future generations. We may not be able to fix your disease now so that you don't have these worries, but there may be something down the road that can help future generations, like my granddaughters, should they be affected by limb-girdle.

James Valentine, JD, MHS (02:02:47):

Right.

Tomie B. (02:02:48):

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I would like to know before I leave this world that there's something that's going to help them so that at my age, they can do all the things they would like to do.

James Valentine, JD, MHS (02:02:58):

Yeah, absolutely. Thank you, Tomie. I think that was very well said. Bryan, I'll give you the final word before we conclude this first session of the morning.

Bryan S. (02:03:10):

Thank you. My last words on it is not only is there a physical impact, here's a financial impact with this disease. My fear is my wife. We've been together for 28 years. I want to make sure she's taken care of. Every day, you're playing with less and less cards to make that happen. That's such a fear that you dwindle your savings and you're left with nothing and you're gone and they're left to going to make it happen in their advanced stage.

James Valentine, JD, MHS (02:03:43):

Absolutely. Thank you, Bryan.

Bryan S. (02:03:46):

Thank you.

James Valentine, JD, MHS (02:03:46):

And really thank you to our whole Zoom panel here and those of you have contributed by calling and in writing. I think we've learned a lot about what daily life looks like and your worries for the future from living with these sarcoglycanopathy, subtypes of LGMD. We're now going to transition to the other two subtypes that we're covering in today's meeting. LGMD subtypes 2A and 2I, to try to explore many of these same topics before later today, we come back all together to talk about current and future treatments.

(02:04:29):

If we can pull up our slate of discussion questions. Now as we do that, for all of you, in case you stepped out and you're just stepping back in. For those of you that are living with LGMD subtypes 2A and 2I, we'd like to spend some time with you now understanding which symptoms have had the most significant impact in your life, how those symptoms have changed over time, and maybe understanding the variability in those from day to day, maybe best days versus worst days, but also how those symptoms translate to impacts in your daily life and those activities that are important to you that maybe you can't do it all or as fully. Finally, looking towards the future, understanding your greatest worries and concerns about living with LGMD.

(02:05:19):

And so, just like earlier, we have a great opportunity now to hear from some of your peers. To kick us off on this topic, we have Jane, Dan, Brooklyn, and Carol who will be sharing. Jane, take it away.

Jane L (02:05:39):

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My journey with limb-girdle muscular dystrophy began at age four or five when I started showing symptoms. My preschool teacher noticed I was having trouble keeping up with my friends on the playground and that I would consistently use the same leg to go up the stairs instead of alternating. This is a major milestone for children. My mother already suspected something was wrong with my hips and took this as a sign to take me to a specialist. I had a muscle biopsy and my tissue sample was sent to the University of Iowa, where I received the official diagnosis of LGMD 2I.

(02:06:09):

At five years old, I didn't understand what having muscular dystrophy meant. I just knew I couldn't keep up with my friends on the playground or at PE. In second grade, my parents wrote a short letter about my disease for me to read aloud to my classmates. I did this in hopes of explaining to them I wasn't being lazy or getting special treatment and to understand why they needed to be a bit careful around me. I read this letter to my classmates every year until sixth grade. 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.

(02:06:52):

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. It was a much more costly risk than any of us thought it would be. 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 cushionoid 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.

(02:07:42):

Looking back, I realized the benefit of steroids was to be able to walk during my high school years and college, but it came at a high price. I was on steroids for five years. When I was a junior in college, 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.

(02:08:05):

Currently, I use a walker inside my house and my manual wheelchair when I leave the house or feel tired. While I'm still somewhat mobile and lead a very busy social and professional life, living with LGMD has created many barriers for me. I am unable to transfer from sitting to standing alone. This means when I go out in public, I rely heavily on friends and family to help me use the restroom or transfer from the car to my wheelchair. 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.

(02:08:48):



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When the pandemic's struck, I moved back in with my parents. I was able to live independently before, but the pandemic has robbed me of my physical strength and I am no longer capable of living alone. While living at home has some advantages, it is not where I imagined I'd be at age 26. I currently rely on my mother as my primary caregiver and we have an amazing relationship. However, it's difficult for her to get things done during the day when she has to constantly worry about my needs. Since I can't transfer independently, she's unable to leave me alone for long stretches of time. She and my father are also unable to travel alone without setting up round-the-clock care, something we have had issues with in the past.

(02:09:28):

My LGMD has also caused me to have several life-changing accidents. In 2014, I fell off my horse and broke my pelvis. I spent a month in the hospital with intense therapy. Thankfully, I was able to prove the doctors wrong by walking across the stage with the rest of my classmates for graduation. While I regained the ability to walk, my strength has been rapidly declining since this first accident. I was lucky enough to walk throughout college since I attended Walford College, a small liberal arts school.

(02:09:58):

This past January, I fell in my bathroom, broke my arm in two places and had to have emergency surgery. 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.

(02:10:25):

I'm currently enrolled in a clinical trial for LGMD and have been on the drug for over a year. We are very hopeful this drug will be approved by the FDA. If it is, it will be the first and only approved drug therapy for LGMD patients. Thank you for listening today about my reality and the struggles and concerns of our patient population and our caregivers. Whatever role you can play in getting more drugs approved into the market for LGMD patients would be welcomed. As time marches on, our muscles switch away and time is of the essence. Thank you.

Dan P (02:11:00):

Hello, my name is Dan and I'm living with limb-girdle muscular dystrophy type 2I/R9. I'm 57 years old and I live in Longmont, Colorado. I was diagnosed with an unspecified form of muscular dystrophy at age 38, and although the diagnosis came as quite a shock, it explained many things that I had experienced growing up. I always seemed to be one step behind all the other kids on the playground and I was never any good at sports. Growing up in Colorado, we would often go hiking up in the mountains and much to the consternation of my older brothers, I would very often have to stop and rest as my legs would grow tired and cramp up.

(02:11:40):

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

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me quite hard and I began to realize the severe impact that my health was having on my life and my emotional wellbeing.

(02:12:12):

Desperate to find out what type of muscular dystrophy I had and determined if there was anything that could be done to treat it, I had a number of genetic tests performed, only to learn that I was negative for those conditions. 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.

(02:12:40):

10 years later, I finally received a genetic diagnosis of LGMD 2I/R9 and I began participating in a natural history study at the University of Iowa. Over the years, I've traveled to Iowa City eight times through study visits in the annual Dystroglycanopathies Patient and Family Conference, and I find it all to be rather bittersweet. I have met many wonderful, supportive people, learned about the science behind my condition, learned about potential therapies being developed, and I've learned about the typical progression of LGMD 2I/R9.

(02:13:14):

However, seeing the declining results of my performance evaluations over the years is quite depressing. For example, the study data has shown that people living with LGMD 2I/R9 typically lose the ability to walk six years after losing the ability to arise from the floor. I lost the ability to arise from the floor in 2016 and the thought of losing my ability to walk terrifies me.

(02:13:44):

In 2015, I was among 20 patients enrolled in the very first clinical trial for LGMD 2I/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.

(02:14:15):

Currently, 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. 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. I also use a mobility scooter whenever I go anywhere in public, as I have had some very bad falls that required complete strangers to assist me, which was extremely embarrassing. 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. I no longer travel by air.

(02:15:03):

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.

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(02:15:33):

My life as it is today is not what I planned for, it's certainly not what I wanted. Limb-girdle muscular dystrophy is a cruel and insidious disease that is slowly stealing my life and my happiness. 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-

Dan P (02:16:00):

... [inaudible 02:16:00] of my condition would be considered a very major victory in my book. Thank you.

Brooklyn (02:16:09):

Hi. My name is Brooklyn Garza and I'm a high schooler living with limb-girdle 2A. This is my mom, Melina. And together, we are going to share my story. It started when I was nine years old. My aunt was visiting from out of state and was videotaping me trying to learn how to do a cartwheel. And I couldn't catch myself with my arms. I kept falling. Long story short, I went to numerous doctors, had highly elevated CK levels, baseline testing for lots of specialists, and two rounds of genetic testing. It felt like forever, but six months later, I had a genetic hit with my calpain 3 gene and a gene of unknown significance, which indicated, I have limb-girdle 2A.

Melina (02:16:53):

We were in complete shocked. How could our precious girl have an orphan disease with no treatment and no cure? We were devastated and scared for what her future would look like. After knowing her diagnosis, I had a terrible mom guilt. Not only did this occur genetically from my husband and I, but I also remember that prior to her diagnosis, I had pushed her to run at her elementary school PE mile. She ended up last in her class and was crying. The worst was nagging her about why she didn't shampoo the top of her head not knowing that she couldn't keep her arms long enough to do that or even to hold her baby sister for long periods of time. I thought she was an athletic, but never did I think she had a debilitating disease.

Brooklyn (02:17:42):

Fast forward to today, the symptom that bothers me the most is how I walk funny. 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. 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 even had to switch schools because the one by my house was too big and would take too much of my energy to get around unless I took a power chair, which I didn't want to do. The elevator also kept breaking, so I felt isolated when I couldn't make it to my classes.

(02:18:24):

I've had boys run past me so hard that I fell to the ground and dropped everything in my hands. I can't pick myself up from the ground when that happens, 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.

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It's so embarrassing. Getting up from a chair is hard for me to do too, but getting up from the ground isn't even possible unless I have something shorter to lean on.

Melina (02:19:00):

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. 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.

(02:19:51):

I have to explain that she can't do stairs and that she won't be able to walk anywhere too quickly or for long periods of time. Brooklyn then must make sure that she is comfortable enough with the friends going to ask for help. 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? Will she feel safe? Is it accessible? 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, defers her from going altogether. I've noticed that as she's gotten into her teen years, it bothers her more socially and has caused her to question what her future will look like.

Brooklyn (02:20:45):

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. Thank you.

Carol A (02:21:15):

I'm Carol. I'm 61 years old and have LGMD 2A/R1. My LGMD journey began around the age of five when I started toe walking and struggled to keep up with my peers. Over the next few years, I developed Gowers sign and unusual gait and experienced occasional falls, plus a high CK level and abnormalities in my deep tendon reflexes were detected. At the age of nine, I was diagnosed with LGMD. At this point, my lordosis was becoming noticeable and it was impossible for me to stand or walk with my heels, touching the floor, physical therapy was unsuccessful, so around the age of 11, I had bilateral Achilles tendon surgeries to release the ankle contractures and improve my walking stability. By the time I graduated from college, stairs were impossible, getting up from a seated position was exceedingly difficult, and my gate was quite precarious, which resulted in many falls from which I couldn't get up without help and included some injuries.

(02:22:17):

It didn't take much for me to lose my balance, a sneeze, being bumped, wind, gravel and uneven surface. At the age of 30, I began using a power wheelchair full time and bilateral double upright leg braces after a fall resulted in ankle fracture. Then at the age of 41, I sustained a fall during a transfer that

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resulted in a femur fracture with medical complications, which ended my career as an occupational therapist. LGMD 2A 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. I am completely dependent on my husband to toilet, bathe and dress me, which results in a loss of independence and dignity.

