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.

Speaker 1: In this episode, you'll hear a recap from our MJFF Parkinson's Webinar. Expert panelists will discuss the latest in Parkinson's research and answer audience questions about living well with the disease. We hope you find the discussion helpful.

Dr. Rachel Dolhun: Hello and welcome. I'm Dr. Rachel Dolhun. I'm a movement disorders neurologist and a lifestyle medicine physician, and I'm also the principal medical advisor at the Michael J. Fox Foundation. This is the Michael J. Fox Foundation's Parkinson's Webinar, which was formerly called the Third Thursday's Webinar. Today, we're going to be discussing Parkinson's disease and other parkinsonisms: how they overlap, how they differ, and how we diagnose and treat these conditions.

Let me introduce our panelists. First, we have Chris Humphrey, who was diagnosed with Parkinson's disease in 2015 and then received a diagnosis of progressive supranuclear palsy, or PSP, seven years later in 2022. Chris lives in Cincinnati, Ohio, with her husband, who's her main support. She's an avid hiker. She's also on the CurePSP Advocacy Advisory Committee.

Chris, thanks so much for being here.

Chris Humphrey: Thank you for having me.

Dr. Rachel Dolh...: Next we have Harriet Adam, who's a photographer and a parkinsonism advocate. She was a dedicated care partner to her husband, Brian, who first received a Parkinson's diagnosis in 2013 and then a diagnosis of multiple system atrophy, or MSA, nine years later in 2022.

Harriet, we're glad to have you.

Harriet Adam: Thank you for having me.

Dr. Rachel Dolhun: And last but not least, we have Dr. Rebecca Williamson, who's a movement disorder and cognitive specialist, as well as researcher at Penn Medicine. She's also the director of the COPE Center, which stands for Comprehensive Outpatient Parkinsonism Evaluation. She's also a graduate of the Michael J. Fox Foundation's Edmund J. Safra Fellowship in Movement Disorders, which trains movement disorder specialists, Parkinson's doctors who are also researchers, all around the world.

We're really grateful to have you here today, Rebecca.

Dr. Rebecca Williamson: Happy to be here. Thank you.

Dr. Rachel Dolhun: Okay. So, let's jump in. We always have a lot to talk about. So Rebecca, I'm going to start with you, and make sure that we're all on the same page. This word parkinsonism, what does it mean?

Dr. Rebecca Williamson: So, parkinsonism is really an umbrella term to encompass a number of clinical signs or symptoms that can have multiple causes. So parkinsonism really has three components that we see on a clinical exam, or that the patient may tell us about based on their symptoms. The first being slowness, and that can be slowness of any part of the body, like slowness of eye movements and blinking, slowness of facial expression, slowness in the arms to complete tasks, slowness in walking. And the second component is stiffness, which patient may tell us directly or we may feel in certain exam maneuvers, like moving your arms and legs around. And then lastly, there are tremors, which is probably the most obvious symptom that people can have. And typically, in parkinsonism, we're looking at a resting tremor, where the tremor is most present when the hand or leg is resting and not holding a certain position or completing an action.

Dr. Rachel Dolhun: So, parkinsonism describes a group of symptoms. It doesn't describe a specific diagnosis, right? There are many different reasons for parkinsonism. Can you tell us just a little bit about each of those big categories of conditions that can cause parkinsonism?

Dr. Rebecca Williamson: That's right. So you commonly think of, when we think of parkinsonism, as idiopathic Parkinson's disease. So that's the regular, typical Parkinson's disease that most of us know about. But there are other causes of Parkinsonism. Other causes we often see in the clinic are drug-induced parkinsonisms. So, that can be caused by certain medications, especially some psychiatric medications that interfere with the dopamine system in the brain and can look exactly like Parkinson's disease. Parkinsonism can also be caused by vascular parkinsonism, which is when there's some scarring or damage to the brain caused by long-term effects of blood pressure, cholesterol, or blood sugar dysregulation. And that can also look a lot like Parkinson's disease. And finally, what we're going to talk more about today, atypical parkinsonisms. So, some people call these Parkinson's plus syndromes, and all of them encompass parkinsonism in some way, but typically have additional symptoms of clinical signs on top of that.

Dr. Rachel Dolhun: And before we move into more of the detailed conversation on atypical parkinsonisms, like you mentioned, can you give us just a teaspoon more on both the drug-induced and the vascular? How might these look a little bit different than Parkinson's?

Dr. Rebecca Williamson: So drug-induced Parkinsonism, we're typically thinking about we call neuroleptic medications, or medications to treat psychiatric disorders that block dopamine, or sometimes medications to treat nausea. And these, often, can look very much like idiopathic Parkinson's disease. And sometimes, if a patient is on those medications and it's unclear whether they have Parkinson's disease or drug-induced parkinsonisms, there might be some additional tests or scans that your doctor could order to try to differentiate them.

