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Welcome to a recap of our latest third Thursday webinar, hear directly from expert panelists as they discuss Parkinson's research and answer your questions about living with the disease. Join us live next time by registering for an upcoming webinar at michaeljfox.org.

Katie Kopil: Welcome. I'm Katie Kopil. I'm the senior vice president and head of clinical research at the Michael J. Fox Foundation. Today, we're going to be discussing some of the research into how Parkinson's and Alzheimer's jointly are answering shared questions about brain disease. We'll also be talking about how that knowledge will eventually lead to better treatments and care for people living with any of these brain disorders. We have a lot of exciting information and complicated information to discuss today. So let me now first introduce our panelists. Welcome to Fred Goldstein, Fred's the founder and president of Accountable Health, a healthcare consulting firm focused on population health. He's also host at the PopHealth Week, a weekly radio show, and has been a care partner to his father who lived with dementia, with Lewy body and his mother who lives with Alzheimer's. Welcome, Fred. Thanks for joining.

Fred Goldstein: It's my pleasure. Thank you.

Katie Kopil: Next we have Dr. Thomas Tropea, who's the Chief Medical Officer at the Institute for Neurodegenerative Disorders. He's also adjunct professor of neurology at the University of Pennsylvania, Perelman School of Medicine, where he works as a movement disorder specialist. His research focuses on biomarkers and genetics for the development of precision medicine for Parkinson's disease. Thanks for joining us, Tom.

Dr. Thomas Tropea: Thanks for having me.

Katie Kopil: And then last but not least, Dr. Melissa Armstrong, who's the Director of the University of Florida Health Mangurian Clinical-Research Headquarters for Lewy body dementia at the Norman Fixel Institute for Neurological Diseases. She's also a movement disorder specialist and her research focuses on understanding treating Lewy body dementia. Thanks for being here, Melissa.

Dr. Melissa Armstrong: Thanks so much.

Katie Kopil: So let's start off by defining brain disorders, and Tom, maybe I'll go to you first. Could you help us understand why do people in research and in the clinical community talk about Parkinson's and Alzheimer's together?

Dr. Thomas Tropea: Sure. Thanks for the question, and it requires a little bit of background and I'm happy to provide that. Alzheimer's disease, as many people are aware, we typically think of this as a memory disorder. While Parkinson's disease tends to be somewhat different, and when we think about Parkinson's disease, most people think about problems with movement or tremor. We know that some people with Parkinson's can go on to develop changes in their thinking and memory, but that's not what we think of as the primary sort of concern in Parkinson's disease. So now, why is it that we talk about these things together? Well, first of all, they're both brain disorders. They originate from changes that occur in the brain that lead to the symptoms that people experience.

But more and more, we're understanding that although we have these designations of Parkinson's like tremor and movement, and Alzheimer's, predominantly memory, that these two things actually, when we look inside the brain, these two things actually can occur in the same person. Meaning you can have the changes that we see with Parkinson's and you can also have the changes that we see typically with Alzheimer's disease. So we talk about them together where more and more we are talking about them together because we understand much more about their underlying biology. So this is why I think you're seeing this webinar, but you're also seeing a lot of talk about these two disorders together in the same space.

Katie Kopil: That's a great background. Fred, maybe I'll go to you. For the two different hats that you're wearing on the call, maybe first with your population health hat, could you tell us a little bit about how prevalent these diseases are in the community, whether that's the US or globally?

Fred Goldstein: Absolutely. So when you think about it from a US perspective, roughly 1.1 to 1.2 million people are living with Parkinson's disease, and a 2022 study found that nearly 90,000 people are being diagnosed with Parkinson's every year in the United States, which has gone up considerably from a few years back when the estimate was about 60,000. We're now looking at this as the fastest increase in frequency impairment for neurological diseases around the world, and it's up about 50% from the previously estimated rates. So what we're thinking also is they estimate by 2050, we'll see about 25.2 million people of all ages and sexes around the world globally living with Parkinson's disease.

Katie Kopil: And you've had that upfront experience across a couple of different brain disorders. Could you talk also a little bit about your experience caring for your parents with different brain disorders?

Fred Goldstein: Yeah, it really... As you recognize and most people on this call would recognize, it's kind of unique for each individual. They have different ways they're expressing the disease or how it impacts their family or quality of life or their caregiving abilities and what they have available, but it's been a difficult situation. I recall the very first call from my father when he called us to tell us he had disease with Lewy body or dementia with Lewy body, and it was sort of stunning. And so now later on as mom a couple years ago began to develop symptoms of Alzheimer's, it really is difficult from a family perspective. And we have frequent calls, we fly out and see her. Fortunately, some family's there, but it's really been a fairly significant effort and load, you would say, on the caregivers themselves. And so there's a lot that's going on there. There's a lot more we could get into, but it's a significant issue, and obviously as we think about it impacts the individual living with it and it impacts the caregiver who's working with them.

Katie Kopil: Yeah, and I think your personal experience living with these disorders as part of your family really underscore the importance of moving research more quickly to get to better treatments that help them. And maybe picking up on the thread, Fred, where you explained when your father called with his diagnosis, I'm sure that was probably a challenging path to get to. Maybe Melissa bringing you into the conversation, could you talk about what makes these brain disorders challenging to diagnose from your clinical perspective?