(02:23:17):

I even struggled to brush my teeth with an electric toothbrush or to wipe my nose. 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. I am unable to cook or help around the house. 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. For transfers, I require maximal assistance, with my husband. I can still do a standing pivot transfer, but they are difficult due to my severe lordosis. My spine is so arched that I am actually looking behind me when my husband stands me up.

(02:24:13):

LGMD 2A 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. Decrease pulmonary cautions have also weakened my voice volume. In addition, I deal with lower extremity edema. I've been wearing custom compression stockings for years, take daily diuretics, and use sequential compression pumps. LGMD 2A 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 require 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. I sleep with my hands on my chest, clenching the bed, remote control, and a personal urgent response device.

(02:25:10):

I fear that if something should happen to my husband during the night, I wouldn't be able to call for help. And we could be stuck in bed for days, if not weeks, until someone decided to stop by and check on us. Extensive muscle weakness and my severe lordosis even impact intimacy. I miss being able to hug or even snuggle my husband. 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. 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 LGMD 2A impacting my life, I am truly running out of ways to adapt. If only there was a way to stop the disease or to at least regain some functional upper extremity strength.

James Valentine, JD, MHS (02:26:27):

Thank you so much, Carol, and to all of our panelists living with LGMD subtypes 2A and 2I for sharing your experiences and really how LGMD is impacting your daily life. So important to hear that. And now, that brings us to our second opportunity today to welcome those of you in our live audience into the discussion now as we focus on subtypes 2A and 2I, specifically. We're going to start with some polling

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questions. Earlier, the polling was limited to those living with the sarcoglycanopathies. We ask now all of those of you that answered those earlier questions to allow just those living with subtypes 2A and 2I and their caregivers to answer these polling questions. So, go ahead and pull out your phone, go to that web browser, go to the tab you have opened.

(02:27:23):

If you're following along on your computer, go to [www.pullev.com/LGMD](http://www.pullev.com/LGMD). In these first polling questions, we want to understand and learn about those different symptoms that impact your life. And so here, we're asking, of all the LGMD symptoms that you have experienced, which have the most significant impact on your daily life. Select up to three. The options are A, cardiac issues, B, contractures, C, curvature of the spine or scapular winging, D, difficulty using hands or arms, E, fatigue, F, impaired mobility, G, pain, H, poor sleep, I, pulmonary issues, J, social and emotional concerns, K, speech and/or swallowing difficulties, L, urinary bowel issues, or M. some other LGMD symptom that you've experienced that has had the most significant impact in your daily life. And again, you can select up to the top three that have had that most significant impact. So, we'll give you a few more moments. I see results are still coming in. As a reminder, whenever we see a polling question that's allowing people to select more than one polling option, the percentages we see are a percentage of responses, not the percentage of people picking any one response. So instead, you can think of these bars as a little bit of a relative ranking to one another. So as it stands, it looks like we are seeing that impaired mobility is the top most significant symptom that's impacting daily life. After that, we see a bit of a drop off. And in the second tier, we see fatigue, social and emotional concerns, and difficulty using hands in arms. And then from there, there's another bit of a drop and we're seeing pretty much everything else then as other's top three, so quite a range of different symptoms that are being experienced by our audience. And we really want to hear about all of those different things.

(02:29:31):

So we go to our next polling question. So here, we want you to think about as a result of your condition, which of the following statements applies best to you. And you can please select that one that does apply to you or your loved one living with LGMD subtypes 2A or 2I. The options are A, that were are there having difficulty with activities involving upper extremities, B you were there having difficulty with activities involving lower extremities and core, C you were there having difficulties with activities that involve both, so both upper and lower extremities and the core, or D, if you or your loved one are not having difficulty with activities at all.

(02:30:23):

So, it's looking like the vast majority of our patients that are represented today with subtypes 2A and 2I have difficulty with activities involving both upper and lower extremities. Although about 10% of people are reporting that they're only having difficulty with the lower extremities and core. And there is maybe one or a few people reporting that they have difficulty only with upper extremities, not lower. No one reporting that they do not have difficulty with activities. So as you then now think about how these impacts of LGMD, we want to hear from you, so we invite those of you living with 2A and 2I and their caregivers to call in and write in. If you'd like to call and share your voices and your experiences, you can dial in at 1-703-844-3231. Again, that number is 1-703-844-3231 as we first talk about the impacts of symptoms and health effects in daily life. Also, if you prefer, you can write in. There is a little comment box that's under the live stream on the website today. You can submit those comments and we'll be

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sharing some of those throughout the program as well. But to get us started on this topic, I'd like to welcome our zoom panel. Some of your peers living with LGMD subtypes 2A and 2I and their caregivers. So, we just did this polling question. We saw a huge number of different symptoms and health effects of LGMD, but we did ask you to try to narrow that down to the ones that are having the most impact on daily life. Noni, I'd love to maybe start with you as we explore this topic. As you were thinking about all the different things that maybe you experience, which stands out maybe as most impacting life for you?

Noni U. (02:32:18):

Sure. My name is Noni. I live in Florida. I was diagnosed when I was 12. I'm 55 now. All of that, it has changed throughout my life. Initially, it was more mobility, transferring, just walking, getting upstairs, but it has progressed now. It has affected my arms quite a lot. I was able to drive before. Recently, I cannot drive anymore. I live in Florida, but I work in Miami, so I would drive every day to Miami. Now, I can't. 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.

James Valentine, JD, MHS (02:33:12):

Yeah. Maybe hearing that that has really been impacting your ability to provide yourself transportation and also how you're able to work, can you tell us, when did you first start noticing the impacts in your arms and upper extremities? Maybe what did you first notice and when did you notice that?

Noni U. (02:33:38):

The arms have been affected from the beginning, but raising my arms, probably the last 20 years or so, it's been getting worse and worse and worse. I can still feed myself but only if I can put my elbows against something.

James Valentine, JD, MHS (02:33:57):

Okay. And in terms of that, then lifting, which has gotten much harder to do, you mentioned, I think it's a really good example, now you can feed yourself but only if you have your arm on a table, how long have you've been needing to do that? And is that something that's pretty consistent from day to day? Is your arm mobility, arm strength pretty consistent from day to day in the more limited capacity that it is right now?

Noni U. (02:34:37):

There are some days that are worse than others. Some days, you're more tired than other days, but it is consistent and just getting worse, consistently getting worse basically is what we could say.

James Valentine, JD, MHS (02:34:48):

Yeah.

Noni U. (02:34:49):

So eventually, I probably won't be able to feed myself.

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James Valentine, JD, MHS (02:34:52):

Right. Wow.

Noni U. (02:34:53):

Not looking forward to that.

James Valentine, JD, MHS (02:34:55):

No, of course not. No, thank you, Noni, for sharing that and how interesting also to hear just that difference between what was most troublesome earlier in your life versus more recently, so thank you for sharing that. I'd like to bring Cindy and Joshua into the conversation. Thinking about of the different symptoms and health effects, those that maybe are most troublesome, what stands out in your minds?

Joshua (02:35:25):

I'm, Josh, 34, from Iowa with 2I. And very similar, transportation, getting around, socializing with people from those limitations.

James Valentine, JD, MHS (02:35:44):

Yeah. So Joshua, as you're thinking about transportation and getting around, what aspects of living with LGMD make that difficult for you?

Joshua (02:36:02):

Being chair-bound, getting... You have to have specialized bands to get around [inaudible 02:36:11]. When those break down, it's not like a buddy can just roll up and give you a ride because you've got a four or five pound chair that you also have to transport.

James Valentine, JD, MHS (02:36:23):

Yeah. And how long have you been chair-bound, if you can tell us how long? When did you first start using maybe mobility assistance devices in general, and how long have you been in, I assume, a power chair?

Joshua (02:36:48):

Right. Yeah, power chair. I got my first scooter in 2009 and then my power chair in 2015. And I've been chair-bound for probably two or three years now.

James Valentine, JD, MHS (02:37:02):

Okay. And then-

Cindy (02:37:06):

This happened after-

James Valentine, JD, MHS (02:37:08):



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Yes. Please go ahead, Cindy.

Cindy (02:37:11):

Oh, I'm sorry. I was just... The chair-bound thing, he was still able to walk very tenaciously holding onto a wall type of situation, but this was after two falls breaking both proximal humerus bones, then we decided that it was time to look for some safer options of independence, mobility.

James Valentine, JD, MHS (02:37:35):

Right. And were falls something that were becoming more frequent, something that were part of daily life for Joshua?

Cindy (02:37:48):

Not daily life. He was really careful, but his weakness started more in the hip girdle than the shoulder girdle.

James Valentine, JD, MHS (02:37:56):

Okay.

Cindy (02:37:57):

Yeah. I mean, it was a big concern and everybody that lives with this disease understands the fragile that comes with it, unfortunately.

James Valentine, JD, MHS (02:38:10):

Yeah. No, absolutely. And Joshua, just to follow up on one more thing with you is you mentioned that obviously, being in a power chair that limits your ability to get around because you're dependent on having an accessible van, are there any other impacts that you would describe? Being chair-bound, not being able to be mobile on your feet. Any other things in your daily life that stand out to you as being most impacted?

Joshua (02:38:46):

Yeah. I mean, you've got to redesign your house for it. As mentioned earlier, I also 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.

Cindy (02:39:26):

There's also the social aspect of it too [inaudible 02:39:29] others have mentioned, all these special accommodations that are required for mobility and health for everyone limits their access to mainstream. As far as the cost of all of those things too, those are things that come out-of-pocket for the most part.

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James Valentine, JD, MHS (02:39:46):

Yeah. Well, thank you both for sharing that. I mean, it's really helped us get a little bit more of a glimpse into all of the different accommodations that are needed and how that makes daily life a lot different. I do see that we have some callers, and so I'd like to bring them into the conversation. First, I see we have Jared from Iowa, who I believe is living with LGMD subtype 2I that would like to share some of the greatest impacts in daily life. Jared, I'd like to welcome you to the program. Are you with us?

Jared (02:40:23):

Yes, I am. Thank you.

James Valentine, JD, MHS (02:40:26):

Yes. Welcome. So yes, we'd love to hear from you any of these symptoms or health effects and how they impact your daily life. What really stands out in your mind, Jared?

Jared (02:40:43):

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.

James Valentine, JD, MHS (02:41:12):

And can you think of one of those times where you had that increase in severity of the weakness that you had to accommodate for? Can you maybe share one of those types of examples and what that change looked like for you?

Jared (02:41:29):

Yeah. The biggest change was in middle school. Towards the end around 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 I think things like that had to be done, I guess.

James Valentine, JD, MHS (02:41:57):

Right. And maybe just a little bit of context over time, how long after that was or how long was that after your first symptoms or maybe your diagnosis?