But they can look very similar. Sometimes, drug-induced parkinsonism can have a few differentiating factors. It can involve both hands or both legs as opposed to one side of the body, but ultimately, it can be very difficult to tease those apart just based on the clinical exam or symptoms.

Dr. Rachel Dolhun: And just to let people know, it's often when you take these medicines for long, long periods of time. And so that's why doctors are asking you about what medications you take, how long you've been on them, to see if that could be a contributing factor and if we can adjust those to ease symptoms or see what's really happening.

And then on the vascular, I often will tell people, "This is like strokes, kind of." Maybe that's simplifying it a little bit, but tell us just a little bit more about that.

Dr. Rebecca Williamson: Yeah. So those changes from high blood pressure, cholesterol, blood sugar can cause some damage to the blood vessels in the brain, and can cause tiny strokes or scar tissue that build up in the brain. And if it affects certain areas of the brain that are also affected in Parkinson's disease, like similar areas, it can look very much like Parkinson's disease or, at least, contain those same clinical signs: the slowness, stiffness, and tremors. And we'll usually use a brain MRI to diagnose vascular parkinsonism, which can show us if there's an accumulation of those little strokes or scar tissue in the brain.

Dr. Rachel Dolhun: That's a really good tease for what we'll talk about later, which is how we diagnose these different conditions and how different tests can help us with narrowing down. One last thing before we move on, Rebecca, you mentioned idiopathic Parkinson's disease. And we should say that Parkinson's disease, as we know it, is the most common cause of parkinsonism. But there's a question about what does idiopathic actually mean?

Dr. Rebecca Williamson: So idiopathic Parkinson's disease is the regular Parkinson's disease that we all think of. And idiopathic really means we don't exactly know the cause of it. So that is what we call just general Parkinson's disease as opposed to these other types of parkinsonisms or atypical parkinsonism.

Dr. Rachel Dolhun: Thanks for that clarification. So as you mentioned, we're going to spend most of our time talking about these atypical parkinsonisms. Now, technically, the term for them is atypical neurodegenerative parkinsonisms because they're causing changes in the brain over time, similar to how Parkinson's causes changes.

But we want to step back and just say, Rebecca, why are we even talking about this altogether? Why do we talk about Parkinson's and other parkinsonisms in the same conversation?

Dr. Rebecca Williamson: I think there can be a lot of overlap between these conditions. And very often, we hear stories about patients who are diagnosed with Parkinson's disease, and then the diagnosis later evolves into one of these atypical parkinsonisms. And I think we're going to discuss that a little bit further later, but that can be because it can be very difficult to tell these conditions apart when the symptoms are early or

mild. And based on how things progress or change over time, we might be able to pin the diagnosis down a little bit more clearly. So, we often talk about them altogether because of that symptom overlap and because of how the diagnosis often evolves over time.

Dr. Rachel Dolhun: And because the community is shared, we have so many people, as we have on our call today, people who may have Parkinson's, and then eventually that diagnosis shifts to a parkinsonism. And so Harriet and Chris, I want to bring you into the conversation. And Chris, I'll start with you. I want to talk about how getting a specific diagnosis or narrowing in on that parkinsonism diagnosis, can, for some people, be a long and challenging process. And as Dr. Williamson said, and as you experienced, many people will start with a diagnosis of Parkinson's, or even just parkinsonism, and then that changes over time, or it's narrowed over time.

So Chris, I'd love to hear from you a little bit more about what that journey was like for you.

Chris Humphrey: Yeah, I was diagnosed with Parkinson's in 2015, and I was still running half-marathons at that point. I was very active, but over time, I noticed that the carbidopa-levodopa wasn't helping at all. And then one day, I fell backwards in my neurologist's office, and he did a quick observation with the eyes and determined that I had PSP. It was really scary. It was really frustrating.

Dr. Rachel Dolhun: And what exactly was the most scary and frustrating?

Chris Humphrey: It was scary because I read about PSP and I realized that there was no treatment. So, that was scary. It was frustrating because I thought that I had Parkinson's all along, and I was still very active.

Dr. Rachel Dolhun: So to have that sudden shift in what you thought you were dealing with, I can understand, would be a lot to take in. And just to mention on the treatments, which is another thing that we'll talk about, when you say there's no treatment, you mean nothing to slow the progression over time, but we'll talk about all of the treatments that you use to ease your symptoms and support life with PSP.

Chris Humphrey: That's right. Yes.

Dr. Rachel Dolhun: And then Harriet, just like Chris experienced, there was a long gap between when Brian was diagnosed with Parkinson's and then when he received a diagnosis of multiple system atrophy, or MSA. How did you navigate that period, which may have come with a lot of uncertainty, and anxiety, and unknowns?

