
# Episode 15: The Power of ALS Registries
## May 10, 2022

(Music playing)

Mindy Henderson: Welcome to the Quest Podcast proudly presented by the Muscular Dystrophy Association, as part of the Quest family of content. I'm your host, Mindy Henderson. Together, we are here to bring thoughtful conversation to the neuromuscular disease community and beyond, about issues affecting those with neuromuscular disease and other disabilities, and those who love them. We are here for you to educate and inform, to demystify, to inspire and to entertain. Thanks for joining. Now, let's get started.

My first guest is Dr. Paul Mehta. He is the principal investigator for the United States congressionally mandated National Amyotrophic Lateral Sclerosis, or ALS, Registry, which resides within the Centers for Disease Control and Prevention, and is responsible for providing medical, scientific and epidemiological expertise on matters related to ALS. Dr. Mehta, thank you so much for being here.

Dr. Paul Mehta: Thank you, Mindy, for having me and thank you for bringing attention to ALS.

Mindy Henderson: Absolutely. I've been looking forward to speaking to you. Would you like to tell us just a little bit more about your background and the work that you do?

Dr. Paul Mehta: Sure. So I've been with the National ALS Registry for, it'll be nine years this October, as the PI. We're a small lit group of individual scientist at CDC ATSDR. And what we do here is we try to figure out who gets ALS in the US, demographics of disease, epidemiology, the incidence, prevalence and

mortality of ALS. And more importantly, we also try to figure out what causes ALS, the risk factors for ALS, why do patients get ALS, and hopefully in the future to mitigate and potentially prevent ALS, which is very, very important.

Mindy Henderson: Absolutely. Could you go ahead and give us an overview of exactly what ALS is and how it presents?

Dr. Paul Mehta: Sure. So ALS is part of the motor neuron disease family. Like you said earlier, ALS is of amyotrophic lateral sclerosis. It is a progressive muscle weakness disease with the death of motor neurons, both in the upper and lower motor neurons. What ends up happening is patients present differently with ALS. Some can present with muscle weakness in the upper body or lower extremities. Some could also have typically walking, difficulty speaking and so forth. Typically, no single ALS case is the same. It's always a bit different when it comes to presentation of the disease itself. Patients in general will have muscle weakness. They can have fatigue, also overactive reflexes as well. So it's just a different amalgamation of sorts of symptoms they certainly can have and how they present to the primary care physician, and eventually, when they go see a neurologist for a diagnosis.

Mindy Henderson: Right. And so I hear frequently in the work that I do that ALS is very hard to diagnose. I hear that oftentimes, it can take several years even to get a diagnosis and to follow those breadcrumbs to get to the correct diagnosis. Is it really the reasons that you just stated and how differently it presents that makes it so hard to diagnose?

Dr. Paul Mehta: Well, right now, there is no specific blood test for ALS, or a specific guess in terms of there are for other diseases out there. You can't just take a blood test from your finger and say, "Hey, I've got ALS." So it's almost like where you're ruling out certain other diseases to figure out, "Hey, do you have ALS?" Sometimes they call it a diagnosis of exclusion when it comes to ALS. And like I mentioned earlier, everyone presents differently. So it can present, for example, with a foot drop, or some could present weakness in let's say their arm or their hand or something like that. And that can also be misdiagnosed because for example, if you're an athlete or something like that, you've had a prior injury, which could be matching ALS, but potentially is ALS. But as a previous sports injury, it could be something else.

So that's why it's difficult to diagnose ALS because like I said, everyone presents differently and the signs and symptoms aren't always there in the beginning. They kind of progress. So you may have difficulties in, for example, speaking. It's progressive, so you're fine, then it gets worse

and worse and worse. Then you go see your doctor to figure out what's going on and so forth. So that by itself makes it a bit difficult to figure out, when ALS is occurring and when it's diagnosed. In general, it can take up to 12 months to go ahead and diagnose ALS.

