UPPER-BODY MOBILITY: PERSPECTIVES FROM THE FSHD COMMUNITY

FDA PATIENT LISTENING SESSION

AUGUST 23RD, 2024

FSHD SOCIETY
LIGHTING THE WAY TO A CURE

PUTTING THE REPORT IN CONTEXT

The report on the following pages summarizes the Patient Listening Session (PLS) held with the FDA in August, 2024. As FSHD is a heterogeneous disease, this conversation couldn't capture every experience and perspective. Alternatively, weakness in the arms, shoulders, and trunk is a common symptom in other conditions, and the experiences shared here may be applicable across disease spaces.

By reporting on this meeting, the FSHD Society hopes to ignite an ongoing conversation that recognizes the importance of upper body mobility.

WHY UPPER-BODY MOBILITY?

Most people have a narrow understanding of mobility and consider it to be synonymous with ambulation or a person's ability or inability to walk. However, for an overwhelming majority (96% according to multiple studies) of those with Facioscapulohumeral muscular dystrophy (FSHD) suffer a loss of upper-body mobility, characterized by weakness in the upper arms, shoulders, and trunk. This facet of the disease has an outsized impact on a person's ability to perform tasks of daily living and maintain their independence. Whereas people who struggle with ambulation have options for assistive technology like canes, scooters, and wheelchairs, those facing decreased upper body mobility currently have limited or no options for interventions. The impact of decreased upper body mobility on a person's quality of life can be more severe than ambulation. Despite this, there is a concerning lack of research or even conversation about the topic. We encourage the world to think of mobility as a whole-body issue.

ABOUT FSHD

Facioscapulohumeral muscular dystrophy, or FSHD, is a relentless, progressive muscle-wasting disease that has been clinically diagnosed in an estimated 8,000-10,000 US citizens. It is a genetic condition, which can be either inherited or occur spontaneously. The onset of symptoms can begin at any age, and anyone can be affected. Patients experience lifelong weakening of skeletal muscles throughout the body. Those with FSHD commonly suffer from debilitating muscle weakness in their shoulders and upper arms, leaving them unable to perform tasks of daily living. This includes basic activities such as washing their own hair, picking up a baby, or lifting a utensil to their mouths. The effect is not just physical; it extends to mental health, contributes to social isolation, and places a financial burden on patients and caregivers.

ABOUT FSHD SOCIETY

The FSHD Society is the world's largest research-focused patient advocacy organization for facioscapulohumeral muscular dystrophy (FSHD), one of the most prevalent forms of muscular dystrophy. For over 30 years, the Society has driven major advancements in research and treatment development, with the mission to end the pain, disability, and suffering endured by one million people worldwide living with FSHD. The Society supports families affected by this disease through programs like BetterLife, which empowers patients with tools to track symptoms and connect with researchers, and FSHD Navigator, a service providing personalized assistance to help handle the challenges of living with FSHD. Our promise to patients is that as long as we are here, no family need ever face this disease alone.

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FDA PATIENT LISTENING SESSION AUGUST 23RD, 2024

Remarks and Briefings

The FDA opened the meeting with a welcome to the facioscapulohumeral muscular dystrophy (FSHD) community and appreciation for sharing their perspectives. Financial disclosures were read, and the FDA welcomed staff from all three medical product Centers [CDRH (Devices), CDER (Drugs), and CBER (Biologics)] and the Office of the Commissioner. Mark Stone, the CEO of the FSHD Society, set the context of the meeting by briefly describing FSHD. It is a relentlessly progressive genetic condition that is currently clinically diagnosed in an estimated 8,000 – 10,000 Americans. Over 96% of FSHD patients struggle with arm, shoulder, and upper trunk weakness, but this symptom is frequently overlooked as a benchmark for disability or disease progression. A decline in upper-body mobility has an outsized impact on a person's ability to perform tasks of daily living, and therefore maintain independence.

Patient & Caregiver Testimonies

Amy is an FSHD patient and advocate. FSHD has affected members of her family for a combined 140 years, across at least 4 generations. Amy described how upper-body mobility profoundly hinders her independence. She shared clips from the short film The Reinventor, in which she describes some of the things she's had to give up as her disease progresses: her career, playing golf (and the social and physical benefits it provides), and finally, painting. Showing several examples of how she struggles and compensates to do daily tasks such as lifting a utensil to her mouth or put on a jacket, Amy described her arm and shoulder weakness:

"Imagine that there is a rope tying your arms to the trunk of your body and only with a great deal of effort can you raise them a few inches. THAT is how you live 24/7."