Dr. Melissa Armstrong: Well, I think one of the big challenges is that it starts subtly. It's not that all of a sudden families notice something or the person living with it notices something. It's a gradual thing, and so it kind of comes on people slowly and that can make it harder to recognize. There can also be a lot of different symptoms that are kind of weird to put together. So we know that people can have constipation as an early symptom. Maybe you're not thinking, "Oh, my constipation is leading to my Parkinson's disease." So I think it's the different kinds of symptoms and also the fact that they can start so slowly.

Katie Kopil: And I think what you're talking about, this overlap of symptoms, and you don't go to bed one night and wake up in the morning with something that's completely new, that there's also this clinical exam that leads to the way that things are diagnosed, and that might change over time based on what progresses in somebody's lived experience. And maybe, Tom, you could say a little bit about why a clinical diagnosis might change for somebody over time.

Dr. Thomas Tropea: Yeah, the symptoms that bring you to go see your physician or a neurologist or whoever it is that you are seeing for this, may be just the first symptoms that you experience, and so maybe it is that you have say tightness or what we call rigidity in a limb, and that's the first thing that brings you to see a doctor, or maybe it's really the memory changes or personality changes or whatever it may be that bring you to see a neurologist or a physician. However, all of these disorders do... They take time to manifest, but they also take time to understand what is going on. So you may visit with a physician on your first visit, and frankly, in my clinical practice, this happens not infrequently where I say, "I've got a suspicion, but I can't really say. You don't meet the criteria for this, but this is what I suspect."

I think what also makes this, to sort of add to the great comments from Melissa, is that we don't have great diagnostic tools outside of the clinical exam. And so yes, we have some imaging techniques and there's some new research methods that we can use for detecting the proteins related to Parkinson's disease, but they're not really part of the clinical diagnostic set. This is a huge area of research.

Katie Kopil: And I was sharing with the panelists before this call, I just came from an annual women's health wellness exam, and I am happy to say that I'm cancer-free, but that's because there was a radiologist at the appointment and there are these diagnostic tests that are used routinely. And so maybe Fred, you could relay the counter experience of what that uncertainty feels like for families that receive a diagnosis of a neurodegenerative disorder where there isn't as much routine biologic testing.

Fred Goldstein: Yeah, it's nerve-wracking, obviously, because you're not really sure. Although my father was a professor of medicine, so he sort of understood it and was able to then explain to us what he thought might go on over the coming years, but it's really a tricky one to... And it does create a lot of uncertainty because you just don't know how, where, when things are going to happen. So I think it's definitely a tough one. And as the doctors talked about, you're sort of unclear as to what is going on until they make that diagnosis, and then when they do, what does that mean and where does it go from there?

Katie Kopil: This mirrors most community member stories about the uncertainty, but we are excited to get towards the end of this webinar where we're talking about research, which we hope is going to change that paradigm. Before we get there, maybe we could talk a little bit more about the overlap between what we do know about Alzheimer's, Parkinson's, and Lewy body dementia. Melissa, could you help us understand some of the nomenclature here, maybe starting with Lewy body dementia, which can be used as different acronyms and those words in different orders. What is it and how does it fit in to this constellation of conditions?

Dr. Melissa Armstrong: Well, first, I just want to admit that the vocabulary is kind of messy. We have terms that are really similar, but when we think about the term Lewy body dementia, it really includes two different paths or two different diagnoses. So people receive the diagnosis dementia with Lewy bodies when the memory and thinking problems are there right up front, they may have hallucinations, they may have some Parkinson movement problems, but really the main problem at the beginning is memory and thinking. And then on the other side of this umbrella term of Lewy body dementia, we have Parkinson's disease dementia, and that diagnosis is given to people who have a diagnosis of Parkinson's that's based on their physical symptoms at the beginning, but then over the course of their disease, they develop more memory and thinking problems as well. So when we think about Lewy body dementia, it has people with the memory problem first in DLB, and also people with Parkinson's that go on to develop the memory and thinking problems later.

Katie Kopil: And Fred, I know you've had this personal experience with a constellation of alphabet soup thrown at you, Parkinson's dementia, dementia with Lewy bodies, Lewy body disorder. Could you talk a little bit about your family's experience navigating those different terms or what your reflections have been on your dad's journey?

Fred Goldstein: Yeah, it was really... he had DLB. So his cognitive came first and early, and so it was really kind of a massive change for him and my mom and the family because he had to retire from his work, although he didn't want to, because he felt cognitively he was going to be at risk at some point. So he retired early while he still physically was able to do the work and things, and that made it very difficult. And then to see over time how that disease progressed was tough on the family.

And we were very fortunate because each of the kids, my two brothers and two sisters have different skillsets, and so we began to fill in to help with those based on our expertise to help caregiving for him. And as an example, he loved fishing, he'd stick him on the front of a boat, put the life fest on him and he'd sit in that chair and fish, and it requires a lot of thoughtfulness from the caregivers as to where is this individual, what are they able to do? And then also the hallucinations and things can be really difficult, going at a theater or something, and suddenly the individual is... My dad would be saying, "Hey, there are four people over there. What are they doing?" Things like that are very tough.