And there's a concerted effort by MDA and other groups to make sure we can go ahead and make that diagnosis delay a much shorter, in terms of having it not as long as 12 months, making it hopefully less than 12 months, three to four months, and letting providers out there be aware, hey, if there's a question, go ahead and refer to a neurologist. If you have something you've not seen before or something, for example, if there's fasciculations in your tongue, which is presenting from the patient itself, to go ahead and refer to a neurologist or go ahead and make that referral just to be on the safe side so we can potentially catch it early. But to go ahead and catch it early is very, very important.

Mindy Henderson: Okay. So it sounds like there's a lot of discussion about trying to work toward earlier diagnosis of ALS, for obvious reasons. The earlier you diagnose, the earlier you can treat. So it sounds as though like there's nothing exactly that's really, for lack of a better term, like an ALS calling card, that if you see a particular thing, you should really think about looking into ALS.

Dr. Paul Mehta: Yes, that is correct. Other diseases have calling cards out there. Let me give you an example, like a heart attack. Heart attack can present typically in a very, very standard sort of way. So you can have a referred pain in your arm, you could have sweating, you could have chest pain and so forth. And it happens all acutely, let's say in a heart attack.

But with something like ALS, it's happening gradually. I mentioned athletes. You athletes out there who are very active. People are very active and, "Hey, my loved one tripped, my husband tripped, my spouse tripped," and so forth. And that certainly could be very, very common. But when it's happening more and more often is where we want to say, "Hey, let's go ahead and refer you to a specialist to figure out to make sure it is not ALS or maybe it's something else happening as well." Every single patient presents differently. Every single patient progresses differently as well. Some patients progress slowly, some patients progress very, very fast. So it just depends on the patient themselves and the actual disease characteristics too.

Mindy Henderson: And so the fact that it does present so differently in everyone. Is that part of or all of what makes it so

challenging to attempt to research and better understand and treat the disease?

Dr. Paul Mehta: I would say yes. I think because it is not a set standard of symptoms which happen with ALS, they differ from patient to patient. So that makes it a bit more of a challenge for clinicians to say, "Hey, I think you may have ALS," or "You may not have ALS," and so forth. For example, you could have someone who goes to the emergency room because they've tripped and they could be diagnosed well, "Hey you're potentially just tired." And they may get sent home and then a month or two later, they're back in the ER because they've tripped and they've had, let's say now a head injury begins resulting in their fall. It is a disease which can occur in anybody, whether it's males, females. And what we have seen it generally occurs in males more so than females.

Mindy Henderson: Okay. And you mentioned athletes and firefighters, I think a minute ago. And this is something that I've recently learned is that firefighters and athletes are actually at a higher risk for ALS than some other people. Can you explain the relationship between those factors where you may have a very physical role in some sort, but then the relationship between that and the genetics that causes ALS?

Dr. Paul Mehta: So you mentioned firefighters. So firefighters are certainly exposed to chemicals throughout their occupation, and we're not sure if those chemicals potentially could cause or make them at greater risk for ALS. And that's one of the questions we want to answer. Athletes also, because they're doing a lot of stressful activities to their bodies and so forth, and that by itself can release for example, oxidative stress and so forth. And so we're not sure if that by itself could be a factor for ALS, and certain athletes as well. There is some research that was done in Italy, which showed soccer players were at greater risk at ALS. And that potentially could be because of hitting each other's heads when they're heading a ball or so forth, and getting a concussion. But more research needs to be done in that area, figure out if that certainly is the case or not.

Another fact, another group, which I want to mention is vets, military members.

Mindy Henderson: Yes.

Dr. Paul Mehta: They are actually at twice the risk of getting ALS than those who've not served. And we're not sure why, and that's really important for us to figure out why are our veterans at twice the risk of getting ALS than non vets? That's certainly a

question we want to answer through research. Our vets are great patriots. They do a lot for the country and they give up a lot as well. And so it's certainly important for us to make sure hey, and find out the answers for them.

You mentioned genetics. So about 90% of ALS is considered sporadic, meaning to say there's a potentially a link to the environment. And about 10% is considered familial ALS, or FALS. And that's due to a certain number of genes that they may inherit. And those genes make them more likely to potentially get ALS than those who don't have the gene itself. There's certain genes that come to mind. One is the SOD1 gene, as well as the C9orf72 gene, which are the two most common genes related to ALS. But like I said, about 90% of ALS is sporadic, potentially linked to the environment, and 10% is genetics.