Supplementing this demonstration, Amy discussed the mental fortitude required to live with a progressive disease. Required to adapt to her circumstances over and over again, she is never sure what the future holds.

"My greatest fear is being forced to rely on caregivers for my every need 24/7. Slowly, but inevitably and progressively, I am being forced by my upper body's growing weakness to yield my independence and personal identity as I become a burden on society, family, friends, and self."

Patient & Caregiver Testimonies Continued

Maggie is a high school student and FSHD patient starting 10th grade. She struggles at school to raise her hand in class and take notes necessary to study. She shared her frustrations with the way her physical limitations bar her from developing a healthy social life; Maggie is unable to join the sports teams her friends are on, has been forced to give up beloved hobbies, and is denied opportunities available to other students. Recently, Maggie traveled to Washington, DC to advocate for those with FSHD. On this trip, Maggie was accompanied by her mother, but she asked a flight attendant what she would need to do in order to travel independently one day.

"The attendant responded that they didn't consider a health issue a disability if it didn't cause the person to need a wheelchair. This makes me mad. That is just so hard to hear and deal with as a person with upper body weakness. She suggested I travel while using a wheelchair so that it would indicate that I needed help."

Maggie is trying to live a "normal" life and wishes for a treatment that is available to all.

Heloise is a Bioengineering & Medicine student at Stanford University. She is doing everything she can to beat her FSHD, including researching it herself, although lab tasks like pipetting are becoming increasingly difficult to perform due to her upper body mobility. Heloise described living with the constant fear of uncertainty caused by the inability to plan for the next phase of disease progression. Diagnosed at 13, she used to fear losing leg function:

"Now I know that my arms are what give me independence."

She most misses the small tasks that allow her to participate in family life, such as setting the table with her siblings.

Heloise is planning for an uncertain future. Though she wishes to have a family of her own, she fears being unable to carry a pregnancy or hold and comfort a child. She is building her career around her weakening muscles through research and medicine, but she fears that as she continues to lose strength, she will have to give up her calling and change course again. She describes living with an ever-present anxiety:

"Imagine your favorite thing to do in the world. It could be sipping on tea while watching the sunset, playing a sport, or holding your child. Now, imagine it being ripped away from you and knowing there's nothing you can do but watch. This is what it's like to live with FSHD."

Evan and his wife welcomed their son Hal in June 2023. When Evan first started using his wheelchair, he thought that losing the ability to walk would be the worst part of his weakness. Since having Hal, he found that upper-body weakness has been his greatest struggle, especially as it relates to parenting. The loss of experiences Evan expected to have with

his son – lifting him into the air, playing catch, or teaching him to play guitar someday – are what drive his hope for a treatment. Simple acts of caring for his child, such as comforting, feeding, and changing, are made difficult or impossible with upper-body weakness. The emotional toll of having to rely on his partner for help and inability to engage in parenting activities as he'd always imagined, is a particularly heavy burden.

For Evan, a slight improvement in mobility would make the world of difference: Reaching an additional inch would mean not needing to ask for help showering. A bit of additional strength would help him change Hal, and a small increase in endurance would allow him to hold Hal longer. Evan hopes for a treatment that would halt his disease, so that he can care for his growing family the way he's always imagined.

Back in 2020, Jack shared part of his story during the Voice of the Patient Forum. For Jack, a close and loving relationship with his family is of paramount importance. He described the emotional toll of meeting his grandson at the library and struggling to pick him up safely. He then reflected on his disease progression and state of mind since that meeting four years ago. He now has nine grandchildren, all under age six, and can't pick up any of them.

"It's a poignant reminder of how FSHD has not only taken a toll on my physical capabilities but also on the cherished moments of bonding with my grandchildren."

Jack takes an optimistic outlook, gleaning lessons of resilience and adaptability. His struggle with FSHD has also taught him how to cherish the moment. However, he wishes deeply for a treatment that would stop or slow the progression of the disease. Physical limitations and consequently, the loss of simple tasks that others take for granted, has a heavy emotional toll.

Debbie is Maggie's mother. She described the fear and heartbreak of watching her child being held back by her body. Though Maggie is resilient, as her friends are growing into their adult bodies, she is becoming weaker.

"I reject the idea that this is a slowly progressing disease," Debbie said. "I've seen her rapidly lose function. We need this to slow down."