Harriet Adam: Yes. Similar to Chris, Brian was diagnosed in 2013, and he was diagnosed with a very mild case, we were told. He was working, he was running, he was doing all the things. And then it just seemed, to me, I was his primary caregiver, that it didn't seem mild to me anymore. It seemed like we were constantly changing the medication more, and then adding and taking away, and always looking for the right cocktail. And I felt like things were progressing quickly. Didn't seem mild

to me. So, we talked to his doctor and decided that he was a candidate for DBS, which, if you have MSA, you typically are not a candidate for DBS. But we thought maybe that would provide some relief, even though tremors weren't the main issue. And after he did the DBS, it really didn't provide a lot of relief because he had MSA.

We saw another doctor and then we did a study at NIH, which confirmed, even though Brian and I felt like we knew. That was at the beginning of 2022. So I think when you go online, I don't know about... With Chris, it sounded like your situation happened while you were in the doctor's office. Brian and I had a little bit more time to try to figure out why things were moving as quickly as they were and couldn't find all the information that we wanted, but we did find MSA online and just felt like this is what it is. It's hard to confirm it because he was responding a little bit to the medication when they would change it less and less.

Dr. Rachel Dolhun: It speaks to the difficulty of diagnosing, but mainly of living with this uncertainty and lack of clarity. And I'm curious to hear a little bit more when you mentioned, "The doctor said it was mild, but we didn't think it was mild." How did you go into those conversations? And I think Chris, if you have anything to add in here. I think you had something similar where you brought up to the doctor, "Hey, I wonder what's happening here. Are we... Is something different than what we think it is?"

Harriet Adam: Right. I almost feel like there's so much uncertainty that the uncertainty becomes certainty, if that makes any sense, where we would have so many questions. But we really only saw our neurologist physically, probably, every couple of months. And if there was a problem, a lot of times it was handled by changing medications, and you have to wait a little bit to see if it provided relief. And I think because there's no case that's exactly the same with Parkinson's and everybody is so different, that Brian's changes were subtle. They were subtle to other people. They were much more apparent to me because I was his caregiver. And are you looking at a change in behavior or something that's happening with eye movements or body movements because it's just a blip, because of a change in medication, or is it the new normal? And does the new normal mean that we're moving faster and things are accelerating, or you morph into things? And I don't know if, Chris, your situation felt like that as well.

Chris Humphrey: I was really frustrated that the carbidopa-levodopa wasn't working, and I brought it up to my neurologist. That was the same visit where I'd fallen backwards. So, I think he was more focused on the falling, but I was more focused on the medication. I was up to four tablets four times a day, and a fellow wanted to give me more. And I said, "No, I didn't want anymore. I wanted to stop taking it because it wasn't working."

Dr. Rachel Dolhun: It's so helpful to hear both of your personal experiences. And Harriet, I especially like what you said about the uncertainty becoming the certainty. And we're going to talk a little bit more about all of these things you're bringing up: the uncertainty, the medication not working.

But in order to get us there, let's talk a little bit more, Rebecca, with you about these different conditions. How do they differ from Parkinson's? What helps us define them and narrow in on them?

Dr. Rebecca Williamson: Yeah, it can get very confusing very quickly with these conditions, and can be challenging because there's often a lot of overlap between them. Idiopathic Parkinson's disease really contains those three symptoms that we talked about before under parkinsonism: the slowness, stiffness, and tremor. And these other atypical parkinsonisms usually contain those symptoms with some additional symptoms on top of them. So for progressive supranuclear palsy, or PSP, it can look like a lot of different things, but classically, the things that we look for to help make this diagnosis are problems with eye movements. Specifically, difficulty moving the eyes in all directions: left, right, up and down. Or slowness of eye movements, especially those quick eye movements that you make to look from one thing to another. In PSP, we might also hear, like Chris mentioned, early balance problems. So, a lot of patients with PSP might have a lot of falls earlier on than they would if it was idiopathic Parkinson's disease.

And in the office, your doctor might do a test where they pull you backwards and see if you can recover, instead of nearly falling down to the ground. Hopefully, that doesn't happen in the office. And then in multiple system atrophy, or MSA, there's parkinsonism, or sometimes what we call cerebellar problems, which is problems with coordination. And on top of that, we see a lot of autonomic symptoms. So, those are symptoms that involve the nervous system that controls our automatic bodily functions. We might see things like constipation, blood pressure problems where the blood pressure doesn't respond properly when changing positions, urinary retention or other urinary issues, problems with sweating or temperature regulation. And then in corticobasal degeneration, again, this can have a lot of different subtypes or different presentations, but some of the classical symptoms we look at are things like dystonia, which is an overactivation of muscles in one part of the body. So, the patient might have some abnormal posturing or positioning of an arm or leg.

We also look for something called apraxia, which is abnormal communication between the brain and the body. So, some of those automatic movements that we all just do for granted, like walking or picking up something from the table, there can be a breakdown in that automatic voluntary movement. And both PSP and CBS can have some cognitive changes that come along with them as well. And then finally, dementia with Lewy bodies, again, has that parkinsonism, but typically has more cognitive symptoms and dementia that start very early on in the course of symptoms, typically within the same year that the movement or motor symptoms begin. Can often be accompanied by hallucinations, especially visual hallucinations where the patient may be seeing people or animals in the room with them, cognitive fluctuations where there can be confusion or changes in level of alertness throughout the day, and behavioral changes as well.