Jared (02:42:16):

First symptoms were probably kindergarten age, five, six years old. I wasn't diagnosed until 10 at the University of Iowa. From there, progression was relatively slow until high school. My freshman year, I started using a scooter to get in between classes and then at extracurricular activities. Basically as soon as high school ended is when I started using a power chair part time. And then like I said, back in 2018, the power chair was full time, and that's where I am now.

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James Valentine, JD, MHS (02:42:54):

Right. Wow. And maybe now thinking forward to today, how would you describe your progression since then and how that might impact your life differently?

Jared (02:43:09):

[inaudible 02:43:09] physically, I haven't seen as much progression. Internally, my heart, 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.

James Valentine, JD, MHS (02:43:25):

Sure.

Jared (02:43:27):

And that seems to be the biggest change for me.

James Valentine, JD, MHS (02:43:31):

Okay. And then, is that something that you can sense or feel the worst thing of the cardiomyopathy in terms of activities of daily life or is this something you're mostly just monitoring with your doctors?

Jared (02:43:48):

I did before the medications, there was definitely a difference since being on them. 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.

James Valentine, JD, MHS (02:44:04):

Wow. Well, thank you so much, Jared, for sharing all of this. It's so helpful to hear your experiences. I'd like to bring Peter from New Jersey, who's also called in living with 2A and wants to share some of his experiences. Peter, welcome to the program. Are you with us?

Peter (02:44:26):

Hi. How are you?

James Valentine, JD, MHS (02:44:27):

I'm doing well. What would you like to share?

Peter (02:44:30):

I just want to talk about my journey with LGMD a little bit. I was diagnosed in 2006. I was eight years old, but luckily, I didn't experience any symptoms until I was about 19, probably 18, but 19 is really when I first started to notice it.

James Valentine, JD, MHS (02:44:47):

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Yes.

Peter (02:44:48):

And since then, it's just been... It started with my legs. Stairs was the first place I ever noticed it. And since then, it's been a slow progression, but at the same time, it's been a pretty fast progression. My arms do feel weak now, but luckily, I'm still ambulatory. I'm very blessed to still be able to walk. I could still stand up on my own. I still have some independence, granted maybe some independence in a unique way from able-bodied people.

James Valentine, JD, MHS (02:45:14):

Yeah. And can you maybe paint a little bit of a picture of what that difference would look like so we can understand a little bit?

Peter (02:45:22):

Yeah. So when it started, I went to a culinary school and I was working in a restaurant in New York, so very physically demanding job, but that's what I love to do. I knew I had the disease, so I knew it was a risk I was taking. So in a field as demanding as that, it was really easy to notice. Where I was working in Manhattan, the prep kitchen was downstairs, so when I started the job, I was able to bring all of my prep up the stairs, no problem. And then just basically night and day, one day, I noticed it was a little harder. I need to use the railing. So I prop my tray of ingredients up on my other shoulder and I use my left arm to pull myself up the stairs, and I still looked pretty normal doing it [inaudible 02:46:06]. I was still able to hide it. At that time, basically, no one except for my really good friends and family knew what I had. And even so once I started experiencing the issues, I tried to hide it from people for as long as I could and I probably hid it until 2020. So, I've been living a little more openly about it in the past two years, but I still try to close it off as much as I possibly can.

James Valentine, JD, MHS (02:46:33):

I see. And maybe in terms of hiding it, were there things that you were avoiding in life socially? Obviously, you were talking a bit about impacts in the workplace. What else in life was being maybe limited a bit by that and trying to only do things that maybe were less apparent with your impacts?

Jared (02:47:04):

Yeah. So, 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. A big thing that I do is what I do now is I still work in food, but I write about food. So in a way, I was thankful that I found that because I probably wouldn't have found that if not for the disease and I do love doing it. But with something like that, if I'm going to a restaurant I've never been before, the first thing I do is look up photos of it. The first thing I do is use Google Maps to see if the entrance to the restaurant is a step.

(02:47:53):

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Because if it's a step, if it's one step and there's a railing, I don't have that much of an issue with it. But if there's steps without a railing, it used to be that I was just embarrassed to do it, but now, it's at a point where I actually can't even physically get into the restaurant. So, that's something I have to know before I go anywhere. So, I'm always thinking about how I might do that. If I'm in a room of people sitting in a chair and I have to use the bathroom, I'll sometimes [inaudible 02:48:20]. I can stand up decently easily, but it is a little awkward. I'll wait until everybody is simultaneously looking not at me, and then I'll stand up and use the bathroom. So, I'm always just thinking of stuff like that. I'm always thinking about how I can do something in a way that is seen by the fewest amount of people.

James Valentine, JD, MHS (02:48:35):

Right. Wow. Well, Peter, thank you so much for sharing some of your experiences living with LGMD. Really vivid descriptions to help us understand, so thank you. I do see we have a number of written comments that are coming in, so I do want to check in. Jen, what are we seeing in terms of impacts reported on symptoms and health effects?

Jennifer Levy, PhD (02:49:00):

Hi, so we've had several comments come in. One is from a 70-year-old woman with 2A. She says, "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." We also have a comment from Kristen in Pennsylvania. She is living with LGMD 2I. She says, "The symptom that most drastically affects my life all day every day is the struggle to get up from a seated position. I'm 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's too low. It is extremely difficult to travel by plane because I really struggle to get up from the seat."

James Valentine, JD, MHS (02:50:01):

Wow

Jennifer Levy, PhD (02:50:01):

James Valentine, JD, MHS (02:50:01):

. Some really great-

Speaker 3 (02:50:00):

... Seat. Wow.

James Valentine, JD, MHS (02:50:02):

Some really great written comments that have been coming in and we apologize if we can't get to all of them today, but know that we are seeing them all, and we'll be incorporating those into that Voice of

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the Patient report. I do want to broaden the discussion. We have already been talking so much about not just the symptoms, but how they impact daily life. But we have a couple of polling questions to understand different worries being selected as a top three by our audience. So now that we've gotten this input from polling, I want to give last word on this topic to one of our callers. We have Cindy from Pennsylvania, who's living with LGMD 2I. I know, Cindy, you were reporting some of the things that you've already experienced, but I was wondering if you might be able to share also related to that, some of your worries. So I'd like to welcome Cindy to the program. Are you with us?

Cindy (02:51:01):

I am. Thank you.

James Valentine, JD, MHS (02:51:03):

You're welcome.

Cindy (02:51:04):

Hi. I have LGMD 2I and I was diagnosed with this about four years ago, but started progressing from the time that I was 25 until today, which I've turned 55 this year. Some of the daily struggles that I deal with, and I think something that really hasn't been discussed yet, 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. And then within years after that, I progressed to using a cane, then a scooter, and then starting about four years ago now, I started using a wheelchair.

(02:52:08):

Throughout that time period, I had a successful career as a corporate attorney and was able to support myself and my family. About three years ago, I had a significant fall, broke my pelvis and my vertebrae, spent two months in an inpatient facility unable to see or be with my five year old twins, my husband and my dogs for those two months. At that time, I went on disability with the hope of returning to work several months later, but struggled to heal from my fall and decided to stay on disability. Since that time, I've been struggling to try to get back to work but have not been able to. And I think something that we really need to all think about and talk about is the significance of this impact of this disease on mental health.

James Valentine, JD, MHS (02:53:01):

Yes.

Cindy (02:53:02):

It's far reaching. It is deep. And I sometimes refer to this disease as death by a thousand cuts because each one of these losses, each cut goes a little deeper into your psyche as an additional layer of loss, grief, and stress to what you were already handling, and the impact that it has on not only your psyche, but those around you-

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James Valentine, JD, MHS (02:53:25):

Yes.

Cindy (02:53:26):

The people that are caring for you, the people that are watching someone that they love disappear in front of them, and the impact it has on particularly is a relationship that you're closest with, like your spouse that didn't really anticipate being a caregiver at the age of 45 for the significant other. And these are all things that we carry around as families. And we try to keep our nose down and try to keep working, try to keep caring for our families, but this weight is heavy and it's a very large burden on all of us.

James Valentine, JD, MHS (02:54:05):

Yeah. Well Cindy, I mean, that was extremely, extremely well said and well put. I think we do need to hear about and I'm glad that you shared not only the physical impacts, but the emotional, social and mental ones as well. So I appreciate that. So at this point, I know we're over time for this session. I thought it was important to hear those additional voices. But I am going to take us to our break. We have at this point a 20 minute break. We will be resuming at 1:20 Eastern time. So we look forward to really expanding on what has been a tremendous morning of learning about what it is to live with LGMD. And in the afternoon, coming back and focusing on what it is that you all have to try to help manage and live with and treat your condition and what you're looking for from future treatments. So we look forward to that discussion and until then we'll be going to a break. Hello, my name is James Valentine and welcome back to the Externally Led Patient-Focused Drug Development on limb girdle muscular dystrophy, subtypes 2A, 2C, 2D, 2E, 2F and 2I. We're very excited to have you back after a wonderful morning of hearing from all of you about understanding what it is to live with limb girdle muscular dystrophy and how it impacts your lives. I do want to address that we understand that there was a outage that affected some of your connectivity to the end of that morning session and you may have missed some of that last discussion on what it is to live with. LGMD 2A and 2I. Fortunately, despite that global temporary global outage of YouTube Live, our livestream has been restored. I will say if you have any other issue from this point, moving forward, all you need to do is refresh your webpage and it should fix the issue.

(03:16:29):

And also, fortunately the end of that session was recorded. So it will be available on-demand along with the rest of the program as soon as today's meetings complete. But now I'd like to take us into our second topic for the day, which is to hear and learn from you all about the different treatment approaches that you currently have available to you, as well as understand from you your goals and preferences for future treatments. If we can pull up our discussion questions for the afternoon, we're going to be asking you to weigh in on some of these things including what are you currently doing to manage you or your loved ones LGMD symptoms? When we talk about these different treatment or management approaches, we're casting a wide net. We are of course talking about those drugs and medical treatments that you have available perhaps to help manage some of the specific symptoms of your condition, but also clinical trials that you've participated in, and maybe things outside of traditional medicine, more holistic approaches, even things in daily life like different lifestyle modifications, diet exercise, and the like.

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(03:17:38):

So thinking about all of those different things, we want to hear from you about how well those help treat the most significant impacts of your LGMD, whether or not those treatments are helping. We do want to also understand some of the most significant downsides of current treatments that you have available whether that's side effects, the burden of keeping up with the treatment regimen, or anything that you would identify as being a downside. And finally, we'll make sure to save some time to talk about your thoughts and views on what would represent a meaningful next future treatment for LGMD. Understanding that while we all want a cure, we do want to understand what would be important to you short of that cure. So to get us started on this topic, it's my pleasure to welcome a panel of your peers who'll be sharing their experiences and insights. We have Sammy and Kelly, Andrew, Paul, Rachel, Patrick, and Catherine. Sammy, and Kelly take it away.