Katie Kopil: And maybe from Fred's care partner, caregiver experience and what Melissa shared clinically, there's a lot of overlap and symptoms across these conditions, and Tom, maybe you could tell a little bit more about the overlap and these symptoms that couldn't be seen or what's more distinct about one condition versus another from your clinical experience.

Dr. Thomas Tropea: I mean, we focus really mostly on the motor symptoms or tremor and walking challenges that can happen in Parkinson's. We've also talked a little bit about the memory issues that can happen predominantly in Alzheimer's disease. First, I'll say that the overlap here is that although we call these... We use the sort of term memory changes, but really in Lewy body dementia, so Parkinson's disease and dementia with Lewy bodies, you see a somewhat of a different flavor of changes in thinking in memory. And so they don't always look exactly the same. It's a little bit hard to tease apart, but dementia with Lewy bodies and Parkinson's disease dementia have a little bit less of what we consider to be memory changes. So loss, inability to recall things, and a little bit more focused, like we just mentioned. So hallucinations can occur, some difficulties with navigating your own space, ordering tasks are a little bit more common in people with dementia with Lewy bodies and Parkinson's disease dementia.

That being said, in Alzheimer's disease, you can see a little bit of movement changes as well. And so again, this sort of ties back to this whole idea, why are we talking about these things together? Because sometimes there are overlapping symptoms and you generally get a diagnosis based on the primary syndrome, but you can experience a lot of these other symptoms. I would also say that across all of these things like lethargy, depression and anxiety, constipation are all very, very, very common. So some of these things that we don't typically associate as a primary symptom of one of these disorders actually can occur across all of them. And when we look actually at data about what people say bothers them the most, there's actually a lot of these other generic symptoms that people report. Movement problems and memory are, of course, what brings you to the doctor, but sometimes depression can be one of the most invasive challenges or sleepiness, daytime sleepiness or lack of motivation that can happen across all of these things.

Katie Kopil: This discussion of the different symptoms and how they overlap or how they can coexist is really helpful. We have a question from the audience, Tom, maybe you could comment on this, within the Parkinson's space. Why is it that Parkinson's is more prevalent in men and maybe Alzheimer's is more prevalent in women? Is there some biology to explain this?

Dr. Thomas Tropea: Oh, it's a really great question and actually an active area of research. So I do think that the population-based estimates are correct. I think it is slightly more common for a man to be diagnosed with Parkinson's and slightly more common for a woman to be diagnosed with Alzheimer's disease, and there are lots of theories about why this may occur. There are some biological theories. There are some what we'd say of how gene changes may affect your risk of developing one of these disorders may differ between males and females. So there's a lot of theories out there, but I'm not so sure that we have a definitive answer about why one sex is more at risk for one versus the other.

Katie Kopil: And maybe this also connects to your point earlier that there's not necessarily a definitive test that helps distinguish across these conditions, but maybe, Melissa, you could talk about what tests are available that help in clinically diagnosing the conditions that we see here.

Dr. Melissa Armstrong: Sure. Well, as we've discussed, I think most of the time it is still based on the doctor asking what symptoms have you been having, the physical exam. Really, we still rely on that very core part of a doctor visit, but there are some emerging tests in the field of Parkinson's disease and dementia with Lewy bodies. There is a skin biopsy that some doctors will order now the back of the neck, near the knee, near the ankle to look for signs of the protein involved in Parkinson's in the skin. For both Alzheimer's and Parkinson's and DLB, you can get a lumbar puncture with cerebrospinal fluid testing to look for the proteins that are not normal in these different conditions, and in Alzheimer's disease, there are some brain scans that can be used to help in diagnosis. But in terms of the test for people with Parkinson's disease and dementia with Lewy bodies, I would say we're still very early in that process, and most of the time those are diagnoses really made in the clinic.

Katie Kopil: And maybe this is a good time to talk about what is happening in the brain. We do understand from the imaging scans, from the underlying biology, proteins... We're not talking about steaks and chicken and fish here. We're talking about the pathophysiology of the disorders. And maybe Tom, you could help us with an overview of what's happening in the brain and how that relates to the clinical diagnosis that Melissa just explained to us.

Dr. Thomas Tropea: From a general perspective, we think of both of these two disorders among others as neurodegenerative disorders, and so in neurodegenerative disorders, one of the common themes among them is that a certain flavor of a protein, yes, not chicken and meat, it's just different proteins that occur in the body, for reasons that we are not entirely sure of, misfold, and so they sort of misfold into an orientation that either prevents your body from clearing it normally, or it induces clumping or joining among those different proteins, and when that happens, they get gunked up in the cell or around the cells and they end up getting deposited. And so you've probably heard of some of these protein names, alpha-synuclein is the one that we typically associate with Parkinson's disease and dementia with Lewy bodies. We also talk about amyloid beta and tau, and those are typically associated with Alzheimer's disease. I started the whole conversation by saying these things don't occur by themselves. And so even in people with Parkinson's, there can be some accumulation of amyloid in tau, and vice versa.