In their family, they tend to focus on the positive, but that has not stopped Maggie's younger siblings from worrying about her. Debbie knows that they will take care of each other, but what she wishes most is for Maggie to have the freedom to chase her dreams, whatever they may be. For now, that could look simple:

"There are functional improvements that come with small changes, like being able to write or type for FIVE more minutes to get homework done, or to move your shoulder an extra 10° so you can reach a cup to your mouth."

Patient & Caregiver Testimonies Continued

Debbie's hope is to watch Maggie at her high school graduation, able to reach out to receive her diploma, shake hands, and hug her friends.

Archer is a student, volunteer, and advocate with FSHD. She discussed the point in her FSHD journey at which she could no longer wash her own hair and needed to hire a personal care assistant. It is both frustrating and embarrassing to be so young and forced to rely on others for these types of tasks. Changing clothes, preparing food, showering, housework, and driving are all keys to independence. Beyond these, Archer described making various adaptations to participate in college courses, hobbies, and activities. There are precious few things that are unaffected by upper-body mobility.

In addition to the health and safety concerns of upper-body weakness, Archer is mindful of quality-of-life issues. To her,

"the most devastating thing of all is that FSHD took away my ability to wrap my arms around my fiancé and give him a hug. I want to be able to hug my best friend, my sisters, and my parents. It's a way to show you care about someone and a way to bring comfort and happiness. FSHD took away my ability to make that connection with people. It's the thing I miss the most."

Clinical Perspective

FSHD is unique among muscular dystrophies for its pattern of progression. Although every patient is different, in FSHD we often see patients experience facial and scapular weaknesses first, with progression moving downwards. Weakness in the trunk is also a significant driver of pain, and the source of compensatory movements. Dr. Johnson noted that this distinct pattern can cause significant morbidity and alterations to daily life, including one's livelihood.

Data supporting these experiences is difficult to capture. Upper arm, shoulder, and trunk muscles are not typically measured and may be missed altogether by a general practitioner. Additionally, people make unconscious compensations, which obscure the problem even further. For the purposes of research, changes in scapular rotation are very difficult to measure, as moving your shoulder involves several muscles. It would be most beneficial to this population to measure disease progression in a way that captures function, as the clinician's goal is to help the patient maintain function as long as possible.

Facilitated Discussion

Following the testimonials, moderator James Valentine asked the panelists, "What about the question of future treatment? We would like to see a complete cure. We would like to know what you would like from a future treatment? What would that treatment outcome mean for you?"

Facilitated Discussion

The panelists had the opportunity to expand on their previous statement. The following is a summary of each of their replies:

Amy

I would be very happy to halt the progression. We compensate and adapt. It is like a constantly moving target; it's relentless. Improving muscle growth and function would be a gold standard. I want to get some normalcy back in life. The most important function is being able to raise my arms higher, to put on a shirt or comb my hair. Just a few inches would be hugely impactful.

Maggie

I agree with Amy – To stop or slow the progression of the disease would eliminate the worry of waking up with another muscle deteriorating.

Debbie

Even slowing the progression might mean that existing compensations would last for longer. The fear is overwhelming – Maggie is only 15 now, what could happen over 70-80 years? You never know where you are at with FSHD. There are huge emotional impacts.

Heloise

I am on the same page; a cure would be a miracle. In the meantime, stopping or slowing progression would be magical, and would help me continue living life independently. I have found small adaptations, but one day those may no longer work. Will I be able to power through the MD PhD program and career I want? Stopping or slowing disease progression will alleviate the constant anxiety.

Evan

When I lose my legs, I have a wheelchair, and that helps life a lot. There is nothing for my upper arms that can bridge those gaps. There is nothing for hand strength. Assistive devices would be helpful.

Jack

Slowing disease progression would be a win. Stopping it would be great. Rebuilding muscle would be fantastic. In my 40's, I could carry a case of beer. Five years ago, I could carry a 12-pack, and today I can carry a 6-pack. I don't want to have to buy beers one at a time.

Archer

Slowing progression would be wonderful; I don't want to keep losing skills. It is terrifying and devastating to think of losing it all. I have tried to learn to drive but can't, and I have to be driven everywhere. In an ideal world, I would have hope to drive myself someday.

Dr. Johnson

The panelists are spot-on. Anything that would slow progression is a welcome improvement. More is better.

Q & A

With the time remaining, the meeting moved into an open question period. The following captures a summary of each question and what was discussed.