Mindy Henderson: Interesting. So what are the different therapies and treatments that are available for ALS right now and how do they differ?

Dr. Paul Mehta: So right now, the two therapies out there is one's called Riluzole, or Rilutek, and one's called Edaravone, or Radicava. In these two therapies, what they do in general, they just prolong life for about two to three months on average. Some patients more than two to three months, some patients less. It all depends on the patient themselves. Those are the only two drugs currently approved for ALS by the FDA. There are other drugs that are currently in clinical trials and hopefully they'll have a good trial outcome.

One of them is AMX0035, or Amylyx, a company itself. And the FDA is going to be deciding exactly if that's going to be approved or not. But right now, Mindy, there's only two drugs out there for ALS. And I think that certainly is a frustration for patients because there's only two drugs out there. And on average, like I mentioned, these drugs are only prolonging life by two or three months. And we certainly need to have more drugs in the pipeline for potential for clinical trials, as well as for approvals. And there's a hunger for that, and that hunger needs to be met. Reverse the disease or prevent disease itself, those are certainly very, very important.

Mindy Henderson: Yeah. So the two drugs that exist today, are they drugs that would you choose one or the other, or can they be used in parallel?

Dr. Paul Mehta: They can be used in conjunction. It all depends on the neurologist and on the provider, if they want to go and take them in conjunction or not. And one of them is the IV infusion drug, which is Edaravone, or Radicava. There's a currently a

clinical trial on Radicava, Edaravone, to see if an oral pill is going to work, which I think would be a very, very good thing. And then the other one is actually is also pill or an oral suspension, Riluzole, or Rilutek.

Mindy Henderson: Great. Let's turn to the ALS Registry and talk about that for just a second. Can you explain to me exactly what the ALS Registry is and why someone should register what the benefits are?

Dr. Paul Mehta: Absolutely. So the ALS Registry was formed back in 2008. Because ALS is devastating, it's a game changer, it's a life-changing event, there was a concerted push by patients and caregivers to have the registry. And once Congress passed the ALS Act itself, they tasked CDC to go ahead and establish the registry. We launched three years later on October 2010. And from there, we like to describe ourself as a multifaceted research platform. So we do the number of cases of ALS in the US, the incidence, the prevalence, the mortality. Then like I said, we also want to figure out what causes ALS ,the risk factors behind ALS. And this is done by having patients come to the registry and take risk factor surveys about where do they live, where do they work, what were they potentially exposed to. We currently have 18 risk factor surveys in the registry that patients can take at their own leisure and in any order, and these risk factor surveys help researchers figure out the unknowns of ALS.

I like to say there are more unknowns than knowns about ALS at this point. And what we are doing at CDC ATSDR is to figure out those knowns, and we do that by funding research through academia, as well as having patients take our risk factor surveys, as well as being counted. It's very important to be counted and having joined the ALS Registry, and coming to cdc.gov/als and signing up. And from there, we can give you information about a bio repository, which is a national ALS biorepository, where we go to patients homes and go in and collect their blood, completely for free. And that blood is used to look for areas such as genetics, biomarkers and so forth, disease progression. We also work with big drug companies out there as well. Sure you've heard of Amylyx, I mentioned earlier.

We've helped to work with Brainstorm, Cytokinetics, Biogen as well as Mitsubishi Tanabe Pharma in their clinical trials. So they come to us for recruitment assistance and we send their information to our pool of ALS patients. And those patients will, in turn, will go ahead and contact the drug company about the clinical trial itself. And so this is called a research notification mechanism where we'll go ahead and we're like a matchmaker. They come to us, we give them

information about the clinical trial. They'll go ahead and contact the drug company to see if they're eligible about this clinical trial. So it's a great resource.

And I also mentioned research. We currently have funded 21 research institutions out there of higher learning to figure out what causes ALS and those risk factors. So for example, whether it's pesticides, insecticides, metals, if that's a risk factor, genetics. We're also funding different groups out there internationally. One group we funded was Trinity College out in Dublin, and they were looking to see why the ALS population in South America gets ALS at a much lower rate than let's say the Caucasian population in Europe. And that's certainly interesting to say, "Hey, how come this particular demographic group is getting ALS at a much lower rate than those let's say in Europe?" And so from that, we can certainly learn and see why that is the case.