Sammy and Kelly B. (03:18:37):

Hi, my name is Sammy Browzo and I'm 14 years old. I live in Lancaster, Pennsylvania, and I was diagnosed with the congenital form of limb girdle muscular dystrophy type 2I/R9 when I was two years old. My mom and I would like to tell you about how this disease has negatively affected my life and share the things I do to help make things easier for me each day. This is my mom, Kelly, and she's going to tell you about my story. Thanks, Sammy. Sammy was diagnosed with the compound heterozygous mutation LGMD 2I, after seeing multiple specialists in clinics all over the Northeast. 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. Sammy has had to wear night splints since she was three years old to help with ankle contractures. When she was younger, she used to put up a big fight and hated wearing them. In fact, her older sister, who's not affected by LGMD, used to wear a pair of stretching boots out of sympathy just to help encourage Sam to wear hers. Laying in bed with thick plastic boots with your toes sticking up in the air that are hot, sweaty and very uncomfortable, and they are impossible for her to sleep in. But as Sammy has gotten older, she now realizes how much they help with her heel cord stretching. She still doesn't sleep in them, but she does wear them for several hours each day. At the age of eight, Sammy was prescribed corticosteroids in the attempt to combat her physical decline and improve her strength. However, after just a few days on prednisone, Sammy suffered from headaches, stomach aches and a racing heart and sleepless nights. Although she refused to take the prednisone after only one week, this resulted in a long-term diagnosis of anxiety for which she has had to receive mental health support and counseling for several years. Since she was diagnosed, Sammy has been a participant in three different natural history studies. Initially she was enrolled in one at the National Institute of Health in DC, where she was initially diagnosed with this disease. Then she began participating annually in one at the University of Iowa as part of the Dystroglycanopathy Family Conference when she was five years old.

(03:20:44):

And most recently she started a study three years ago with the GRASP Consortium in Richmond, Virginia, which was for a lead in study for a current clinical trial. Sammy's neurologist warned us that around the time of adolescence, we would notice a significant progression. They were spot on. 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 a single floor living, which



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keeps her independent throughout the day. We installed higher toilet seats and have counter height seating in the kitchen and dining room. We also added a ramp to go outside as well as a heated pool, as swimming is such a white great way for her to stay active in the summer months. She has an electric scooter that she can use for long distances, such as going on family walks or in around amusement parks.

(03:21:31):

Over the past few years in school, we have had to request new accommodations to support her independence. She has an elevator key that she uses as steps are very difficult for her, which works great unless the elevator is broken. She even got stuck in the elevator for nearly two hours when she was in the sixth grade. She now needs to have higher counter height seats and elevated desks in her classroom and separate higher table seating in the cafeteria, as the little circle bench seats are impossible to get out of for her. Sammy has an adaptive commode in the nurse's office, as the accessible bathroom is far from accessible for her condition. 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.

(03:22:19):

So in the fall of 2020, she underwent a bilateral heel cord lengthening procedure. During her recovery, she had to wear cast on both legs for six weeks and endured serial casting while recovering from the surgery to increase her ankle flexion. 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. Thankfully, she is still able to walk despite the surgical trauma, but she has lost the ability to rise from a seated position, as her back no longer hyper-extends to help with her standing up.

(03:23:05):

Sammy has participated in a clinical trial for this condition and has been receiving the trial medication for over a year now. We are so grateful to be able to contribute to this research and hopefully help bring a much needed treatment available to our beloved 21 community. As wonderful as it is to be included in a trial, there are certainly challenges involved. 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 that 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. If a treatment or cure were to become available for you, Sammy, what would you do differently with your life?

(03:23:50):

Probably the first thing I would do would be to run to the ocean and jump in the waves without the fear falling. But it would be great to just go around school and go shopping with my sister and my friends and not get tired and not worry about falling down.

Sammy and Kelly B. (03:24:00):

... With my sister and my friends and not get tired and not worry about falling down. And if I did fall, it would be amazing, if I could just get back up on my own. Thank you. Thanks.

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Andrew R. (03:24:12):

Hi, my name is Andrew. I live in Canterbury in the UK, with my son Thomas, who's nine years old. I'm 41 years old. I have lived with limb-girdle muscular dystrophy for over 22 years. The disease has progressed to the point where I now rely on a powered wheelchair to get around. 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. When the specialist doctor in London told me, I had a genetic diagnosis of limb-girdle muscular dystrophy. I was told it's a rare disease and I had to remember three things. Firstly, there's no cure for this disease. Secondly, there are no treatments for this disease. And thirdly, the best I can do, is to concentrate on quality of life. The scientist then said, "There's a ray of hope. We've just managed to map the human genome and within your lifetime, effective treatments and even a cure are more than likely."

(03:25:08):

The condition is progressive. And so, whilst I'm grappling with the mental health implications of knowing I have a condition that has resulted in a wheelchair, eventually will contribute to my early death, I also have to deal with the physical limitations, which can change on a daily basis. Sometimes, I look at other disabled people who've had an accident, or corrective surgery, or partial paralysis, and I think, "At least, they can live with the knowledge that their condition is stable." Living with a progressive muscle wasting disease never gives you the peace of mind, 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?" I currently use aquatherapy, which is useful for keeping the weight down, getting all the joints stretched out. It's good for mental health to have that freedom of movement.

(03:25:55):

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. I also use a standing frame, which is particularly good for stretching the calves, it's good for breathing as well. I have an all-terrain powered wheelchair, that allows me to go off road. Occasionally, even on the beach, which I often get stuck. I live in a historic city with lots of cobblestone streets. Having something with big wheels makes it easier to get around, without getting bumped, or jarred too much. In the past, I've tried two exoskeleton suits and the technology isn't quite there to give freedom and independence. One of the suits has electrodes that are attached to the body.

(03:26:44):

The slightest movement is then amplified by the hydraulics. The other was controlled the same as a power chair would be, with a joystick, and that's quite slow, clunky movements. And I use these treatments, while knowing that despite it being over 20 years since I was diagnosed, there is no other treatment, or cure available for my condition. Living in a digital world where news spreads instantly, you read about the latest treatment, or cures for other diseases and you wonder in anticipation, "When will it be my turn?" 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.

(03:27:38):

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Since then, no other trials have been relevant for my condition. I know there won't be a magic pill that will suddenly make me spring up out of my wheelchair, run carefree on the beach again. But, as the disease progresses, I find myself wanting to go back to the previous step. I wish I could once again stand up out of the chair. Could I do that without having to push with my arms, or walk up a flight of steps, without having to virtually crawl, or get up from a toilet independently, would be a dream come true. Any treatment that could hold the progression of the disease, or give me that ability to go back one step would be amazing.

(03:28:12):

For many years, I'd speak very positively about the future, telling strangers I'd meet in the street, "Scientists can reverse the disease in mice, it won't be long for me now." One day I overheard my young son tell a carer, "I can't wait until I'm older, there'll be a treatment for my dad. He'll be able to play football like other dads." Going back to the statement, I was told when I was diagnosed, they all still ring true today, some 22 years later. However, now being severely disabled, quality of life is much more difficult to concentrate on. I hope one day a treatment, or cure is ready. I can dare to believe again this disease won't beat me.

Paul J. (03:28:53):

Hi, my name is Paul and I live in Napa, California. I'm a 65 year old married man, with one grown child. My earliest LGMD symptoms were lack of muscle developments, which was noticed about the time I was five. A duck wobble was noticed in my gate, from this time I started to walk. I had also been born with short Achilles tendons. And therefore, had to walk on my toes, until I had corrective surgery at the age of 15, in 1972. Due to poor leg development muscles, they gave out on a regular basis, causing me to fall, as far back as I can remember and continuing until I had to start using a wheelchair. I also had great difficulty with climbing stairs, hills, and traversing uneven ground. All these symptoms were attributed to difficulties during my birth and I received no therapies, or medical care, aside from the achilles tendon surgery, until I was in my early 30s.

(03:30:11):

I was finally diagnosed with muscular dystrophy when I was 35 years old and further diagnosed with LGM 2C when I was about 40. In early 2005, 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. I was experiencing the progression of the disease with more rapidity and would quite often fall. It was like a train coming at me and I couldn't step off the track. 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. I began requiring interventions from my LGMD symptoms, when they were exacerbated by a lengthy hospital stay, following multiple abdominal surgeries, due to a poor outcome of appendicitis in 2005.

(03:31:39):

Upon my release from the hospital, I had three months of at-home physical therapy to regain my ability to walk. 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. I could still stand and sit up unaided. In 2007, I began using motorized scooters that eventually progressed to a power wheelchair. At about the same time, I started

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using motorized wheelchairs, 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.

(03:32:57):

I'm also taking various heart medications and blood pressure medicines. I have daily in-home caregivers during the day, my wife cares for my needs overnight. 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. And I leave the house four, or five times a month for doctor appointments and very rarely to visit friends. It's quite painful to be placed in the Hoyer and to sit in my wheelchair. I take all pain medications on these occasions. Considering that LGMD is a progressive disease, my current treatments help maintain a better standard of living. However, they do not replace full function, or constitute anything more than palliative care and assistance.

(03:34:03):

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. I hope that one day there are other gene, or other therapies to stabilize the loss of muscle mass and/ or muscle repair, short of a complete cure. Thank you for your time.

Jacob DeCandi (03:34:48):

Hi, I am Jacob DeCandi and I'm five years old, almost going to be six.

Rachel D. (03:34:52):

My name's Rachel. My son Jacob, is kind, funny, sweet, smart, and adventurous. He loves playing outside with his Marvel superheroes, especially Spider-Man and was awarded fabulous friend at the end of kindergarten this year. Last fall, Jacob was diagnosed with LGMD type 2D/R3. As a parent, this diagnosis was terrifying, heartbreaking and blind siding. My husband and I knew, we need to do whatever it took to learn more about LGMD and became devoted to advocating for him and the entire LGMD community. Jacob is always on the go. He loves to run, climbs on whatever he can and barely sits still. At the last checkup for an LGMD study he's in, the physical therapist, told him to sit and recharge to 100. He told her he's already at 500, that's just how he is. But, with this constant activity, his legs begin to hurt after a while and we need to constantly remind him to sit down, relax, slow down, and stop running. It's the constant battle of letting a five year old boy be a five year old boy and having him rest, because we know his body needs a break.

(03:36:09):

There's also a feeling of guilt, that if one day he isn't able to do some of these things. And we know maintaining activity is important to supporting muscle strength, so it's that balance. Jacob was diagnosed with LGMD after he suffered a case of Rhabdomyolysis last Summer. His CK was extremely high and we were in the hospital for three days, while he was hooked up to an IV. After that event, one of his doctors recommended that he drink at least 48 ounces of water a day, due to his non-stop

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activity. There have been times when there was traces of myoglobin in his urine and we need to make sure he drinks extra water that day, until it becomes light again.