Dr. Rachel Dolhun: That was a really helpful overview, but probably a lot for a lot of people to take in. And I think one of the things I hear, and that comes up a lot, is how do I know what's Parkinson's? Especially when I'm early with Parkinson's and I'm not familiar with all the ways it might be showing up for me. How do I know what's

what? How, as a doctor, are you keeping tabs on these things and looking for what we call red flags? Things that would make us think, "Maybe this isn't Parkinson's disease. Maybe this is something else."

Dr. Rebecca Williamson: It can be really challenging. I think one of the most frustrating things as a medical provider and the patient is that a lot of times, it's seeing how things progress over time, that we really understand what the diagnosis is. So in that first visit, it may not be clear if this is Parkinson's disease or something else, and it's seeing how things change or how symptoms develop over time that we get a little bit more clarity. Of course, everyone wants to have that definitive diagnosis right away, but sometimes that's not possible. There are some things on the exam that we look for that might give us those red flags, and hone in on something we want to monitor over time or something we might want to do some additional testing to figure out. So, your doctor might look at your eye movements, might look at your balance. And then there's things that you tell us as a patient that can also trigger some red flags when we're asking you about your symptoms, and how they've developed, and what you've noticed.

So if you're having a lot of falls earlier on in the course of your symptoms, if you're having a lot of those autonomic symptoms like the constipation, urinary problems, blood pressure issues. So in my initial visit with my patients, I'm going through a checklist and asking them about all of these different kinds of symptoms, some of which patient may not realize could be associated with their parkinsonism or not. So we're going through each of those, and some red flags may be going off in my mind as we go through about things I want to explore further.

Dr. Rachel Dolhun: And things you have to keep an eye on. As you said, that's frustrating, mostly for people and families, but it's also frustrating for us as physicians that we don't have better diagnostic tools to tell us right now what it is. It's largely, we have to watch and see how things change and what symptoms come up. Two questions I can imagine a lot of people have on this. We keep saying earlier on. So a lot of these things can happen to some degree, remembering that everything, every symptom doesn't happen in everybody. And if it does, it happens to a different extent or in a different way. But when we say we're worried about these things happening earlier on, what is the general timeframe we're thinking about?

Dr. Rebecca Williamson: I would say in the first year or two of having parkinsonism symptoms, if there are things that are not quite expected, especially those early falls, or really significant balance problems, or blood pressure issues in those first, maybe 1, 2, or 3 years, then those red flags are going off in my mind.

Dr. Rachel Dolhun: And same question around how quickly the disease progresses because, of course, progression is different in everyone. And so, how do we gauge whether the progression seems a little bit faster than we'd otherwise expect?

Dr. Rebecca Williamson: This can be such a challenging thing to figure out because in idiopathic Parkinson's disease, the progression is so variable from one person to another. So, it's hard to say, "This person's progressing more quickly than they should." But I think if you have someone who's progressing quickly, say, over significant

differences, needing assistive devices over maybe the first 1, 2, 3, 4 years, combined with a lack of response to the medication, then that's when we are thinking more about these atypical parkinsonisms.

Dr. Rachel Dolhun: And Chris and Harriet, I want to bring you back in. So Chris, when you hear all of this, are there things you wish other people knew about PSP, or you wish you knew when you were before your diagnosis?

Chris Humphrey: I guess, I wish everyone knew what it was. It's so rare that people don't know. When I fall in public, I'll often say I have Parkinson's because people know that. So, I wish that people just knew what it was.

Dr. Rachel Dolhun: And you're doing some of that work yourself with your advocacy work and just by being here today.

Chris Humphrey: And I usually now say that it's PSP, but for a long time I would just say it was Parkinson's. Even after I had my diagnosis, because it was easier, people understood it.

Dr. Rachel Dolhun: And Harriet, for you, how does this resonate for you? What, maybe, changed when you realized you had the diagnosis of multiple system atrophy, especially as a care partner?

Harriet Adam: I believe that it certainly confirmed that I wasn't crazy in my own head with thinking that something was different. I feel like we lived a full life, and Brian was a very positive person, which, I don't know that it changed how we lived. But certainly with Parkinson's, you're always told that you can continue doing what you want to do and that you could go on for a really long time. And I think with MSA, you have the possibility that things are escalating faster, so you might be more limited in a shorter period of time. So I think for us, I think knowledge is power. And so it helped us be aware of these things, to never take anything for granted. And maybe today's going to be the best that it's going to be. You don't know what tomorrow is, but today might be the best.