Mindy Henderson: Very interesting. So it sounds like it's really fairly patient driven to go and register, or are there are also doctors who input information into the registry as well?

Dr. Paul Mehta: No, we don't, at this point, have doctors inputting information. I believe the MOVR system is that way for MDA, but we currently don't have it that way. It's all patient driven. Patients can come in, sign up with the help of their caregivers, or even with the help of let's say an MDA clinic personnel as well, they can help them sign up too and so forth. So it is all patient driven where they come to our registry to go ahead and sign up. The registry also gets their cases from CMS centers, centers for Medicare services, centers for Medicare and Medicaid services, as well as the VA system. We have agreements with them to go ahead and get their cases into the registry as well.

Mindy Henderson: That's fantastic. Well, it certainly sounds like the registry is well positioned to provide hope to ALS patients just in the work that you're doing and the answers that you're trying to uncover. As we wrap things up, what do you think is, with the trends that you're seeing in the research and the things that you're learning, what do you think is the most exciting thing happening in ALS research today that might provide potentially patients or families who are listening with some of that hope?

Dr. Paul Mehta: Absolutely. First of all, I want to say our registry is for patients. It's their registry and we are caretakers of that registry. There's been so much attention to ALS, but I always say there's always going to be more attention paid to ALS. ALS is a rare disease, but it's not a rare disease if you get ALS. So it's a life changing event. And therefore, I think it's

very important to make sure ALS gets the attention it needs and deserves out there, especially for research, especially for realizing, hey, these are people out there who've got this disease, it's a life changing event. And frankly Mindy, the ALS patients I've met throughout my time as the principal investigator there, are some of the nicest individuals out there. They're very altruistic individuals, very, very humble people, and they really touch their heart.

And for me, I think just seeing what's happening these days in the ALS community, with the research out there, with the potential therapeutics coming online, fingers crossed, that these will be approved and new ones will be coming up online as well. It's really, really important. For me, as a clinician and a researcher, it's very important to share that hope and to share that optimism with the ALS patients and the community, because we want something to help these patients to like I said, either to slow, halt, reverse or prevent their disease. I think it's very important. And there certainly is a lot of excitement out there, whether it's at CDC or whether it's other clinics out there.

For example, Massachusetts General Hospital is a huge clinic out there as well at Johns Hopkins also has a very, very big center out there as well. They're all groups that want the exact same thing. We want to make sure we have therapeutics out there that could help these patients make ALS a livable disease, make it where these patients can enjoy time with their family and pretty much and hopefully lead a life where they can, like I said, enjoy time with their family and just be with their loved ones.

Mindy Henderson: That's great. If you don't mind, let's give that URL one more time so that people can register.

Dr. Paul Mehta: It's cdc.gov/ALS.

Mindy Henderson: Perfect. And I'm going to put that in the show notes as well, just in case anyone listening doesn't have a pen handy. Dr. Mehta, thank you so much for your time and for all of the incredible work that you all are doing and for sharing your knowledge with us today.

Dr. Paul Mehta: Thank you, Mindy, and thank you for having us. I appreciate it.

Mindy Henderson: My next guest is Dr. Elisabeth Kilroy. Watching the progression of her father's and brother's muscular dystrophy ignited Dr. Kilroy's passion for understanding the intricacy of the neuromuscular system and human movement. Dr. Kilroy has a ton of super impressive credentials, and I love

speaking to people that are so much smarter than me. I'm going to go ahead and just let you, Dr. Kilroy, if you don't mind introducing yourself and telling us a little about your background.

Dr. Elisabeth K...: Yeah. I'm Elisabeth Kilroy. You can call me Dr. Kilroy if you want, but it still feels so surreal and just out of place for me. But I currently serve as the director of MOVR, which is MDA's patient registry. And so my journey to becoming the director of MOVR really starts, as you mentioned, my dad and brother have an unknown type of muscular dystrophy. Taking a step back, it became a family tradition to watch the Jerry Lewis telethon on TV every year. And I just have such a vivid memory of me sitting on the living room floor in my Power Ranger onesie, telling my brother that when I grew up, I was going to answer telephones during the telethon.