(03:36:53):

It breaks our hearts that our sweet boy has to worry about these types of things. Things that parents and children normally don't even think about. 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. Jacob is worthy of the right to a treatment that will help him play sports with friends his age, or even keep up with them on the playground. He 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. Having a treatment like gene therapy, would ideally address the symptoms I mentioned, that Jacob 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.

(03:38:44):

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. I don't think that there's much parent might do for their child. When an LGMD 2D treatment does become available, which will hopefully be soon. Fully understanding the treatment would be critical, knowing what the treatment is, how it will affect him, potential side effects, and what the risks are, would be among the top questions for us.

(03:39:32):

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 re-occurring 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.

Patrick M. (03:40:10):

From 1972 to 1984, my life was normal. Well, looking back now, there were signs, but I never noticed, nor would I have acknowledged them. As a kid, no one wants to be different. When you realize you are, due to a physical problem, even at age 11, you start to question the whole world. "Why can't I run like everybody else? Why do my calves feel like they're on fire when I try to run? Why do I lose my balance

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when trying to climb on the playground? How come I'm out of breath when I reach the top of a normal flight of stairs? Why did I randomly get chosen from a class of sixth graders, to help some lady who showed up during my class who told me she was a PT? What does that mean? And why is she sitting with me in a closet, next to the gym, making me stand on one leg and asking me all kinds of questions? Does she know that I ache a lot? Can she see it? Now, somehow my parents suspect something."

(03:41:01):

Three different doctor's offices during the school year. Everyone, even an orthopedic specialist tells me, I have flat feet, but nothing else is wrong. I know something is wrong, something's seriously wrong, I could feel it. I just didn't grasp that having trouble running, would someday lead me to several power wheelchairs, a few hospital stays, worrying about my weakened heart and damaged lungs, experienced discrimination in my workplace and in public, as well as spending tens of thousands of dollars out of my own pocket, simply to attempt to live as the rest of able-bodied adults do. I had no idea that women I dated, did so, because I was funny, driven and a great guy. But, when things got serious as in living together, or a marriage excuses were made, but I knew that they had all they could take.

(03:41:47):

Anyone that decides to spend time with me, becomes a caretaker, and the vast majority of people can only mentally and physically handle that for a little while. The exception is my wonderful wife, Vanessa. While I was drafted in the world of muscular dystrophy, Vanessa enlisted. We have our highs and lows, like all married people, but our support for each other is unwavering and that is key. Here are a few things that you do each day that require almost no thought, but require full assistance, for a 49 year old man, living with limb-girdle muscular dystrophy. Getting out of bed, scratching your head, getting on and off the toilet. 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. Brushing my teeth, shaving, getting dressed, tying my shoes, eating breakfast.

(03:42:39):

While you are listening to me speak right now, you may have checked your phone, scanned a quick email, or effortlessly raised a cup, or glass to your mouth, without even thinking about it. All of these simple acts, to me, require planning, preparation, and assistance. I have lived like this for so long, that my mind is sharp to solve problems all day. They are in addition to all the ones that come up for all of us. Broken car, "I need new clothes, the dog needs to go to the vet, the kids have swim lessons, we really should get an estimate on the roof, we could have a little tree work done in the yard." Those are all things for all of us that require research, thinking, planning, and finally, action. Having a glass of water, or feeding myself carries similar effort for me. I can't open the fridge if I want a snack.

(03:43:26):

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. 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. What I do understand, is that I live in the best country on earth, the United States. We have the most talent, the most resources, and some of the most progressive laws to help the disabled. None of this is enough. I can still breathe normally, but in

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the future, should my lungs fail, someone drills a hole in my throat and puts a tube in, this is the best we can do.

(03:44:14):

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. These are the therapies and treatments for muscular dystrophy, not good enough. From 1985 when I was diagnosed until now, I've been told that better treatments, and even a cure is just on the horizon, coming into focus, or just around the corner. 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.

(03:45:02):

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. 40 years of having muscular dystrophy is enough, I'm done. Actually, I was done 30 years ago, but here I sit. My name is Pat Motion and this is my journey.

Kathryn Bryant Knudson (03:45:28):

My name is Kathryn Bryant Knudson and I live with LGMD 2I/R9. 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. When I was diagnosed, the only recommendation was palliative care, management of symptoms and assistance with durable medical equipment. 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. There are currently two possible treatments that show great promise. One is gene therapy and the other is a treatment called ribitol, which helps to act as a shock absorber, so the cell acts more normally. In the last two years, we have seen first-time potential therapies for LGMD 2I and other forms of limb-girdle.

(03:46:40):

A successful treatment for me would be to see the disease progression slow down. I don't have an expectation that a treatment for muscular dystrophy would allow a person who was in the later stages to be able to walk again, that's unrealistic. I use a wheelchair currently, and for me, 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. 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. Another thing that's important, is that I still have a lot of muscle groups that are very strong. For example, for the most part, my arms are still unaffected.

(03:47:37):

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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. A treatment that would slow the disease down will allow me to keep this independence in using my arms and my hands. This allows me to be independent, without relying on others. I feel very frustrated when I'm in a clinical trial and things that matter to me are ignored. And I feel like the emphasis is on things sometimes, that just aren't as important to me. A treatment that would slow progression, would mean that I may not have to use a ventilator one day. I wouldn't be able to communicate well with an assistive breathing device. It's a huge burden to carry, or put on the back of a wheelchair. The fear of my heart and lungs greatly overcomes any concern about walking.

(03:48:29):

In terms of risk, I'm willing to do a lot. However, I wouldn't participate in a trial if I thought it was a great risk to my life, but I would do a trial that has short-term side effects. And I'm happy to endure anything like that for a positive outcome later. I've actually had the opportunity to participate in trials. I'm in two natural history studies for 2I. In fact, one natural history study has been 15 years long. My concern is that some subtypes of LGMD are so rare, it's difficult to find patients with strict inclusion criteria. 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.

(03:49:27):

I feel like I already have enough burden to deal with already. 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. 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. 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. We pray to God that we see treatment sooner, rather than later. I hope stakeholders consider how we can effectively do trials, while also helping patients lessen the burden of disease.

James Valentine, JD, MHS (03:50:54):

Thank you, Kathryn, and to all of our panelists for this session, who have really started to lay out the range of things that this community is trying and using and willing to do, in order to having a effective treatment and what that might look like for them. We now come to our third opportunity today to expand the conversation to all of you who are live in the audience. And in this session, it is open to all of our people living with LGMD, with subtypes 2A, 2C, 2D, 2E, 2F, and 2I. We aren't splitting this afternoon session out as we try to explore those things that you're currently doing to help manage and treat your LGMD. But, to get us all thinking about this topic and understand the experiences in our audience, we're going to start with some polling questions.

(03:51:50):



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So, if you didn't happen to be with us this morning, you can go ahead and we're going to be asking you to go to a webpage, so you can pull out your phone, go to a web browser, open a new tab in your web browser on the computer, if you're following along that way, and go to [www.PolLEV.com/LGMD](http://www.PolLEV.com/LGMD). Again, that's P-O-L-L-E-V.com/LGMD, and we will be putting up different polling questions throughout this afternoon's session. So, our first question, for our audience is, which of the following medications do you use to manage LGMD symptoms? And here we really are focused on more medications. We'll have another polling question on some other types of approaches to managing LGMD. But, here we want you to select all that apply. So, the options are A: Dietary and herbal supplements.

(03:52:42):

B: Investigational drugs, that might be accessed through expanded access, or clinical trial. C: Medical, or recreational marijuana, Cannabidiol, or CBD products. D: Medication for anxiety, or depression. E: Over-the-counter medications, things like acetaminophen, or ibuprofen. F: Prescription pain medication. G: Steroids. H: Some other medication that's not named above, or I: If you're not currently using any medication, or your loved one that you care for, is not currently using any medication. As this is our first polling question of the afternoon, where we're asking our audience to select more than one option. And this will apply to any question that is like that, you're seeing percentages of total responses. So, the percentages are not the number, or the percentage of people picking any one option. So, you can view these bars as relative ranking amongst each other.

(03:53:46):

So, while results are still coming in, as it stands, it looks like some of the top medication approaches that are being used by our audience today, include over-the-counter medications and dietary and herbal supplements. So, we'd like to hear, which of those things you're using? What you're using them for? How they're working? We also see that after that, there's a number of people that are using medications for anxiety, or depression. As well as, each of the other types of medications that we list here, including investigational drugs that are still in development, but might be accessed through expanded access, or clinical trials. And we do want to hear about clinical trial experiences as part of this session. We also have a number of people who are not currently using any medications. So, we'd be interested to hear about your decisions to not use medications based off of maybe, where you're at with your LGMD story, or journey. And maybe, some of the trade-offs that some of these medications bring. If we can now move to our second polling question.

(03:54:55):

So, here we want to go beyond just medications and supplements. We want to know what else are you using to help manage your LGMD symptoms. And we want you to select all that apply, of those things that we have listed here, which include A: Braces, kinesio tape, other things along those lines. B: Complementary therapies like a chiropractor, acupuncture, or massage. C: Counseling, or therapy. D: Diet modifications. E: Exercise. F: Mobility aids, things like cane, walker, scooter, or wheelchair. G: A modified home environment. H: Physical, or occupational therapy. I: Surgeries. J: Urinary incontinence devices. K: Ventilation devices. L: Water, or aquatherapy. Or, M: Some other approach to try to help managing LGMD symptoms, that is not listed here. And you can select N, if you are not currently using anything to manage your symptoms, or if your loved one that you care for, is not using anything.

(03:55:59):

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So, it looks like some results are still coming in, but as it stands, mobility aids, seems to be the top non-medication approach to trying to manage LGMD symptoms. After that, we're seeing, a modified home environment being reported as perhaps, the second most-common approach. Then, followed by more of a clustering of things like exercise, PT & OT, diet modifications, complimentary therapies, ventilation devices, and really just, everything here being used by a number of people and much smaller compared to the first polling question. A number of people saying, that they're not currently using anything to manage symptoms of LGMD. We have one more question for you here to start us off and get you all thinking about current treatment approaches. So, if we can go to our third polling question.

(03:56:57):

So, thinking about everything that was covered within those first two polling questions, medications, supplements, other approaches to managing, we want to know, how well does that current regimen control your symptoms overall? The options are A: Not at all. B: Very little. C: Somewhat. D: To a great extent. Or, E: This is not applicable to you, because you are not using any treatments, or other management approaches. So, basically you're not using anything that was listed on those last two slides. So, as you're thinking about and selecting your response to this question, I want you to think about what is coming to mind and driving your decision. If you're one of the people that are selecting somewhat, what is helping? How would you describe that, somewhat control of your symptoms? But, also where are the gaps? What is not being controlled? If you're one of the people that have said, "To a great extent." Similarly, what were your most...