And there wasn't any aha moment. We were sad to hear it because there could be much faster progression. Whereas if it had been Parkinson's, we'd be like, "Okay. Maybe we..." But we were told that the treatment is the same, so I don't know the fact that if we knew... If we had known earlier, I don't know that would we have still tried carbidopa-levodopa? Yes. I mean, at least the route that we were going. And if they had said, "You could still do DBS because it might..." Brian would've jumped on that. He would've loved to have done a trial. So, he would've done anything. We were limited because he had the DBS, so we couldn't. But I don't know that there's any other treatment that we could have done. So I don't know if knowing it early, other than having the knowledge of it, it might've been more frightening for us.

We always said that Brian had Parkinson's, but then even now, I say it was atypical Parkinson's MSA because I still feel like people can understand that, but it's nice for them to know that it was not the typical. And I've had several people

that have said, "Wow, I'm thinking that my father, my uncle, my husband, they experienced some of those things. I'm going to look into that."

Dr. Rachel Dolhun: I think as you said, for so many people, knowledge is power. And for a lot of people, it's having that diagnosis. And even though, of course, you don't want that diagnosis, and you mentioned the sadness that came with it, you know now what you're dealing with.

On that note, let's go. We're getting a lot of questions about what tools there are and how we can make a diagnosis. And so Rebecca, I'll invite you back in to talk a little bit about what are the diagnostic tools that are available. These are growing. We have a spinal fluid test that was just validated in the last couple of years that can help a little bit with this, but tell us what the tools are that can help and how they can help.

Dr. Rebecca Williamson: Yeah. So, it's exciting we're getting a lot more tools to help with this diagnosis, but there's still a lot of work to do. So these diagnoses, really, are still made based on the clinical exam. So what your doctor is doing in the office to examine you, and what you're telling your doctor about your symptoms, and how they've developed. The specific tools that we have to support a diagnosis, so if there's uncertainty based on the clinical exam and history, then we might turn to these other specific tests. So, a DaTscan is a specialized brain scan that we can do to look at the part of the brain affected in Parkinson's disease and parkinsonisms. That's most helpful in idiopathic Parkinson's disease. It can be abnormal in these atypical parkinsonisms as well, but sometimes it can be normal, which can make things a little bit more confusing.

A brain MRI, as we discussed, can also be helpful. There are a few signs on there that can help support a diagnosis of some of these atypical parkinsonisms. And then there's, as Rachel mentioned, these newer, we call biomarker tests, looking for specific proteins that are involved in these conditions. So, two newer tests that look for a protein called synuclein, which is one of the protein that causes Parkinson's disease, MSA, and Lewy body dementia. There's a skin test and a spinal fluid test that can help us to identify that protein and support those diagnoses. And I think those are the main things that we look for at this point. Unfortunately, we don't have good tests to detect some of the other proteins that can underlie PSP and CBS, like tau and TDP-43, but lots of research is going on to look for ways to identify those biomarkers.

Dr. Rachel Dolhun: Thanks for that really helpful overview. I think one of the things to remember is that we have some tools, we are working on many more. As you hear, we need better tools that can diagnose more accurately and earlier, but the tools themselves don't make a diagnosis. They're in conjunction with your doctor's expertise, your exam, your medical history, the things that you're seeing change over time. So, those tools are one piece that can help us, but they're not the be-all, end-all.

And Rebecca, I want to stay with you for one second just to go onto DaTscan a little bit deeper, because we get a lot of questions about this often for both

Parkinson and parkinsonism. Can you tell us a little bit more about that test? And again, how it can help us with these diagnoses?

Dr. Rebecca Williamson: Sure. I would say, not everyone needs a DaTscan to make a diagnosis. So if someone clearly has Parkinson's disease in the office, it may not be necessary, but if there's a lack of clarity in the diagnosis, then it can certainly be helpful. And the test itself is a nuclear medicine scan. So, there's something injected into the body that binds to a specific part of the brain involved in the dopamine transport system that is affected in many of these conditions. And when we look at the scan result, we're looking for a degeneration in this area of the brain or, in other words, like a damage or loss of cells in that part of the brain that can indicate some abnormalities happening there. Like I said, it's, I think, most helpful in Parkinson's disease, but I will often order it when I'm concerned about these other conditions. And if it's positive or abnormal, I think it can help support those diagnoses as well.

Dr. Rachel Dolhun: And one thing to underscore there, as you said, it shows us that there's an abnormality in the dopamine. And we know with both Parkinson's and these atypical parkinsonisms, there's an abnormality in the dopamine. So, it doesn't help us separate those. It can help us separate some of those conditions we talked about earlier. So, drug-induced or vascular. Even essential tremor, which a lot of people wonder about that versus Parkinson's. It can show us and separate those conditions that don't impact the dopamine, but they can't separate the Parkinson's from the atypical parkinsonisms.

We have so much to still talk about we have to move on. But very quickly, Harriet and Chris, I'd be interested to hear from you about the tests. Did you have any of these done? Did they help you?

Chris Humphrey: They had a brain MRI. And when I looked at the results, I thought I said I didn't have PSP, but my doctor thought differently.