Mindy Henderson: Oh my gosh.

Dr. Elisabeth K...: It's surreal to actually be working at the MDA, but not actually be answering the telephone.

Mindy Henderson: Oh, that's so cool. I love that story.

Dr. Elisabeth K...: Yeah. So fast forward a few years, and I was sitting in the hospital trying to understand why doctors were telling me that my father would never walk again because he had a spinal cord injury. And as you said, in the intro, it ignited my curiosity for understanding human movement. And then fast forward a few more years, and my brother received the diagnosis of muscular dystrophy. And I really found myself trying to understand why doctors were telling him that they do not know what type of muscular dystrophy is, nor what gene is causing it. You heard on the news the buzzword of human genome sequencing, and we can identify all your genes. And I didn't understand why they didn't know why his muscles were wasting.

And at that time, I was also recovering from my third knee surgery. And I was really frustrated because I wasn't gaining back the strength that I wanted to, or the muscle mass that I lost from being on bedrest with my knee. So from there, I chose to study exercise science and neuroscience in college, and really fell in love with the basic science researcher and being in the lab and really trying to understand the intricacies of human movement, how muscle responds to injury and how muscle responds to stimuli, like strength training or inactivity.

And then after college, I wanted to pursue a PhD. My dad has his PhD and I always wanted become Dr. Kilroy too. So

now we can duel it out and see who's the better Dr. Kilroy. But then once I completed my PhD, I went on to do training in a gene therapy lab, so really trying to push out cures for these diseases. But I really learned that being at the lab bench wasn't where I could have the biggest impact. I really wanted to interact with individuals with neuromuscular diseases, interact with clinicians, researchers, drug developers, policy makers. And so that really led me to becoming the director of MOVR, where I could interact with all these individuals and have as big of an impact as possible.

Mindy Henderson: That's amazing. And I have to say, I suspect your brother and your father are probably incredibly proud of you and these are such hard things to go through in life. But as cheesy as it sounds, when your pain becomes your purpose, it's such a special thing. And I love working for MDA myself. And hearing about the work that you all are doing on MOVR is amazing. So I want to jump right in. Let's start with MOVR. Do you want to just start out by explaining to everyone what is MOVR and when was it created?

Dr. Elisabeth K...: Yeah, of course. So MOVR stands for the neuromuscular observational research data hub, and it was launched in 2019 after seeing how successful MDA's pilot registry, the United States Neuromuscular Disease Registry, or USNDR, and it was really started to see if MDA could fill the gaps in the data shortage for neuromuscular diseases, and also, just the availability of this data. So the USNDR collected longitudinal data from 26 MDA care centers. And there was about 2,700 participants diagnosed with one of four diseases. So it was ALS BMD, DMD, and SMA, and it really represented the first centralized registry to house data on multiple neuromuscular diseases with the standardized framework for collecting that data, meaning data is collected using an electronic form and it's standard for all the diseases. So the data is coming in and it's very easy to use, very easy to analyze.

So MOVR now represents a more rigorous or expandable platform with seven different diseases that are captured. So now we're capturing, in addition to ALS, BMD, DMD and SMA, we're now capturing also FSHD, LGMD and Pompe disease. So it's still powered by the nationwide network of care centers and it's available to every care center. So care centers can elect to activate the MOVR study protocol and become a MOVR site. So now they can start, when they see patients in the clinic, they can ask them if they would like to participate in MOVR. Every time they come back to the clinic, the data that is collected at that visit is then entered into MOVR. So there is an onboarding process for the care

centers, but our long term goal is to hopefully make sure every care center becomes an active MOVR site.

Mindy Henderson: That's fantastic. And I think at last count we had something like 163 care centers. That's a lot-

Dr. Elisabeth K...: Right now we have 60 MOVR sites, so we're almost there.

Mindy Henderson: We're getting close. Okay. So what are the plans to expand to other conditions? I would imagine that it's pretty methodical and the criteria is probably pretty specific each time you add a new condition to the MOVR database. But what does that look like, the consideration to add a new disease? And like I said, what are the plans to expand?