James Valentine, JD, MHS (03:58:00):

... stent, similarly. What were your most troublesome symptoms and how have those really been addressed to a great extent? So whichever one you select, we want to hear from the range of experiences with the degree of control of symptoms. So it's looking like we're seeing just over 40% of our audience reporting somewhat, just under 40%, reporting very little. A little over 5% saying that current treatments are helping to either a great extent, but about the same amount saying, not at all. And then we're seeing about 6% of people saying that they're not doing anything right now to help try to manage or treat their symptoms.

(03:58:47):

So now that you've had an opportunity to think about this, I'd like you to consider calling in and sharing your treatment experiences. What's helped? Maybe what if you'd like to call in, we invite you to by dialing in at 1703-844-3231. And that phone number is 1703-844-3231. We'll get you in the queue and try to bring you into our discussion. But to start us off in thinking about these issues of current treatments, I'd like to welcome our zoom panel for this third and final discussion of the day. Maybe we can start with Michelle. Michelle thinking about all of those things, maybe we can start by thinking about what has maybe been the most useful or most helpful in addressing the symptoms and health effects of LGMD. So I'd love to hear your thoughts on that.

Michelle and Austin C. (03:59:45):

Thank you. My name is Michelle. I'm the mother to a 15 year old boy named Austin, he was diagnosed with LGMD 2D R3, approximately a little over five years ago. So the most common things that we use as

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supportive measures for this would probably be mobility aids. That is the most that he's affected by and we've seen that change over the years as things have progressed.

James Valentine, JD, MHS (04:00:19):

So maybe can you share a little bit about what that manifestation of mobility limitation started to look like? And how did you decide that it was time to maybe start introducing some mobility assistance devices?

Michelle and Austin C. (04:00:37):

Sure. So when symptoms first started, we noticed some weakness and some frequent falling and certainly a lot of fatigue so we started with a manual chair. Approximately a year after that, we noticed again, more frequent falls, more injuries because of that and more weakness in the shoulders. So we moved to a power assisted wheelchair, and that lasted for about 15 months or 18 months or so until the weakness progressed in the top where he wasn't able to move the chair as much even with the power assist. And so we moved to the power chair, which gives him more maneuverability and takes the fatigue off of those muscles and being able to use it throughout the day.

James Valentine, JD, MHS (04:01:26):

Right. And so having that available now, what aspects of daily life, activities in daily life has that help him continue to engage in or reengage in?

Michelle and Austin C. (04:01:39):

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, also going out into the community, not having to worry as much again, about falling or that fatigue in the shoulder area, pushing the manual chair. So it certainly gives him a lot more flexibility to be able to do those things that he wasn't able to do before.

James Valentine, JD, MHS (04:02:12):

Wow. Well, that is wonderful to hear Michelle, so thank you for sharing some of those experiences around mobility assistance devices. I'd like to bring Jordan into the discussion while we're on this topic of maybe what has been most helpful of these different treatment or broadly management approaches?

Jordan B. (04:02:32):

Thanks. Yeah. My name is Jordan and I am a patient with LGMD2A, located in New York. Yeah, I would echo what Michelle said, clearly mobility devices are, I think for many people, the difference between being home bound completely or being able to be out in the world, whether that be school or a job. Outside of that, I would say most of the treatments or therapies are extremely mild in the sense of whether they're potentially effective and just general. My view is basically more around trying to stay as healthy as possible so that when there is a more specific treatment for this disease, that I would be able to benefit from it as much as possible.

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James Valentine, JD, MHS (04:03:33):

And if you think about these changes and what you're doing to help access and increase mobility, are there specific, important activities that are really driving the need for using these devices? And just maybe to give us a little bit of an insider color into your day and your life, maybe if you have an example to share to that effect.

Jordan B. (04:04:04):

Yeah, physical therapy is important to try to retain range of motion, obviously. I have heel core 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. And then also just being at less risk of injuring yourself by accident. So I think the physical therapy is important just for trying to maintain day-to-day mobility.

James Valentine, JD, MHS (04:04:52):

And I guess it might be hard to pinpoint something very specific, but just this added flexibility, which translates this added mobility for you and doing some of these things, are you notice certain things that you're able to specifically continue doing, whether that's some kind of activity within the house or within daily life, what does that translate to being able to have that?

Jordan B. (04:05:30):

Yeah, I think one thing that I would emphasize, I think this has come up in some of the videos, is that 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.

James Valentine, JD, MHS (04:06:24):

Yeah. Thank you so much, Jordan. I see that we have a number of written comments that are coming in and so on this topic of maybe things that have been most helpful. Jen, what are we seeing from the web?

Jennifer Levy, PhD (04:06:36):

So we have a few comments. One is a 42 year old woman with LGMD2A. She says, "My partner does range of motion activities on me five nights a week before I go to bed. That helps me sleep better. I am careful with my diet, so is not to gain too much weight or encourage other health problems. 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."

(04:07:13):

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We also heard from the parent of a 14 year old with LGMD2E. They say, "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."

(04:07:32):

And we have a comment from a 54 year old with LGMD2I, who says, "There's no medicine or treatment, but I take meds for heart issues. I try to keep my stress low, stay as active as possible without further damaging my muscle. I eat healthy and I attempt to keep my weight down."

James Valentine, JD, MHS (04:07:49):

Great. Well, thank you everyone who's been writing in with those comments. It's great to hear some of those things that have been helpful for you. But we do want to expand the discussion. We certainly want to continue hearing about those things that maybe have helped the most. But we also recognize that maybe there are things that you've tried that maybe haven't been as useful, or you're not sure, maybe even how useful it's been.

(04:08:14):

As well as things that maybe whether or not they are helping they come with some downside or trade off. And so we want to explore those topics. And as part of that, we're going to get started by doing a polling question together. So go ahead and go back to [polleEV.com/LGMD](https://polleEV.com/LGMD), whether that's on your phone, on a new tab in a web browser. Here we want to know what are the biggest drawbacks to your current treatment approaches. And here you can select up to three. The options are; A, the high costs or co-pay, or it's not covered by insurance. B, limited availability or accessibility of the approach to you. C, negative side effects. D, that it's not very effective. E, the number of pills or medications needed per day. F, it requires too much effort or time commitment. G, some other biggest drawback of your current treatment approaches that you would identify as a top three approach, or H, this is not applicable because you're not using any treatments.

(04:09:27):

So we'll give you a few moments here to think about this and let us know what those greatest drawbacks of current treatments are for you. So as it stands, it looks like some of the top biggest drawbacks are both the high cost co-pay and inability to get insurance coverage, as well as limited availability or accessibility. So particularly on that would be interested to understand is that based off of where you live or some other barrier to having some treatment approach be available to you. We're seeing as a close third, that the current approaches are just not very effective at treating those important aspects of LGMD.

(04:10:19):

Although again, here, we're seeing each and every one of these drawbacks in some number of people's top three, so we're very eager to hear your experiences with current treatments. And again, if you're interested in sharing your thoughts, some of your experiences, we encourage you to call in. Again, that number is 1703-844-3231. You can call it at any point during this discussion to share your views and experiences. But I'd like to check in with our zoom panel and Lisa, we haven't had a chance to hear from you yet on this topic of current treatment approaches. Maybe as you're thinking about some of the things that might represent downsides again, whether or not maybe the treatment is actually providing some benefit. Is there anything that comes to mind for you as a top drawback?

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Lisa V. (04:11:15):

Hi, I'm Lisa Veda. I live in Wichita, Kansas. I have limb girdle 2IR9. I'm also a pharmacist and a health economist, married to a physician with two grown children who are also in the medical field. So I was able to research medications and such, but one of the big things that's happened recently, I use a scooter when I'm outside of my house. And for the longest time I was able, because it only weighed about 30 pounds, I could take it in and out of my car. But in the last couple of years, I haven't been able to do that myself. So I got creative and went to my local Wichita State University and worked with bioengineering students to put a customized lift in the back of my car, that would allow me to get it in and out of the back of my small SUV without damaging the car.

(04:12:16):

And so I think in dealing with this, sometimes we have to get creative. One of the biggest things that I see besides cost and not necessarily monetary cost, but the cost on, "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.

James Valentine, JD, MHS (04:13:08):

Yeah. That's really powerful to hear just the burden of taking that one step, traveling, even local transportation, it sounds like with the YMCA example. So have there been things, you mentioned being able to go and swim. Have been things that you think might have been beneficial to you? Maybe even exercising things in daily life that you have to limit, which may in turn be restricting the benefits that you could be getting from those things.

Lisa V. (04:13:48):

I think all of us will say, if you've ever worked with a good therapist versus a bad physical occupational therapist, that that can make a difference because sometimes if they don't understand, specifically your muscular dystrophy, they may try to push you too hard or they may try have you using equipment that you shouldn't. Early on I actually went to an exercise physiologist who specializes with older patients and those with Parkinson's and she had me practice certain things like getting in and out of getting out of my car or going up and down a stair, just one stair, using the railing.

(04:14:38):

And how to do exercises that would benefit me and how to do those activities in a way that I wouldn't cause myself more harm or actually cause myself to become off balance and fall.

James Valentine, JD, MHS (04:14:52):

Wow.

Lisa V. (04:14:52):

And I think it's very important to make sure that whoever you're using that they're well educated about your specific type of muscular dystrophy.

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James Valentine, JD, MHS (04:15:02):

Yeah. That makes a lot of sense, Lisa. Thank you so much. I do see that we have a phone caller that wants to share her one of her treatment experiences. We have Anita for Missouri who has LGMD subtype 2I. So I'd like to welcome Anita to the show. Anita, are you with us?

Anita (04:15:23):

I sure am. James, how are you today?

James Valentine, JD, MHS (04:15:25):

I'm well, I'm eager to hear about this treatment experience. Is it something that's helped? Something that maybe hasn't been so helpful, whatever it is, I'd love to hear about it.

Anita (04:15:39):

Absolutely. In fact, I was just listening, I think her name was Lisa.

James Valentine, JD, MHS (04:15:41):

Yes.

Anita (04:15:42):

And I really loved what she had to say because similarly I do aquatherapy. I've done... Oh my goodness, over the last 40 years, quite a few things. But my take, and this is just my journey. I use a power wheelchair. I'm 61 years old. Fortunately I can get up out of my wheelchair. It lifts and raises me and I can stand out of it, support myself and use a walker to sit on a lift or whatever it is. So I have the benefit of that and being able to still move. And I think, my point today would be just no matter how little you can move, it's so important to move those muscles and being in the water is just the best thing that you can possibly do because it takes gravity out of the equation.

(04:16:34):

And being with someone who knows how to work with you in the water and address your needs every time you're with them. Because one day you may feel one way and the next day you may feel another way. Basically, oh, probably the last 10 years, I go once a week and swim with a swim coach and we do all kinds of work in the water. And then I also have a, she's actually a yoga instructor, but I would consider her almost an OT because she comes to my home and I'm fortunate enough that she works out with me and then does stretches on the bed, and I do that weekly. And then I also have an exercise bike, and I listen to videos and I do drumming with salad tongs for 20 minutes. Whatever I can find just to move that day a little bit just makes me feel better.