Dr. Rachel Dolhun: And that's an important point, that the MRI can't show us. It shows us the structure of the brain, but it can't show us specifically any of these one condition. So, we're looking for things there, like, the vascular. Are there little strokes? Or are there other changes that could be contributing that we would do something different about? So, that's an important point. Thank you for raising that.

Harriet Adam: Brian had several of those tests at NIH when he went in 2022 and was in a study. He stayed for five days and was under the care of Dr. Goldstein. They did almost all of these tests that you're talking about. And they also did an ultrasound of his heart, where he concluded, after looking at all of these tests and he had took Brian off of his medication, that is when he confirmed that it was MSA because it was a compilation. He did the tilt test and all of those. He was there for five days. So, we did leave with a new prescription or we just left... We have the information.

Dr. Rachel Dolhun: It helps solidify the diagnosis. And what you're talking about too, is what we call broadly autonomic testing. So, we're looking at your heart and your blood pressure. And again, we see that that's more impacted in something with multiple

system atrophy. So sometimes we'll test that system to help us see, "Is that significantly impacted?" and that would lead us, maybe, more in that direction of diagnosis. We've been talking a lot about the challenges in diagnosing Parkinson's and other parkinsonisms. And of course, as we keep saying, the more information we have about what these diseases look like, the more certainty we can give, the better we can diagnose them. So the Parkinson's Precision Medicine Initiative is recruiting volunteers, and that includes people from all backgrounds, both with and without Parkinson's, who can help move research forward.

I want to move into treatment. And Rebecca, I'll bring you back in here. So, we've been talking a lot about diagnosis. But once we have a diagnosis, even before we have a diagnosis, what are the tools we have to ease the symptoms of parkinsonisms?

Dr. Rebecca Williamson: So once we diagnose an atypical parkinsonism, we're really emphasizing a lot of the therapies in our multidisciplinary team in helping to support the patient with the disease. So we'll bring in our physical and occupational therapists, speech therapists, palliative care specialists, social workers, sometimes nutritionists. All these people can be really helpful in providing support, and equipment, and all of that stuff that helps us to support the patient. There are medications that can help with symptoms, but as we've mentioned briefly before, there's no medications right now that can slow down or cure the disease. I think what I see in my patients is the patients that are most active, moving their body, and mentally active, really do the best. So, that's what I'm emphasizing in my clinic. And then as I meet with my patients, I'm going through different symptoms that they have concerns about, asking them about things that I know can be impacted in their disease, and we're addressing symptoms with medications as they come up.

So that could be medications for constipation, urinary symptoms, stiffness, or pain. We are going through each of those in each visit, and seeing what we can do to help with those symptoms pharmacologically.

Dr. Rachel Dolhun: Chris, I want to go to you next because I want to ask a little bit more. With the falls, for example, what were the best supports that were helpful to you for managing a symptom like that?

Chris Humphrey: The best support is my husband. He's my caregiver, and he supports me every day. He's always with me, drives me everywhere I need to go. So, that's a great support. Other than that, I walk a lot. I hike. I've done physical therapy a couple of times, and I practice that at home. I did speech therapy also.

Dr. Rachel Dolhun: And I want to talk about the care partner, the invisible member of the care team, of the Parkinson's or parkinsonism's team. And I'm going to go to you for that, Harriet. But before that, Chris, while staying with you, Rebecca mentioned how important exercise is. You said you're an active walker, a hiker. It's really important to keep that movement in, that exercise in, to eat a healthy diet, to manage our stress. But as we have symptoms, as disease changes, we have to adapt. So, what are the ways that you've adapted to be able to keep those important pieces of your treatment going?

Chris Humphrey: I used to do half-marathons I mentioned before. In fact, I did more half-marathons after my diagnosis than before. But May of 2025 was my last one. I didn't finish it, and I've slowed considerably. I still walk a lot. In fact, I did two and a half miles this morning, but I'm just slower.

Dr. Rachel Dolhun: So, it's somewhat about finding those exercises you can do, acknowledging that you might have to do them in a different way. For a lot of people with falls, it's about adapting to safe exercises. We have to think about how you can be safe. So seated exercises, or standing behind a chair or something you're holding onto. But there are a lot of ways that you can adapt to keep exercise and to keep the things that you love. And your doctor, your physical therapy team, everyone's there to help you do that.

But Harriet, to talk about the care partner, and back to Brian and your optimistic attitude, how do you get support for yourself as a care partner? And which of these tools and treatments were your best supports for Brian?

Harriet Adam: I would say that we started palliative care. We were in palliative care for almost two years, and I can't say enough about that. It was an extra resource for us that, I think, helped us live the way that we wanted to live, and they were part of our team. Brian used to call it his foxhole, people in his foxhole that were helping him. Our neurologist, our physical therapist. As Rebecca said, that we had an occupational therapist. They all became part of this bigger picture of socialization. I think for me, it was humor, and we had to laugh at ourselves because Brian fell. Brian fell all the time, and oftentimes I fell with him. And we laughed a lot, but we also socialized. And being around people, I think, prolonged his life, and it extended my time with him that was really positive, because it can be very isolating. It can be a very isolating disease. And it doesn't just impact the patient, it impacts the whole family.