Dr. Elisabeth K...: Yeah, this is really a great question, and we hear this a lot from industries who are interested in accessing MOVR data, clinicians that are seeing patients in the clinic and other researchers really interested and invested in these neuromuscular diseases. So we want to expand MOVR to include all neuromuscular diseases. And right now we're working on adding CMT, myasthenia gravis, and myotonic dystrophy. But one of the biggest hurdles in adding more indications is what we refer to as a data entry burden. So MOVR's capturing clinic entered data. So when the individual is seen at a participating MOVR site, all of their data is being entered into the electronic medical record or health record, but then that data needs to then be transferred into MOVR.

And this transfer is done manually by research coordinators and trained study staff at that site. So it takes time to complete the data entry process. So we have a standardized set of questions. They have to look at the medical record and then use that to answer these questions. So we're really trying to alleviate this manual data entry by using other data entry methods, such as batch uploading, or integrating the electronic health record with MOVR. And even trying some new things like artificial intelligence and machine learning, to be able to pull data directly from the medical record and put it directly into MOVR.

Mindy Henderson: Okay. So you mentioned a standard set of questions. Is the set of questions that you ask patients, is it the same data that you capture from disease to disease, or is there some variance?

Dr. Elisabeth K...: There is some variance. So for all indications, we capture data using four different forms. So we have a demographics form, a diagnostic form, an encounter form and a discontinuation form. So the demographics form and the discontinuation form are the same. So the demographics form

is going to capture the participant's date of enrollment into MOVR, date of birth, gender, race, ethnicity, insurance type, education, and employment. And then the discontinuation form is going to capture the reason for discontinuation, such as was the patient lost to follow up, did they move to another clinical site, is the patient withdrawing from the study or has the participant become deceased. And if so, what was the date and cause of the death? But then the diagnosis form and the encounter form are unique to each individual indication. Each disease has their own diagnostic criteria and diagnosis method. And then the encounter form is what's completed at every visit. And every disease has different functional measures, disease progression measures and markers, and we want to make sure that's captured for each disease on its own. So there's different criteria and questions in those forms.

Mindy Henderson: That makes sense. So when you mentioned earlier that at the care center, the practitioner will ask a patient if they want to participate in MOVR, if they say yes, are there specific touch points?

Dr. Elisabeth K...: So we do ask that care centers enter data from their normal visits at the care center. Since it is an observational study, we don't make care centers do anything that they wouldn't normally be doing in the visit. And if something is not done at that visit or within 30 days leading up to that visit, we just don't capture it. So for example, for a lot of these neuromuscular diseases, there's a lot of functional tests, like the six minute walk test, or time to climb four stairs, time to rise from supine. And if this isn't being done at that visit, we don't ask the care center director or the physician to do these tests. We just want to capture it if it was already done. Because again, we don't want to burden the sites with more things to do, we just want to capture everything that's already being done.

Mindy Henderson: I see. And I do want to shift gears in just a second and talk about ALS in particular. But just in general, can you tell me a little bit about what we've been able to do with the MOVR data so far?

Dr. Elisabeth K...: Yeah, I absolutely love this question. It gets me like so pride and joy, something that I'm really excited about because it takes time to get data into a database, as you can imagine. But now that we have data from over 4,000 participants, I think the last time I checked we're at 4,400. So it is a lot of data now.

Mindy Henderson: That's fantastic.

Dr. Elisabeth K...: Yeah, it really is. So two of the biggest things that we've been able to achieve or accomplish with MOVR data thus far is to run clinical trial feasibility analyses, and performed clinical trial matching. So for clinical trial feasibility, companies will send us their inclusion and exclusion criteria for their proposed trial and we can then determine how many MOVR participants would be eligible to participate, but also determine which criteria are causing the number of eligible participants to be decreased. And this information can then be used by the company to reevaluate whether or not that specific criterion is really necessary. For example, boys with DMD and steroid use. So a lot of clinical trials are very specific about their steroid regimen, how long they've been on it. And this could impact whether or not a participant is eligible. So are those steroid criteria necessary. And so then the company can reevaluate how they want to proceed in order to recruit the most number of participants as possible.