Q & A Continued

A representative from CDER/OND/ON opened this time by asking: We are the clinical office that would regulate treatments in FSHD. We learned today from hearing about your lived everyday experience. What would success look like to you? When we are reviewing applications and sponsors, we want to make sure that if we see a successful drug trial that the benefits are going to have impact and improve lives. Can you provide descriptions of what meaningfulness in a treatment would look like?

Amy

Life is completely restricted: My upper arms, hands, even not being able to hold my head up. Even regaining just a few inches and be able to function without the pain. It's important to have the respect and personal pride being able to do something yourself. I wear a bra 24/7 because I can't put it on or take it off. I can no longer shower myself; I used to put my elbows up the wall. Safety might be something. We could function in certain areas, but it might not be safe.

Heloise

I've never heard a young adult excited to set the table or do chores. Success to me would be if I could help siblings with chores. I can barely contribute since my arms are too weak. I can't open the cupboard. I wanted to get the cups from cupboard, and almost bashed my head. If I'm able to do that with siblings again, or bring laundry, some of my family dynamics might be restored. I'm the only person in my family with FSHD. They want to be supportive, but there are some things that they can't understand. I wonder how that relationship would be different if I could help them and not just sitting helplessly while they are doing chores.

Debbie

Success would look like some level of independence. I didn't realize until Maggie was diagnosed, that she had to fling her elbow to the side of the shoulder to wash her hair. It isn't necessary to put your hair in a braid, but when other girls are styling hair, it feels important. All of us talked about how emotional it is. We have lost members of our community because of falls and respiratory problems. If disease progression is severe, there could be respiratory issues. I want all of these people to survive.

Jack

We have had a number in the community that have committed suicide.

Debbie

…Which tells you how challenging these issues really are.

Jack

A lot of patients don't have the ability to smile. It is difficult and emotionally taxing. Other forms of muscular dystrophy have a more linear progression, but FSHD often progresses in steps. It's frightening waking up one morning and not having an ability that you had before.

Archer

Right now I'm in my 20s. I'm relying on others. At this age, you are supposed to be finding yourself. I haven't had the time to figure that out.

Q & A Continued

A representative from CBER/OCD asked: Debbie and Maggie mentioned being able to type for just five more minutes to get more homework finished. Can anyone on the panel tell me a little more about the importance of endurance vs. strength?

Evan As a software engineer, the more I'm typing, the faster my hands tire out. Endurance is just as important as strength. You can start off doing something well and very quickly get exhausted. It could be something as small as putting my fingers in different positions repeatedly. Doing that for 10 minutes versus 15 min makes a difference. This is true of walking as well. The quick fatigue is tough.

Amy

Debbie There is also this overall issue of how much you can do in a day. You have less time to accomplish everything.

Maggie There is sleepiness and muscle fatigue that impact each other.

Debbie You can do one thing, and be done for the day and still tired the next day.

From a representative of CDRH/OPEQ/OHTV/DHTVB: Thank you all for being here and sharing your experience. It is powerful and deeply motivating. As a Lead reviewer in CDRH, we are the team within FDA's neurological devices, dealing with acute injury devices, assisted devices, and robotic exoskeleton. Do any of you have experience using any body powered robotic devices? Are there limitations, or do you foresee any rehabilitative potential in robotic devices?

Amy I haven't had an availability of using one. There were two products for arms/shoulders that are sold here, but they are not categorized as medical devices. They are sold to construction workers. It isn't really robotic, but kinetic. It is not attached to a wheelchair. I tried to pursue it, but the company wouldn't sell it to me because it is not FDA approved as a medical device. I spoke to an orthotic company in Germany, but they couldn't ship to the US because it could be confiscated at Customs for safety. There are things are available, but just not available to us.

Debbie We will do whatever we can, but people wouldn't be able to pay for it if it weren't covered by insurance.

Heloise I've never used a robotic device, but I do have a spinal brace that I strap on my lower spine and core. It helps a lot in my day-to-day, but it is uncomfortable, and I can only wear it if I stand a lot because it is too uncomfortable to sit in. It is a pain to put it on. I only put it on when I know when I'm going to move around. My weakening lower body. I hate it being mistaken for a waist trainer. I have a lot of friends who are studying biomechanical engineering and exoskeleton and allowing it to be synergistic with the patients. I don't want to have a huge thing strapped to my arm to lift it. If a device were to be available, I would take it but there are a lot of complications.

Q & A Continued

Evan

I haven't used robotics. I'm interested, but it is an issue of availability. If I could design something, I would want a powered glove that gives me a full grip so I don't drop stuff. For a heavy beer mug, I have to use a straw because I can't secure the grip.