Dr. Rachel Dolhun: It's so beautiful what you share, but for so many, the connection is a real challenge. How did you keep that up when things changed, when there were falls or changes in voice?

Harriet Adam: We have a great family and friends. But if there were places we couldn't go, for example, because maybe there were steps or we weren't invited, I would invite people here. I would create the dinner here or the event here. I would reach out to a buddy if, maybe he wanted some company. But people were good about coming and spending time with him, but he also didn't hide behind the disease, which it's easy for us to do because his voice changed. That might not happen to everyone, but he did still communicate, and his mind was fine. And I think being with other people, and that would've even been the physical therapist and the occupational therapist and the speech therapist, because it was a connection. It was being with people.

Dr. Rachel Dolhun: Yeah, that connection is so important. So, thank you so much for putting a spotlight on that and sharing how you kept it part of your and Brian's life. Before we move to our last slide, Rebecca, could you just spend a moment telling us about palliative care? Because Harriet, you said that was so helpful for you. But for a lot of people, there are many misconceptions around palliative care.

Dr. Rebecca Williamson: Yes, it's a great question. I think palliative care, people often associate with hospice or end-of-life care, and that is one component of it but it's certainly not the only thing that palliative care encompasses. So the way I think of palliative care is, really, care that is focused and emphasizing quality of life. So, that could mean treating certain symptoms like pain, constipation, and especially thinking about maybe non-medication ways to treat those symptoms. It could also mean planning for the future. So looking ahead, thinking about paperwork that's important for everyone to have that can help with planning for end-of-life, whether that's 20 years or two years down the line. Or just anything else that emphasizes the quality of life and figuring out how to make sure you are living your best life, and doing what you want to do in the face of this disease. I don't think there's ever a time that's too early to get involved in palliative care.

Dr. Rachel Dolhun: Yeah, that's a great point. We often talk about it as extra support that's available from the time of diagnosis onward. And Harriet, as I think you alluded to, it often is good at helping support care partners and family members. And it brings in other components that your doctor may not talk about as much: the emotional side, the planning-ahead side. As you said, spiritual, if that's important to you. So, it really tries to support the whole person and the whole full family unit living with Parkinson's or parkinsonism.

Harriet Adam: Yeah, we had a social worker which was a wonderful... It gave Brian the opportunity if there were... He worried about me because I took care of him, and I worried about him because... And there was a safe place for him to... And sometimes they just talked football, but it was a good person to have to develop a relationship with.

Dr. Rachel Dolhun: And more connection, right? So last but not least, Rebecca, we'll go back to you to talk a little bit about research. We've mentioned how research into Parkinson's helps parkinsonisms and vice versa. Give us an overview of why that is, and what the most active and promising areas are.

Dr. Rebecca Williamson: I think as we've mentioned earlier, there's been a lot of developments recently in terms of diagnosis in terms of finding these tests that can look for biomarkers, which is really so important to help differentiate these diseases and help us to make an earlier diagnosis. But as we said, the only tests that we have right now are for these proteins called synuclein. And there are other proteins that can underlie these conditions that can build up in the brain that we don't have tests for at all, like the tau, TDP-43 proteins. So one of the big challenges in research right now is to find biomarkers for those proteins, and to be able to implement these tests earlier in the disease course to make an earlier diagnosis. So even when we have treatments, hopefully, sooner rather than later in the future, they may not be effective if we're not giving them early enough before too much damage had happened within the brain. So, we want to make sure that we can make an early diagnosis for patients and an accurate diagnosis.

So, I think there's a lot of different types of research moving forward. There's imaging studies that are trying to identify these biomarkers. There's other types of biomarker research, looking for these proteins in spinal fluid, and skin, and other areas of the body. And then, of course, there's research looking at new

medications for different symptoms to slow down the disease course, medications to try to remove those proteins from the brain to try to slow down these diseases, similar to what's been happening in the Alzheimer's field, where we've seen some success in that arena. So, lots of exciting research happening. Challenging because these conditions are rare, and there can be so much overlap in terms of what's going on in the brain and clinical symptoms, but I think a lot of hope.

Dr. Rachel Dolhun: And staying on that, we're getting a lot of questions around, we keep talking about early diagnosis, and of course a lot of people wonder about early symptoms of these conditions. And in Parkinson's, we often talk about sleep changes, like, acting out your dreams, your smell loss. Are those similar for the parkinsonisms?

Dr. Rebecca Williamson: We typically think of these, we call prodromal symptoms. These symptoms that can happen years before the other symptoms occur, like, sleep changes, especially REM sleep behavior disorder where people are acting out dreams, or constipation, or hyposmia, which is a loss of the sense of smell. Those prodromal symptoms we classically think of in terms of the synuclein diseases. So the Parkinson's disease, MSA, and Lewy body dementia where the predominant protein in the brain is synuclein, often have those prodromal symptoms. So the other atypical parkinsonisms can sometimes occur with those symptoms, but we're classically thinking of it in terms of the synuclein disorders.