Companies can send us their inclusion and exclusion criteria. And then we perform analyses to actually identify eligible participants. And then we send the information about the trial to the principal investigators at the MOVR site, along with the ID numbers of those participants who do qualify or could be potentially eligible. And then the clinician at the site can confirm a participant's eligibility, decide whether the trial would be a good fit and then share that information with the participant, and the participant can decide to reach out to the company running the trial.

Mindy Henderson: I love it. And that's so exciting because I'm thinking back to my own journey with SMA and growing up before things like Spinraza and other treatments were available, there were clinical trials that I knew were out there happening and going on, but I never really knew how to get plugged into them. The idea that now you've got this database where you can proactively identify trial participants of things and make these trials available to them, that's really exciting.

Dr. Elisabeth K...: Yeah. And just like you said, like there's so many trials out there, but a lot of families and patients, they don't always know what allows them to be included or excluded. And also, clinicians are so busy and they see so many patients, it's hard for them to learn about a trial and then be able to immediately go and say, "Okay, I know this participant, this participant and this participant would qualify and be a good candidate." Now, we're doing that heavy lifting for them and then they ultimately just get to go back and view the data and make sure that yes, they would be a good fit.

Mindy Henderson: That's amazing. So I spoke with Dr. Mehta from the ALS Registry also for this podcast. And it sounds like, I'm sure

there are other differences, but the difference that's really sort of in my mind become one of the primary differences between the ALS Registry and MOVR is that the ALS Registry is largely patient driven. So patients register on their own and share their information. MOVR is initiated by a physician. And while a patient has to consent to participate, it's incumbent on the doctor to approach a patient about it. Is that accurate?

Dr. Elisabeth K...: Yeah. So once the patient consents to participate in MOVR, that's it. The rest is on the clinician and the study staff. So again, the biggest thing that separates MOVR from other registries, data captured in MOVR is clinic entered and it's transferred directly from the medical record. So this not only ensures continuity among the data from different sites, different participants, but it sets MOVR up to become a very rich source of data that could be used for regulatory submissions. So the data can be used to show the FDA that a drug or therapy is safe and effective, or if participants in MOVR are serving as a natural history or comparator arm for a trial, they have all this good clinic entered data rather than a patient trying to answer questions that they might not fully understand or [crosstalk 00:36:48] expected.

Mindy Henderson: Gotcha. I mentioned ALS a little while ago. May is ALS Awareness Month. So I'd love to zero in a little bit on the data that's collected in MOVR for ALS. Can you tell us about the kinds of data that you collect around ALS?

Dr. Elisabeth K...: Yeah. So ALS is actually one of my favorite data sets to explore and analyze because there's over 2,000 participants that have been collecting data in MOVR. So I had mentioned earlier about the different case report forms. So for ALS, the diagnosis form captures data around the date of symptom onset and the date of diagnosis. As we know, symptom onset to diagnosis can be relatively long. And so we're trying to understand what is the fastest way to make that timeline shorter. We also collect which body regions were first affected, upper extremity, lower extremity, was it the bulbar. And then we collect whether genetic testing was done and what the results were. So the genetic testing, there are some candidate genes out there known to lead to ALS. But then there's also some sporadic cases too. So we want to understand that. And then one of the main diagnostic tests right now is the revised El Escorial criteria, so we capture that. And then also family history. So trying to understand if anyone in your family also is battling ALS or has battled ALS.

Mindy Henderson: It's such a complicated disease. From what I understand, not being a doctor, but it's hugely variable from patient to patient, which must make it really, really challenging.

Dr. Elisabeth K...: And that's what's really cool about having so many participants. 2,000 is a huge number. And so I mentioned the diagnostic form. But really the bread and butter of MOVR is the encounter form, because this is capturing the longitudinal data, so at every clinical visit. And so this is collecting information about clinical trial participation, falls and hospitalizations. One of the functional tests for ALS is the ALSFRS scores. So that asks you about climbing stairs, walking, swallowing, using your hands. It also looks at nutritional therapy use, mental and cognitive status, medications, disease progression, assistive devices, pulmonary and cardiology, functional measures, and then also who the patient was seen by at that visit and referred to. And I think the referral data is what's really interesting to me because what are the most common practices that participants are being referred to, and why could that be.