(04:17:29):

And being that we have muscular dystrophy, we get to know our bodies so much better. And we have to, in order to go forward. We know what works for us, what doesn't work, and we have to advocate for ourselves. And when we're with someone who says, "Do this," or "Do that," and we know it's not a good idea, or we know it's pushing our bodies too far, we have to take that step and be an advocate for ourselves. And say, "No, no, that's not going to work for me." Or "I can't push it too far. I can't let my

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muscles burn. I can only go so far." And they really appreciate that I'm educated that I can tell them, "I can do this, but I can only do this to a certain degree."

James Valentine, JD, MHS (04:18:19):

Well, you said something really important Anita, that I want to follow up on. You talked about these different, we can call them exercises, we can call it just moving and staying active, but the aquatherapy, the yoga and so on. You said that when you're able to be active and do some of these things you feel better. Can you maybe describe, is that feeling better in terms of making some of your symptoms feel less bad? Is it feeling better in terms of energy that you have? Can you just describe that a little bit for us?

Anita (04:18:50):

Yeah, absolutely. I think it's a little bit of everything. It makes you feel better about yourself, number one. It makes you mentally just as if you were to go to the gym, sometimes you don't want to go to the gym, but once you do it and you get it over with and you leave the gym and you get in your car and you feel better about yourself because, "Okay. Yeah, I got that done, check." So it's a little bit like that.

(04:19:16):

Yes, it may not be something that we're looking forward to, but it's something that we need to do. And once you do it, I think it maybe releases those endorphins that just makes you feel better that you've done it. So everything, even I know, I'm educated enough to know that that's not going to stop my progression. It's not going to make a difference in my disease where all of a sudden, the more I exercise, the better I'm going to get, I know better.

(04:19:43):

But I also know that just sitting and doing nothing is the... if at all possible to move in any way, you've heard the old term, if you don't move your muscles, you lose those muscles. And I just believe that we're on that road anyway. So whatever we can do in the now is the best avenue and it just makes you feel better. And also meditation, someone else mentioned today, mental awareness. 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.

James Valentine, JD, MHS (04:20:47):

Yeah, absolutely. Well, Anita, this has been so incredibly helpful to hear both on the physical side, but also on the mental side, what has been helpful? I want to bring in another voice, it looks like we have Michelle who is living with LGMD subtype 2I, that has some other treatment approaches we haven't heard much about yet to bring in the conversation. So Michelle, I'd like to welcome you to the program, are you with us?

Michelle (04:21:16):

Hi, I live in Michigan and where I live there, we're not really close to really good therapies. So I have to drive quite far if I'm going to. But I had started using chiropractic care actually, before I was diagnosed. I



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started because I was pregnant with my third child and I knew the first two pregnancies were hard. So I started going to a chiropractor and about three years into going, I was diagnosed and I talked with my chiropractor and he made it very clear that he couldn't cure me. I made it very clear that I understood he couldn't cure me.

(04:22:03):

And I wasn't looking for a cure. But what he did say is that because the muscles were going to be so fatigued, that he would be able to, if I fell or if something went out, he'd be able to help put it back in. And I think that has been a huge part of the past 20 years, being able to still walk and I think it just moves me better.

James Valentine, JD, MHS (04:22:37):

Okay. Are you able to notice certain things, parts of movement or activities, day-to-day when you are getting that maybe when you've gone some amount of time without having that type of support and help from the chiropractor?

Michelle (04:23:00):

I definitely notice the difference. In fact, I try to go every two weeks, but the summer was busy and so I couldn't go and my body tells me. Now I want to say that I had a really bad experience when I was 19 with a chiropractor and so I knew that if I ever sought out, which I wasn't going to, forever, for a long time. If I ever sought one out, it had to be like ones that talk about gentle. And the more I learned, my particular one practice is called Gonstead, it's a Gonstead method. He doesn't force anything. He doesn't "Jerk me or crack me," horribly. 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. Now I know we could do it at home, but honestly, my husband is not always a fan of just sitting there massaging me for a half hour. So I usually have to pay money to do it.

James Valentine, JD, MHS (04:24:21):

Sure. No, that-

Michelle (04:24:25):

And I loved what the last caller said about water therapy, aquatherapy. I wish that was an option for me. I could go to the Y, but then I don't have the support and my insurance doesn't cover chiropractic or massage, very little physical therapy if I were to go. So I would love to have-

James Valentine, JD, MHS (04:24:55):

It makes that difficult to access. Yeah. Well, thank you so much, Michelle. It's great to hear about some of these alternative treatment approaches when we don't have things that are directly addressing the disease. It's still very valuable to hear about how some of these things make life a little easier, maybe provide a little bit of relief from these symptoms. Keep the calls coming, we see more people are starting to call in. But I do want to check in, because I also see that we're getting a number of written comments on the broader topic of maybe things that haven't been so helpful or represent some treatment downsides.

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Jen (04:25:42):

So we've heard from Teresa she's 68 years old and lives with LGMD 2A and she is based in Poland. She says, "In my case, physiotherapy, by an experienced physiotherapist plays an important role. The problem is that it's difficult to pinpoint the moment when physiotherapy can do more harm than good."

(04:26:03):

We also heard from Viola, from Italy. She says that her 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. She says that these treatments only help slow down the worsening, which happens anyway. He's also taking steroids, but that causes eating difficulties and problems with his bones.

James Valentine, JD, MHS (04:26:30):

Wow. Well, thank you. And thank you for those who have been writing in, keep those comments coming as well. I want to bring in another one of our callers, actually, someone else from Michigan. We have Ferran who has a son with LGMD subtype 2D, wants to share some of their treatment experiences. So Ferran, I'd like to welcome me to the program. Are you with us?

Ferran (04:26:56):

Hi. Yes, I am. Thank you so much.

James Valentine, JD, MHS (04:26:58):

Yes. Welcome.

Ferran (04:26:59):

Oh, yeah. My son, he's nine. He has 2D and for his treatments, we focus on physical therapy, really working on stretching. We do stretching daily, but he sees his physical therapist every week and they work on some mild exercises as well. We're just really trying to maintain his mobility as long as possible and that flexibility is such a huge piece to that.

(04:27:27):

He also wears night splints on his ankles every night. He actually got acclimated to those pretty quickly, so that was great. He's part of the natural history study 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.

James Valentine, JD, MHS (04:28:01):

Yeah. Well, can you tell us a little bit about that relative stability that you were describing? How have you noticed things have been stable for now? Maybe the best way to do that is comparing that to what it looked like before, maybe when things were progressing a little bit more.

Ferran (04:28:21):

So he really just got diagnosed in October. So we started physical therapy and that's actually how we found out that he had muscular dystrophy.

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James Valentine, JD, MHS (04:28:30):

Oh wow.

Ferran (04:28:31):

The physical therapist has been working with him on certain strengths 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.

James Valentine, JD, MHS (04:28:55):

Yes.

Ferran (04:28:55):

I know that's not going to be the norm for his whole life, but that was really encouraging. So we definitely love physical therapy and we intend to continue it for as long as possible. The progress of his physical therapy, it's small and minimal and our hope is that it at least keeps him where he is at as much as possible.

James Valentine, JD, MHS (04:29:23):

Yeah. You mentioned going up steps. Are there other types of activities involved in physical therapy where you're... because those are the things that he's doing there, you at least get a sense that those things are either staying stable or maybe even getting... like with you said with his hip strength, even some little boost.

Ferran (04:29:48):

Yeah. So a big focus is heel striking when he walks. That's a big thing, it helps prevent him from tripping. That's always a struggle on the playground. Being able to stabilize his body when he is playing tag with his friends or running around, having proper heels strike when he's walking makes a big impact on his ability to stay upright and not injure himself.

James Valentine, JD, MHS (04:30:15):

That makes sense. Well, I just want to thank you so much for calling in sharing your son's treatment experiences. And I'm glad to hear those... I think we're hearing a little bit of a theme here about how even some of the really small things can make a big difference in people's lives. So I appreciate that. I want to make sure that we do have time also to talk about what you all are looking for from future treatments. I think we can all agree that what we want is a cure for LGMD and each, not just LGMD of course, but also each of your subtypes.

(04:30:54):

But short of that cure, maybe there's other things coming down the pipeline that are being developed that might provide you some benefit that is short of that. But we'd like to know what might represent a meaningful treatment benefit, even if it is short of that cure.

(04:31:11):

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So for the final time today, we'll ask that you please go to that polling website, pull out your phones, go to that browser, open that tab on your web browser, on your computer, go to [poleEV.com/LGMD](http://poleEV.com/LGMD) and please let us know, short of a cure what would represent a meaningful benefit to you in a future treatment for your or your loved one's LGMD. And here we want you to select your top choice. So would a meaningful treatment be A, lessening pain or fatigue. B, preserving cardiac function. C, preserving respiratory and lung function. D, regaining strength and/or muscle function. E, slowing or stopping the loss of muscle function. Or F, some other meaningful benefit from a future treatment that you would select as your top choice that isn't on-

James Valentine, JD, MHS (04:32:00):

... get from a future treatment that you would select as your top choice that isn't otherwise listed in this question. And maybe multiple of these would represent meaningful benefits to you. And so, if you call in and write in, we'd like to hear ... Certainly, you don't have to just limit your answer to one. For polling, I think it's helpful to get a sense of where people are thinking. But we want to hear what did you pick? But maybe was there a close second amongst these treatment options? We know this is a difficult question to have you just pick one top choice.

(04:32:45):

All right. Well, it's looking like, as it stands, that over half of our participants today, they're saying that a meaningful treatment would be to regain strength and/or muscle function. And about a quarter of people are saying that a meaningful treatment would be slowing or stopping the loss of muscle function. So, kind of those two options related to muscle function being very high on people's list of what would represent a meaningful treatment or their top choice, rather, for a meaningful treatment. But we do see about 10 people saying preserving respiratory and lung function, 5% say preserving cardiac function, and some number of people saying even lessening the symptoms of pain or fatigue alone would be their top most meaningful benefit short of a cure, as well as some saying something else that wasn't listed here.

(04:33:37):

So, regardless of whether you pick the thing that was selected by the majority of people or only 1%. We want to hear about those different experiences and encourage you to call and write in.

(04:33:52):

But I'd like to start with our Zoom panel on these, reflecting on what, short of a cure, an ideal next future treatment might look like. And Michelle, maybe we'll start with you this time. Thinking about that, those options, maybe even things that weren't listed, what would you seek or hope for, short of a cure?

Michelle and Austin C. (04:34:18):

So, 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.

James Valentine, JD, MHS (04:34:34):

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Yeah. And are there certain aspects of muscle function, whether that's certain aspects of mobility or certain activities that you would say these are the key things that would be important to preserve as much as possible?

Michelle and Austin C. (04:34:53):

Mm-hmm. Certainly walking would be one. 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. So, I think that would be really helpful.