The important thing actually is where these protein deposit makes a difference, and so when you have diffuse alpha-synuclein around the entire brain early, we typically think of dementia with Lewy bodies. When it occurs a little more focally, predominantly in the lower part of the brain and the brainstem, we think that is what leads to Parkinson's disease at least early on. However, over time, they can change, and so they can move, they can sort of migrate and occur in different areas. So that's the general about what's actually occurring in the brain in these disorders.

Katie Kopil: One of the things that I know I had struggled with learning about this when I was in graduate school is what does it mean? Why is protein misfolding a problem? And had a colleague give a great analogy. I was thinking of a piece of paper. When it's flat, it can go through the printer just as it's intended to do. It's supposed to work just that way. If you crumple it up, it's not going to work the same way, it's not going to go through the printer, and there's something about the underlying biology here that the protein has to be in the right shape to serve its proper function. Maybe pulling on the point that Tom had brought up about where proteins get misfolded leading to different conditions, Melissa, maybe you could talk a little bit about how the parallels exist in the Alzheimer's field with where we see different protein smiths holding there versus maybe in something like dementia with Lewy bodies.

Dr. Melissa Armstrong: Well, to Tom's point, it is very similar between the diseases. They are different proteins in general that we think is the main cause of these different diseases, but we do think pretty much across these diseases that misfolding is the problem. In Alzheimer's disease, we talk about the protein's amyloid and tau instead of the protein synuclein that we talk so much about in Parkinson's disease and dementia with Lewy bodies, and for reasons we don't totally understand, amyloid and tau may, when they clump and cause problems, may go preferentially to those memory centers of the brain.

But there are other kinds of presentations of Alzheimer's disease where people have trouble with their vision or have trouble with their language, and that's because sometimes those proteins are causing problems in the vision or language parts of the brain. But to Tom's earlier point, it's also important to note that while we say Lewy body diseases are about this nucleon, we know in dementia with Lewy bodies, for example, that over half of people may have amyloid changes in the brain too, and so there is some overlap, and that's really something that is having a lot of research done now.

Katie Kopil: And this relates to an audience question. Maybe you could just put a fine point on it. Is there a continuum, a spectrum between Alzheimer's and Parkinson's, or does the field think of them as truly separate disorders?

Dr. Melissa Armstrong: I would say that Parkinson's and Alzheimer's are really considered separate right now. They are primarily linked to different proteins that tend to affect different parts of the brain, but I think there is increasing recognition that if we look at the brain either before or after someone dies, that people with our clinical diagnoses can have signs of both, and exactly how that works and how that changes what people experience is really an area of study.

Katie Kopil: And this is a great transition to highlight this shift in our knowledge of brain disorders. Maybe staying with you, Melissa, at least within the Fox Foundation, think of an analogy now when we hear about cancer and how it used to be treated on just one sort of clinical disorder where the cancer was in the body, but now there's subtypes, molecular markers, genetics, and also importantly, tailored treatments for those biologies. And so could you just say from a high-level perspective what's changed and what you see being a standard of care now for oncology? As a neurologist, I'm sure you feel very comfortable.

Dr. Melissa Armstrong: Well, certainly for different cancers now, the chemotherapies used to be really broad chemotherapies that said, well, as a chemotherapy, cancer is a fast-growing cell. So old chemotherapy said, "Well, we're going to target all of those fast-growing cells, and most of those fast-growing cells are cancer cells," but hair grows fast and that's why people lose hair. Stomach lining grows fast and that's why people get nauseous. So that old approach was really broad, kill the fast-growing cells. But now a lot of cancers do have targeted therapy, immunotherapies that say, "We're going to target this specific cancer," or even within certain cancers, there are different kinds and we're going to target this specific kind. And so I think the hope is that for diseases, we say, rather than taking this broad approach, we're going to be able to narrow in on something specific for an individual.

Katie Kopil: Right. That's what people want to hear regardless of the conditions that they're living with. And Tom, maybe you could talk about where you see the field on the path to personalized treatments that Melissa was talking about, especially when it comes to Parkinson's and Alzheimer's to mention with Lewy bodies.

Dr. Thomas Tropea: Pertaining to Parkinson's, I think one of the most important transitions that occurred in oncology, we'll stick there for just a moment, is their ability to detect the abnormal cell was greatly enhanced because what do we do with cancers? Oftentimes we can take it out. Well, we're talking about brain disorders, so of course we're not going to take out the bad parts of what's occurring. So we need to function in a system where we have to use things like biomarkers, which are basically either blood tests or spinal fluid test or skin to detect and predict what's going on in the brain, and we need to use imaging tests. So we're moving in that direction. We've been moving in that direction for years. We've had some great breakthroughs in our ability to detect and measure the abnormal protein.

And so I think the earliest evidence is that when we look at clinical trials and how they were enrolling for years, some people in those trials actually didn't even have alpha-synuclein in their brain because we can go now and we can look using tests to say, "Actually, we were giving you a drug that was intended to target alpha-synuclein, but you didn't even have alpha-synuclein." So the first step towards precision is actually clarifying the use of biomarkers. And so this is one of the big things. And I'm very involved in the Parkinson's Progression Markers Initiative, the PKMI study, and so this is one of our major goals, of course, is to develop these types of biomarkers.