Dr. Rachel Dolhun: And what about genetics? Are there genetic components to these parkinsonisms? We see some genetic changes that increase risk for Parkinson's. Is it the same with parkinsonism?

Dr. Rebecca Williamson: For the most part, these disorders are majority not genetically inherited. That's also true for idiopathic Parkinson's disease, but we are learning more and more about genetics. And as you mentioned, there are some genetic variants that increase risk for Parkinson's disease. There are some genetic variants that can increase risk for the tau disorders, PSP, and CBS, but for the most part, they're not genetically linked.

Dr. Rachel Dolhun: And I'm going to continue with the rapid fire of questions from our audience. So one person says, "My wife has Parkinson's disease, but doctors keep pointing us to parkinsonism. And at the end of the day, what adjustments do we need to make to treatment?"

Dr. Rebecca Williamson: So as we've been hearing from Chris and Harriet, a lot of times, the treatment doesn't necessarily change in terms of medications available. We'll often try the same medications, like, the carbidopa-levodopa for atypical parkinsonisms as we do for Parkinson's disease. So sometimes, it can be more information to have this diagnosis, but like we've mentioned, it doesn't necessarily change the management, though it might change your outlook in terms of the prognosis because we know that these diseases can progress a little bit more quickly.

Dr. Rachel Dolhun: And that gets to another question we were asked. That's, "If the treatment doesn't change, why is it important to pursue a specific diagnosis?" And I think it's what you just said, Harriet. You said earlier, "Knowledge is power. We know what to

do with this. It also helps with prognosis." And even as we just talked about research, getting into research trials, that's of interest to you.

One other question, maybe you could put a finer point on this idea that the parkinsonisms don't respond as well to levodopa. So Chris, that's something that you said. How do we know something isn't really responding to levodopa? And then also, there are many different variations of levodopa now. There are pills, there are inhaled forms, there are infusions. Does the formulation make a difference?

Dr. Rebecca Williamson: So I think when patient doesn't respond as well, we're meaning that they don't notice an improvement of symptoms after they take the carbidopa-levodopa. And I think the formulation of the carbidopa-levodopa doesn't really change that assessment, except that sometimes different formulations can be better tolerated for one person for whatever reason. So when we're thinking about response to the carbidopa-levodopa, we want to make sure that the person is able to get a high enough dose of it in their body without having side effects before we determine that there's been a response or not. A lot of people do have side effects to this medication and just can't tolerate taking a high enough dose that would help their symptoms. So, that can sometimes be a confusing point. But if they're at a decently high dose, like Chris was at quite a high dose without a big change in her symptoms, then that would tell us there's a lack of response.

Dr. Rachel Dolhun: And back to you, Chris and Harriet, we have questions from people about what should they be asking as a person living with Parkinson's or parkinsonism as a care partner? If I'm uncertain, what kinds of questions can be helpful at guiding these conversations?

Harriet Adam: I feel like in some ways, it's all of these symptoms that you get that come up. Brian had the orthostatic hypotension, so he had blood pressure issues. So once again, is it something that happened just this week, or is it happening all the time? And if it happens all of the time, if we're taking the [inaudible 00:51:16], midodrine, or whatever medication you take for that, then the different changes that we make in the medications, typically what I found was that we would try these things, but you have to wait a month or wait another month. So in the meantime, you keep a notebook. I kept a notebook. I have several binders. But I do think that it helped to be prepared when I talked to the doctor to make the notes, to maybe write down what Brian's blood pressure was if that was to happen. And when he took his medication, how often were these things happening?

Because I think it's hard for the doctor when they only see them once in a period of a couple of months and they're just listening to you. And as a care partner, I would say also, listen to your gut and your heart. When the doctor would ask Brian how he was doing, Brian would always say, "I'm doing great." And I would say, "Well, you fell on Tuesday, you fell on Friday. On Sunday, your blood pressure was..." He didn't look at things like that. And so a notebook, I think, was a good thing to have.

Dr. Rachel Dolhun: The notebook and another perspective which you gave, Chris, which I'm sure your husband gives, that input from family members and care partners is so valuable to us as doctors.

Chris Humphrey: Yeah. My husband goes to all of my appointments with me, and he's very active. So, he knows there's things that I don't notice. That's great. Then he talks to the doctor about it.

Dr. Rachel Dolhun: We could talk all day. I wish we had more time. There's so much to talk about with both of your experiences, Rebecca, with your expertise, but I'm afraid we are at the end of our hour. So I want to thank everybody for being here today, for being part of our community. Thank you to our panelists for sharing your experience, your time, and your expertise.

For more, you can, of course, visit our website, but you can also follow me on Instagram where my handle is @racheldolhunmd. Thank you so much and have a great day.

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