Mindy Henderson: Interesting. How is ALS MOVR data feeding into clinical research or trials?

Dr. Elisabeth K...: Yeah, so we actually get to partner with researchers to combine data, so combining data from MOVR with other data sets, as well as starting to collect new types of data. So we're currently working with a company to set up a study that would be run side by side with MOVR. And this is really trying to track what is living with ALS like, day to day, versus just at that clinical visit. So I think we can definitely back clinical trials by for example, recruiting participants to participate in a company trial and still be involved in MOVR and combining those data sets.

Mindy Henderson: That's great. What do you think is the most exciting thing happening in ALS research today?

Dr. Elisabeth K...: It's just always been a fascinating disease because it's so different. Every individual is affected so different. Every new paper comes out and it's just a whole different view of what ALS is. It's just one of those diseases where you just keep learning about and you keep making progress and understanding, but then something new comes up. As a scientist, it blows my mind. And it's frustrating. Everyone you know, you at least know one person in your life that has battled ALS and it can just be really hard. But one thing that I really am loving is all the different tools that we are developing and we're using to understand the disease.

So for me, that is like when I looked up this question last night, like what's new on ALS, to prep myself, I was just amazed by all the different animal models. So they're using Drosophila, so fruit fly, C. elegans, so worms. Zebra fish. So I'm biased because Zebra fish was what my PhD used. And

mice. And there's so many different models in knocking out the different genes to understand what happens when you no longer have that gene, using different techniques. So for example, with flies and worms, it's very easy to manipulate their genes and add environmental stressors. So you can understand what happens when they don't have this gene. What happens to the nervous system? What happens to the muscle.

And then with Zebra fish, they're completely transparent from fertilization up to 15 days, and now nerding out. So being completely transparent, you can literally visualize the nerves growing and the muscles being innervated by these nerves. So it's really great to see all these papers utilizing all the old techniques, new techniques and developing even more techniques with the technology that we have and the science we have. So I think that's something that is really most fascinating to me in the ALS world.

Mindy Henderson: Yeah. Interesting. And again, not a scientist, but what is coming to mind for me in listening to you explain this and the different kinds of animals and organisms that they're looking at, I would think that would be incredibly helpful in getting to all of the different ways that ALS can present.

Dr. Elisabeth K...: I think that when we look at science, we have to look through multiple lenses, and this is really allowing us to look at multiple lenses. And multiple sizes. Going from a little tiny fly, all the way up to a little mouse, their systems are different, but they're the same. So it's really cool to understand a disease in multiple different contexts.

Mindy Henderson: That's really interesting. Unfortunately, I'm going to have to wrap this up. But are there any final thoughts that you'd like to share with our listeners about ALS research or MOVR, in general?

Dr. Elisabeth K...: Yeah. I just want to say my family's motto is adapt and overcome. So every day is a new day that brings new challenges. So I just ask listeners to keep fighting, fighting against ALS and all the other neuromuscular diseases. And as a researcher, I know we are on the brink of bringing a lot of effective and life altering therapies to you and to individuals with these diseases. And one thing that I've learned is that strength is in numbers. So the more participants in MOVR, the more data we have to generate hypotheses, to make conclusions. And the more individuals we have raising awareness about these rare diseases, the more power we have to influence policies and support therapeutic development. So with Congress passing the act for ALS, that's huge. Not only for ALS, but all neuromuscular

diseases. So I ask everyone to keep adapting, overcoming and keep fighting the fight against ALS.

Mindy Henderson: So well said. Thank you so much for your time and for being here today. I appreciate it.

Dr. Elisabeth K...: Yes. Thank you so much, Mindy.

Mindy Henderson: Thank you for listening. For more information about the guests you heard from today, go check them out at mda.org/podcast. And to learn more about the Muscular Dystrophy Association, the services we provide, how you can get involved and to subscribe to Quest Magazine or to Quest Newsletter, please go to mda.org/Quest. If you enjoyed this episode, we'd be grateful if you'd leave a review. Go ahead and hit that subscribe button so we can keep bringing you great content and maybe share it with a friend or two. Thanks everyone. Until next time, go be the light we all need in this world.