Katie Kopil: Great, and we're excited about this precision testing, the right treatments and the right people. And we've been talking about a lot of proteins here, and we know that those are part of the disease pathology, but I also wanted to call out genetics, and Fred, I know you're comfortable talking about your experience with genetic testing. Maybe you could just share some of the reasons you've done genetic testing and what you've learned about your risk factors in the hopes of having better precision treatments in the future.

Fred Goldstein: Sure. So I actually made the decision when I got... I think it was a Facebook post that said, "Hey, if you're maybe at risk for Parkinson's, you should do a genetic test." And it was the MJFF way back. And my father had passed away at that point and I said, "Yeah, I'd like to help in this area and I'd like to know." So I did the genetic screening and one of the risks showed up for Parkinson's, and then I was asked to enroll in the study. And I think it's helped me as I think through, okay, what might my future be like? I don't know yet, but at this point, obviously getting in and getting involved in the study has one, I hope, and as you'll see, has created a lot of data that is helping this field advance, and it's also allowed me to participate and learn things about my own health.

Katie Kopil: That's great. Thank you for sharing. I know you're a passionate research advocate, and we can't thank you enough for all you do, both in participating in research and in raising awareness. Melissa, maybe just to close us out on this topic, could you talk about what research you're excited about, what research needs to happen to get us to that future state that Fred and Tom are talking about with those precision medicines where you started us off with where cancer is today?

Dr. Melissa Armstrong: Well, I think it's going to be a multi-step approach. We're definitely Looking for those treatments that target the alpha-synuclein and people living with Parkinson's or DLB or who are at risk of Parkinson's or DLB, but now that we're learning more and more that if we look at the brain, people may have more than one kind of disease in the brain. We're also going to have to start thinking about whether our treatments need to target more than one protein. So will there be people who have both Parkinson's protein and Alzheimer proteins, or eventually when we have a drug for the alpha-synuclein, they get the drug that targets that, but they may also need the drug that targets the Alzheimer changes. And so I think it'll be a two-step process getting those good treatments for the different proteins, but then also figuring out when we need to combine them.

Katie Kopil: And this is the future that we're hoping for and we're seeing in other conditions today. Maybe just for what this means for people living with these disorders today, I appreciate, Melissa, everything you said that we're learning more every day, but Tom, could you say what this growing understanding of biology, the new drug development, while we're waiting for better treatments, what this means for patients that come to your office today?

Dr. Thomas Tropea: Well, nowadays, I would typically rely on tried and true clinical diagnostic tools, which is essentially come to the office and you do your evaluation with the physician. This is still the gold standard in diagnosis for Parkinson's disease, but rapidly, and in Parkinson's disease, we've already seen this transition in Alzheimer's disease that these diagnoses are really becoming more reliant on the underlying biology detection. And so right now, we offer the gold standard still. I think in the very near future, this will transition to the use of more imaging techniques and more biomarkers before a diagnosis is offered to a patient.

Katie Kopil: And before that becomes standard and people are experiencing a variety of clinical symptoms, Fred, what advice would you give to people living with these disorders, the people with the diagnosis and the family members? How should they talk to their doctors about the way their symptoms are showing up?

Fred Goldstein: Yeah, I think this one is critical because I would watch my father go in for an appointment and he would shine. He'd do really well with the neurologist or whatever he's meeting with, but we had seen things differently. So we would then go and add that extra context to what was going on with my father. And I'd also point out it's complicated. They're seeing a lot of physicians, and one of the issues we had one time with my father, unbeknownst to my mom in the house, had wandered out at 3:00 in the morning and was found at the football field at the high school just down the street. And when we took him in to see the internal medicine doctor in a quick appointment, he said, "Oh, this is just Parkinson's," and we thought, "Wait, that advance is too quick." What happened to him cognitively, at least for us, seemed too fast, and it turned out it was something else.

And so if we hadn't raised that issue with the internal medicine physicians said, "Wait, it's more than that." In his case, he had one kidney, it was clogged up from a statin and the drugs were backed up in his system, and so it was not. And so ensuring that your entire care team has a pretty good understanding and relationship with the different doctors so they can understand it, I think is critically important, and explaining what you see is critically important.

Katie Kopil: I think that's such great advice. And Melissa, on the receiving end of that care team input, what would you add? How do you want your patients and their care team to talk with you about the symptoms that they're experiencing?

Dr. Melissa Armstrong: Well, I think what he said was really important. So I always want to hear from the person living with the disease about what they're experiencing and noticing, but I really want to hear from family as well, what are they noticing? And then we use both of those reports to figure out what is happening and what we need to do. And our appointments aren't really that long. And so I think it also helps if people come prepared, "These are the top three things that I've been noticing as a person living with Parkinson's. These are the top three things I notice as their spouse or their child," so that we can make sure that we use that appointment time well and really focus in on those key issues.