Jack

We would be open to everything including assisted devices. The range of limitations are noted. I'm wondering if there is any thought about rehabilitative devices that could modify the course of progression.

Dr. Johnson

I've had two patients that attempted to get robotic arms, but both faced financial barriers. Regular exercise and rehab can be beneficial in slowing progression. It is difficult for any external device to get at shoulder, core and trunk muscles for effective rehab. DMOs have had some improvement.

Conclusion

On behalf of the FSHD community, as well as all the other disease states suffering from impaired upper-body function, the FSHD Society would like to thank the FDA for providing this platform for patients. This is an important step in amplifying the patient voice and ensuring that upper-body mobility is taken seriously as a significant component of disability and disease burden.

We encourage anyone who wants to learn more about living with FSHD to refer to the Voice of the Patient Report, published in 2020. FSHD is not merely a progressive disease; it is a truly relentless one. For these patients, time equals lives.

Attendees

Six patients living with FSHD and one loving parent of an FSHD patient, were joined by Dr. Nicholas Johnson of Virginia Commonwealth University, and Mark Stone, CEO of the FSHD Society, to broach this important topic with the FDA.

Additionally, over 40 members of the FDA and other regulatory bodies attended this PLS. Representatives from 17 FDA offices/divisions across 3 different Centers were present.

Office of the Commissioner (OC) – 3 offices

- OC/OCPP/PAS - Office of Clinical Policy and Programs/Patient Affairs Staff (organizer)
- OC/OCPP/OOPD - Office of Clinical Policy and Programs/Office of Orphan Product Development
- OC/OCPP/OPT - Office of Clinical Policy and Programs/Office of Pediatric Therapeutics

Attendees Continued

Center for Biologics Evaluation and Research (CBER) – 2 offices

- CBER/OCD – Office of the Center Director
- CBER/OTP/PSPS – Office of Therapeutic Products/ Policy and Special Projects Staff

Center for Drug Evaluation and Research (CDER) – 8 offices

- CDER/OND/ODES/DCOA – Office of New Drugs/Office of Drug Evaluation Science/Division of Clinical Outcome Assessment
- CDER/OND/ON – Office of New Drugs/Office of Neuroscience
- CDER/OND/ON/DNI – Office of New Drugs/Office of Neuroscience/ Division of Neurology I
- CDER/OND/ORDPURM/DRDMG – Office of New Drugs/Office of Rare Diseases, Pediatrics, Urology and Reproductive Medicine/ Division of Rare Diseases and Medical Genetics
- CDER/OND/ORO/DRON – Office of New Drugs/Office of Regulatory Operations/Divisions of Regulatory Operations for Neuroscience
- CDER/OTS/OB/DBI – Office of Translational Science/Office of Biostatistics/Division of Biostatistics I
- CDER/OTS/OB/DBIII – Office of Translational Science/Office of Biostatistics/Division of Biostatistics III
- CDER/OTS/OCP – Office of Translational Science/Office of Clinical Pharmacology

Center for Devices and Radiological Health (CDRH) – 4 offices

- CDRH/OCD – Office of Center Director
- CDRH/OPEQ/OHTIII – Office of Product Evaluation and Quality/ Office of Health Technology III
- CDRH/OPEQ/OHTIII/DHTIIIB - Office of Product Evaluation and Quality/Office of Health Technology III/Division of Health Technology IIIB
- CDRH/OPEQ/OHTV/DHTVB - Office of Product Evaluation and Quality/Office of Health Technology V/Division of Health Technology VB

Non-FDA Attendees

Reagan-Udall Foundation

European Medicines Agency (EMA)

National Institutes of Health (NIH)

- NIH/NCATS – National Center for Advancing Translational Sciences
- NIH/NCATS/DRDRI – National Center for Advancing Translational Sciences /Division of Rare Diseases Research Innovation

DISCLAIMER

Discussions in FDA Patient Listening Sessions are informal. All opinions, recommendations, and proposals are unofficial and nonbinding on FDA and all other participants. This report reflects the FSHD Society's account of the perspectives of patients and caregivers who participated in the Patient Listening Session with the FDA. To the extent possible, the terms used in this summary to describe specific manifestations of FSHD, health effects and impacts, and treatment experiences, reflect those of the participants. This report is not meant to be representative of the views and experiences of the entire FSHD patient population or any specific group of individuals or entities. There may be experiences that are not mentioned in this report.