James Valentine, JD, MHS (04:35:11):

Great. Well, thank you so much Michelle. Jordan, I'd like to get your thoughts on this question as well. Short of a cure, what would represent an important or meaningful benefit from a future treatment?

Jordan B. (04:35:26):

Yeah, I mean think, as I said earlier, obviously the hope would be to get some sort of restoration of function in some form. But if all it did were to kind of stop the progression, that would obviously be a huge relief while waiting for potentially other things in the future. So, just not knowing how the disease is going to progress or at what speed and what's going to be in the future, not having to worry about that would obviously be a massive benefit in itself.

James Valentine, JD, MHS (04:36:07):

And Jordan, when you refer to progression, are you also referring to the muscle progression? Are you also talking about cardiac and/or pulmonary function or all of the above?

Jordan B. (04:36:20):

So, I have 2A where there generally usually is not cardiac or pulmonary. So, for me, it would be more the muscle weakness.

James Valentine, JD, MHS (04:36:32):

Yes. Well, thank you so much, Jordan. And Lisa, to kind of circle around our virtual table here, want to ask you that same question of what would represent, short of that cure, an important next treatment for you?

Lisa V. (04:36:48):

Well, as everyone's mentioned, I think that holding the progression and actually trying to regain some muscle function but thinking as putting my pharmacist hat on, one of the things I often worry about is that so much of our muscle's already broken down and there's lots of scar tissue that's intertwined within our muscle that is functioning. So, I do think that part of a cure is also going to be looking at some sort of enzyme or something that's going to help us deal with the scar tissue that's there that inhibits our muscles to work as properly as they should.

James Valentine, JD, MHS (04:37:27):

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Sure. Well, thank you, Lisa. And I just want to thank our whole Zoom panel here for your contributions. I'm going to go to some phone callers here in a second, but wanted to make sure I at least express gratitude for all of your contributions.

(04:37:40):

So, I would like to check in with our phones. I see we have some callers who want to chime in on our topics around treatments. I'd like to start with Eric from Arizona who I think is living with LGMD subtype 2A, would like to welcome you to the program. Eric, are you with us?

Eric (04:38:03):

Can you hear me?

James Valentine, JD, MHS (04:38:03):

Yes. We can hear you.

Eric (04:38:06):

Hi. Hi, James.

James Valentine, JD, MHS (04:38:08):

Hello. So, we'd love to hear, I know we've been covering a lot of topics here, but in particular if you happen to have any reflections on that topic of, short of a cure, what would you be looking for? And certainly feel free to put that into context by sharing about your journey and maybe current treatments that you've already experienced.

Eric (04:38:32):

Yeah, I'll be pretty succinct. I'll try to give a one minute of context and then I'll answer the question. So, I have had 2A for, I mean, it's probably really been 20 years, but I diagnosed about 10, eight, nine years ago, but it's probably been since I was nine. I'm 33, about to be 32 and I have 2A and I'm 6'7". And so, it's hard to move all those limbs around.

(04:38:55):

And so, right now, I'm doing physical therapy in the pool, which is helping make some things happen. I have had multiple heel cord lengthening surgeries, facial frame, all this stuff. And a couple years ago I had broken my femur because of being weak in the garage and broke it and I have a rod down there.

(04:39:13):

And so, now I use my power chair to go around. I drive with my truck and a joystick, but I can technically walk if I'm holding onto something but everything's so unstable now. If I fall, it's going to be really terrible. And I'm so tall that it's a long fall.

(04:39:28):

And so, 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. And so, it feels like I'm almost not, that some of the people go

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to pulmonary into other problems, but it's so scary and I got things to do, I got to go places and do some things, the driving, I got business things to do and so I can't do it. I have to sit in this chair, this recliner for 10 hours a day or 20 hours a day. I don't know. All day to do the things because I can't go out and do them instead regularly because my back hurts and all the things that you would think hurt. And I do a massage to make sure that because I don't think I have very much scar tissue as someone was mentioning. And so, I'm ready, perfect for the actual thing.

(04:40:17):

But, in terms to answer the question, I think I would love to play piano again. I played it for 15 years and now my arms are only work enough to play and stick with them. I would love to play basketball again. Don't think that's going to happen, but I really just want to be able to walk and sit down and stand up from a chair that's regular size because everything has to be on the cinder block to get me out of it and need caregiver help at times from my parents. And I would like to not have that happen.

(04:40:38):

So, looking to hopefully get a slowing of it or stopping so I can be more stable. If I was able to stay stable and walking around from between my chair, use my chair whenever I need to, that would be great. But I'd really like to get back to doing what I can. Any follow up?

James Valentine, JD, MHS (04:40:55):

No. Eric, that was wonderful both in giving us that context, but really some concrete kind of thoughts around if you could get some improvements, those being able to do those things that are important to you, like playing the piano but even just kind of maintaining or improving that stability and in the context of that feeling of falling. So, thank you so much. We do have one more caller that I want to try to get to before we conclude. I know we're a couple minutes over this final session. We have Tiffany who is from Texas living with LGMD or her son living with LGMD type 2C. So, I'd like to bring her into this discussion around what might represent that next meaningful therapy. So, Tiffany, I'd like to welcome you to the program. Are you with us?

Tiffany R. (04:41:52):

Hi. Can you hear me?

James Valentine, JD, MHS (04:41:53):

Yes. We can hear you.

Tiffany R. (04:41:55):

Okay. Hi, yes, I'm Tiffany and I'm living here in Richardson, Texas. My son Jonathan, he's 15. He has LGMD 2C and, I mean, I had to choose one because the type of muscular dystrophy he has, it 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.

James Valentine, JD, MHS (04:42:29):

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Right. And would that translate into the way that he feels or things that he's able to do in his life if something could benefit his heart or is that really more thinking more towards his future?

Tiffany R. (04:42:44):

That's really more towards his future. Of course right now it would be, and I guess 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.

(04:42:57):

I do know that they're looking at gene therapy, I think, and this is the one that kind of frustrates me, is that I know that steroids have worked with other types of muscular dystrophies and I think it was Lisa when she talked about the scar tissue. I know that steroids can help sometimes with that, but yet they haven't really tried it very much with the LGMDs.

James Valentine, JD, MHS (04:43:20):

Right. Yeah. Well, Tiffany, thank you so much for being with us and helping contribute to this important question. I do want to also recognize that we've been getting quite a few written comments, so maybe we'll close our session today by seeing what we've heard from people writing in on this question, okay?

Tiffany R. (04:43:39):

Mm-hmm.

Jennifer Levy, PhD (04:43:40):

We heard from a 54 year old with LGMD 2I who says, "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." And we also heard from the parent of a 14 year old with LGMD 2I who's based in Pennsylvania. They say, "I think that it is so important to know that a successful treatment would be to just stop the progression of this heartbreaking disease. Hitting a pause button would be considered a win for our teenage daughter with LGMD 2I. Anything that improves her strength and function would just be icing on the cake."

James Valentine, JD, MHS (04:44:22):

Yeah, some really powerful statements there and I think is kind of the perfect way to end what has been really an impactful day with these three sessions with so many people contributing to each throughout.

(04:44:39):

So, kind of at this point, I want to thank everybody, as you're meeting moderator, for just being so open and willing to share. These are truly personal stories that you've been sharing, personal experiences, and I know at times it's the things that we've been talking about have not been the easiest things to talk about when so much of the time we're focused on hope for the future, but in order to have that hope for the future, we really need to first understand where things are now and where we can most help this community.

(04:45:16):



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And so, as the person who's been having that conversation with you all day, I think we've accomplished that. And it's just so tremendous all of what you've contributed, whether it was through one of the panel statements or by Zoom or all of our callers and written comments, really just a tremendous showing by this really vibrant community. So, again, as your moderator, I just want to personally thank each and every one of you.

Jennifer Levy, PhD (04:54:10):

It's now my pleasure to introduce our partner, Dr. Charlotte Drew, co-founder of the Kurt+Peter Foundation, and caregiver of two sons living with LGMD 2C to provide some closing remarks. Dr. Drew, over to you.

Charlotte Drew, MD (04:54:08):

Thank you, James and Jennifer. This has been an incredible day of hearing personal insights to help us all better understand six types of limb girdle muscular dystrophy and their impact on patients and families. On behalf of the LGMD Coalition, I would like to thank the FDA for giving us permission to hold this meeting and to the FDA staff who tuned in today. Special thanks to Shannon Cole and Karen Jackler from the FDA's patient focused drug development staff who guided us through this process. Thank you to Dr. Wilson Bryan from the FDA for your perspectives on the importance of externally-led patient-focused drug development meetings. And to Dr. Katherine Mathews for the very interesting clinical overview of LGMD.

(04:55:11):

Thank you to the Dudley Digital Works media team for all of their technical expertise helping with the meeting. And thanks to James Valentine, Larry Bauer, and to the LGMD Coalition, and especially to Katherine Bryant Knudson, Jennifer Levy, Carol Abraham, Michele Wrubel, Rachel DeConti, Kelly Brazzo, and Jane Lockwood, who worked so hard to plan this meeting.

(04:55:34):

Thank you to our supporters and partner organizations. This meeting would not have happened without you. Thank you to our sponsors, Sarepta Therapeutics, Edgewise Therapeutics, AskBio, ML BioSolutions, Vita Therapeutics, who all help support this opportunity to allow patients to rewrite the reference book on six types of LGMD from our shared experience. But a huge thanks goes to you, my fellow community of kids, men, and women with LGMD 2A, 2I, and the sarcoglycanopathies and their caregivers. Thank you for agreeing to bravely and honestly lay bare the worst that these diseases have to offer. The embarrassing stories, the sad and frightening stories that are all part of our lives. We are grateful for you. Thank you for sharing your experiences.

(04:56:23):

To those of you who step forward to be part of a video panel or to speak on Zoom or to call and write in to share your insights, this meeting could not have been as impactful or enlightening without each and every one of you.

(04:56:33):

In the coming weeks, we'll compile all of the information from today into a Voice of the Patient report, which will be available on the LGMD EL-PFDD website. Today's program will be available on demand

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immediately after we conclude at the same link you are at now. The form to submit comments for the report is open for another 30 days. So, please do consider submitting additional comments, which will be added to the Voice of the Patient report. The video transcript and report, along with a list of supporters and partner organizations is publicly available to anyone once it's published and posted to our website, LGMDPFDD.com. There will also be a link for the FDA website. Thank you to everyone for sharing your voice. The impact of this meeting will be felt for years to come. Now, back to the studio.

Jennifer Levy, PhD (04:57:26):

Thank you, Charlotte. Again, thank you everybody for joining us today and especially to those who shared your stories with us. As soon as this meeting concludes, you will be able to access the recording from the same webpage and stay tuned for the Voice of the Patient report, which will be shared by all of our organizations when it's available in early 2023. Be safe, be well, and we look forward to hearing more of your comments over the next 30 days. Thank you.