Katie Kopil: Great advice that should be used all the time and helping prioritize ahead of time if you can agree on what you want to bring up in that limited timing. It's always a good way to make the most of those brief appointments. So that's what it means today. Now let's go back and take a look ahead to the research that's helping us understand more about the links between these disorders or at least biologic processes that may contribute to these. Maybe I'll start with Tom and then, Melissa, have you chime in to talk about some of the work that you're most excited about that's advancing therapies that target these misfolded proteins that come up across different neurodegenerative disorders. Tom, what are you most excited about?

Dr. Thomas Tropea: I'm most excited for two broad areas. One is around targeting therapies to people where we can identify and measure the underlying biology. So I'm very excited about the biomarkers that are in development. I'm excited about the imaging markers that are in development. So these are some novel tools that we can use to detect the alpha-synuclein like we can do in Alzheimer's disease. I'm also really excited about developments around targeted therapies for individuals carrying certain variants in certain genes. And so this has been a big area of research, and so I think we're going to see a lot of movement on those two fronts in the next couple of years.

Katie Kopil: The Fox Foundation loves talking about biomarkers, and I want to come back to that point in a minute. Melissa, what are you most excited about in terms of advancing these biologically-targeted therapies against these disorders?

Dr. Melissa Armstrong: Well, I'd agree. Biomarkers are a really big part of it. There are people trying to develop brain scans that can detect the changes we see in people with Parkinson's, just like we have some of those brain scans for proteins and Alzheimer's. The field is also looking for blood-based biomarkers, and everybody would love a blood-based biomarker because then we wouldn't have to do things like lumbar puncture or spinal tap. Not everyone really likes those. And then I think another really exciting thing is just all the crosstalk that has been happening recently between the different fields. I feel like in the past we have the Parkinson field and we had the Alzheimer field, and they were really separate, movement disorder specialists, dementia specialists, but I really feel like the fields are coming together now, and I think that crosstalk is really important, especially as we learn how many people have evidence of both kinds of diseases in their brain.

Katie Kopil: I agree that collaboration in the field is really ripe right now and that these opportunities to bring different expertise together that are been thinking about almost a similar problem from different angles is really leading to new insights and knowledge turns much faster. Maybe next to that, I'll say from the Fox Foundation perspective, we have the opportunity to work and alongside with biopharma partners that are developing new treatments for Parkinson's disease, both symptom treatments as well as treatments that attack this underlying biology to change the trajectory of progression, and we're excited that there's over 1150 different treatments that we know are in development today to help improve the lives of people living with Parkinson's and a broader array of drugs being developed across Parkinson's, dementia with Lewy bodies and Alzheimer's.

So I think this is a really exciting time for momentum and tools like biomarkers make those clinical trials more informative. And maybe Tom, to go back, could you talk about not just what biomarkers are happening, but the importance of how you communicate biomarker results to participants? And then, Fred, I'm going to invite you to share your experience getting some of those biomarker results.

Dr. Thomas Tropea: And just by way of introduction, it turns out actually that in order to know if you are even eligible for a trial that is a precision-based trial or a targeted therapy, you've got to know if you actually have that. And so one of the things that we have started to do in the PPMI study is evaluate how best to share that information back with people. In PPMI, we follow people for years and years and years. We collect lots of blood and spinal fluid and imaging, and it is for a research purpose, but we have really wonderful partners in our participants who deserve to actually learn that information. And so what we're doing now is we're sharing back a few pieces of research information, increasing over time to understand how best to inform the field on how to do this and how to do it right and how to do it effectively and how to support patients as they learn that information.

Katie Kopil: And can you talk... There's an audience question about the seed amplification assay test for synuclein and spinal fluid. Could you talk about whether that's part of the PPMI study and what we know about the implications if somebody has a positive synuclein test based on a lumbar puncture?

Dr. Thomas Tropea: The seed amplification assay detects alpha-synuclein as measured in the spinal fluid, which is a reflection of what is occurring in the brain. The assay was developed a number of years ago, but one of the biggest demonstrations of its use was within the PPMI study. And so there's a landmark paper published a couple of years ago showing that that is a very reliable test for detecting alpha-synuclein, but it also turns out that some people with Parkinson's symptoms don't have alpha-synuclein in their brain. So in PPMI, what we've really been studying is why do some people and others do not have a positive seed amplification test, and so that is one thing that we're really focused on in PPMI. I will also share that we share the SAA results back with participants in PPMI.

Katie Kopil: And Fred, you are a very generous PPMI volunteer. Could you talk about your experience opting into getting these results back, your SAA test specifically?

Fred Goldstein: Sure, absolutely, and I think it's one of the greatest things that's been done because usually you don't see this, and I think MJFF taking the input from us as participants has just been amazing. So obviously people are going to have different feelings about this. Some people may say, "I don't want to know," and that's fine, and other people say, like myself, "Hey, I do want to know," and it's actually helped me think through as I've gotten these various pieces of information, clinical information from the study of what's going on and where I am within the context of what we know today. So it's really been good for me to understand that, and I really appreciate the fact that that information is now being released. And we talk about, in the future, maybe some more information, other pieces of information that would be helpful.

Katie Kopil: Thank you for sharing this experience, but thank you also for your advocacy. No insults to Dr. Armstrong and Tropea, but sometimes there's discomfort when there's not a full understanding of what biomarker tests mean and the lack of maybe the prognostic value. They don't really tell you necessarily everything you'd like to know. And so there's sometimes hesitancy to share that back. But your voice, Fred, and the voice of others in our community advisory board for

PPMI have been so powerful. And in a sea change, I think in being able to say that patients have the right to know, and I know it's actually no insult to Tom or Melissa because they are both champions of this as the next rising leadership within movement disorders across the field, and they do this routinely too.

So because we've been talking about PPMI alongside the acronyms of Alzheimer's and DLB and PD, I just wanted to take a moment to call out that the Parkinson's Progression Markers Initiative PPMI study is recruiting volunteers. People from all backgrounds with and without Parkinson's, as Tom was talking about, can help move research forward, and we'd encourage you to join the study that's changing everything by clicking the link in the resource list on the right side of your screen. So with that, we've received a lot of fantastic questions. We'll try to get to as many as we can. And as a reminder, you're welcome to enter your questions into the Q&A box. So let me jump into some of these. We have a question from someone who has Parkinson's that wants to know if they're more likely to get Alzheimer's disease than somebody without Parkinson's. And maybe you could take this both, Melissa, as a clinical diagnosis, but also talk about some of the cognitive changes that somebody with Parkinson's might anticipate that's different from Alzheimer's.

Dr. Melissa Armstrong: Yeah. So we know that people with Parkinson's can also get Alzheimer's changes in the brain, but I don't usually tell people living with Parkinson's that they're at a higher risk of Alzheimer's, just that having one doesn't mean you can't have both. But sometimes when people ask that question, what they mean is not, do I have a higher risk of Alzheimer's, but do I have a higher risk of memory and thinking problems? Because sometimes Alzheimer's and dementia are used to mean the same thing when Alzheimer's is really just one kind of dementia. And when you have Parkinson's, you are at a higher risk of memory and thinking changes as you live with it longer. Now, the memory and thinking changes we see in Parkinson's are different than the memory changes we see in Alzheimer's.

So Alzheimer's in general tends to be very much about memory, but when we think about the changes in Parkinson's, as Tom mentioned earlier, it can be things like trouble multitasking, trouble really focusing and paying attention. And if you can't focus and pay attention and really capture something, it doesn't get into short-term memory or long-term memory. Parkinson's can cause challenges with visual spatial reasoning that can be something affect driving. And a lot of this gets back to that foundational point we made earlier. The diseases affect different parts of the brain. So the Parkinson's memory and thinking changes are from proteins building up in a different part of the brain than the Alzheimer memory changes that we often see.

Katie Kopil: Tom, maybe go into you. There's a lot of different questions coming in about environmental exposures linked to different neurodegenerative disorders, Parkinson's and Alzheimer's. What do we know about that, and are those environmental exposures similar or different across the clinical diagnoses they've been linked to increased risk for?

Dr. Thomas Tropea: Well, when we talk about environmental exposures, what we're talking about is your risk of developing Parkinson's, and so I usually put this into this sort of bucket of three different risk categories, and for any given person, your age and your genetic makeup are things that add to your risk over your lifetime. Of course, your age will continue, your genetic makeup stays the same. And the thing that we have to add on top of that is your environmental exposure. And your environmental exposure can be any number of things. It could be certain toxins that you're exposed to, your eating habits, your sleep habits. There's lots of things that go into that environmental exposure that affect your risk. What most people refer to when they discuss environmental risk are really environmental toxins related to pesticides and proximity to certain areas that have a high prevalence of certain toxins to the body, and we're learning a lot more about that.

Now, what we think is that your exposure to certain environmental risk factors adds to your genetics and to your age. And in most scenarios, it is not the case that the toxin exposure is the absolute cause of your symptoms, it adds to your risk. We're learning a lot more about what those toxins are, and so there's some really great work being done, and I think we'll continue to learn more about how your environment may affect your risk of developing Parkinson's.

Katie Kopil: Fred, anything you'd add from your population health perspective, how people should think about additive risk factors versus causative factors?

Fred Goldstein: Yeah, as the doctor said, it's a broad area in a sense. And so as we begun to understand it better in me not as a clinician, I say, "Okay, I may need to change some things about what I'm doing or potentially what I'm getting exposed to." Back in the day, it was, "Hey, my lawn's got to look like X, Y, Z, and I'm going to go ahead and put these chemicals on it, and so there are things like that and those associations that I've began to talk to and recognize now that I hear other people actually talking about themselves as well in regards to what we're learning and what gets published.

I think it is really important to understand that you need to talk to individuals who really know it and understand it to get a better sense of what that really means and what the risk is. As the doctor said, it adds to a potential risk that you have. And so there are things, I think, as we think about it, whether it's sleep or eating habits or exposure to toxins that we can do to try to minimize potentially those add-on risks.

Katie Kopil: And I think you're getting at this too, that people might also be able to consider lifestyle interventions to help mitigate risk. And Melissa, we've gotten questions about this and I know you're passionate about this, questions about the value of movement and exercise for managing the conditions if people already have a diagnosis. Could you talk a little bit about what you would advise in terms of exercise to help live well with these conditions?

Dr. Melissa Armstrong: Yeah. So for people living with Parkinson's in my clinic, every time I see them, we talk about how important it is to exercise and stay active. There is lots of research showing that people with Parkinson's who exercise do better, and there are even ongoing research studies to look at whether exercise might even be able to slow the progression of Parkinson's. And in those discussions, we often focus on the physical benefits of exercise and staying active and whether exercise might slow Parkinson's down, but there's also a lot of research that shows that that physical exercise and staying physically and mentally active is really good for memory and thinking changes too. So even outside Parkinson's, they've studied exercise for people living with mild cognitive impairment and exercise had benefit. So I think that one of the most important things people with Parkinson's can be doing for both their physical health and their mental and cognitive health is making sure to have a regular exercise regimen and then staying physically and mentally active in other ways as well.

Katie Kopil: One of the questions I know people are probably thinking, what's the right type of exercise to get those benefits? What would you tell people?

Dr. Melissa Armstrong: Well, there's probably no wrong time to exercise, although I do want to emphasize that it doesn't have to be every day. There was even a publication this past year that said, "Could there be too much exercise?" I don't think too many people go all the way to that, but there is a point that might be too much. But I think doing it regularly, in my clinic, I encourage people to start slowly, ramp up, and target three to four times a week.

Katie Kopil: One of the things that I find helpful for myself and also for conversations with community members, the exercise that you're going to stick with is the best one that you can do.

Dr. Melissa Armstrong: Yeah, they've looked at different kinds of exercise and people with Parkinson's and different exercise might help in different ways, but doing it, I think, is the most important. And I'm sorry I interrupted you, Tom.

Dr. Thomas Tropea: I was going to actually say what I tell most of my patients in the office is that I'm not here to prescribe you a certain type of exercise. In fact, I think you're much less likely to do it if it's a prescription. It's just whatever exercise you're going to do every day, and that may be walking, it may be stretching, it may be yoga, it may be running a marathon. Who knows? Whatever it is that you're going to do, that's the one that you should continue with.

Katie Kopil: There are many marathoners in our community, congratulations to them. I'm much more of a yoga person myself. Maybe going back to biology, there were a couple questions around scientific thinking about inflammation, especially neuroinflammation and how neuroinflammation may be a driver across these neurodegenerative disorders and what progress is happening to target neuroinflammation as a way to slow down disease progression or prevent it. Tom, did you want to start?

Dr. Thomas Tropea: Yeah. Well, the problem with that question coming up at four minutes to the hour is that we haven't really been entirely truthful with you this entire seminar because although we're talking about Alzheimer's disease and Parkinson's disease changes in the brain, there are actually a lot of other things that occur. We didn't talk at all about what we would call vascular changes or changes to the blood vessels, we haven't really talked about inflammation, and there are other proteins that can misfold and affect brain cells. So inflammation is actually one of the pathways that can be affected in actually all neurogenic disorders. And is it either a reactionary process, meaning the alpha-synuclein may sort of deposit and cause neuroinflammation, or is it that there's neuroinflammation that precipitates or increases the risk of depositing alpha-synuclein into the cells? These are things that we're learning about, but what we do know is that it is a potential target, and so there are some drugs in development to target neuroinflammation and it'd be great and be excited to see some of the data that comes from that work.

Katie Kopil: Agreed. And I think this fits into what Melissa was saying. There's maybe not just a one-size-cures-all drug that's going to be available, but that there may be a mixture. Melissa, anything you'd want to add to that response?

Dr. Melissa Armstrong: No, I think Tom covered it well. This is really a work in progress. This is an area of a lot of current research, and I think we need to see where that research takes us.

Katie Kopil: And I'll put a positive spin on it. It's not that we're untruthful, there's just a lot to learn. I think of the brain as one of the last unexplored frontiers, like the deep sea and outer space. So we're learning a lot here and all of this is thanks to research, especially research that people like Fred contribute to. And so maybe our last question is for Fred, what message would you send to people on the fence about participating in research?

Fred Goldstein: Well, this may sound strange, but participating has been one of the great joys of my life actually, to be able to say I'm doing something to potentially help maybe myself down the road, I don't know, but certainly others. And so it's really been a fantastic experience for me and I've enjoyed going to the research, to the site. The tests sometimes can be a little bit tough, but we'll work through that, but there really actually overall just an incredible amount of data. And I'm a population health person. Data is the river that flows through population health, and what we're trying to do is create more data. So if you can participate or interested, please do. It's amazing because it's actually making a difference.

Katie Kopil: Thank you, Fred. Thank you to our audience for being part of our community and for joining us today. Thank you, Melissa, Tom, Fred, for sharing your time and your expertise, and I hope everyone has a great day.

Michael J. Fox: This is Michael J. Fox. Thanks for listening to this podcast. Learn more about the Michael J. Fox Foundation's work and how you can help speed a cure at michaeljfox.org.

Welcome to a recap of our latest third Thursday webinar, hear directly from expert panelists as they discuss Parkinson's research and answer your questions about living with the disease. Join us live next time by registering for an upcoming webinar at michaeljfox.org.