Dr. Rachel Dolhun: Thank you everyone for joining us. I'm Dr. Rachel Dolhun, vice president of Medical Communications at The Michael J. Fox Foundation, and I'm your moderator today. Our panelists will be discussing thinking and memory changes that can happen with Parkinson's disease, strategies to lower the risk of these symptoms or ease their effects, and research toward new treatments.

You're able to submit questions throughout the hour. Use the Q&A box near the middle of your screen. You can type your questions there, and we'll do our best to get to as many as we can.

We're also providing the slides from today's webinar for download. You should see a box called Resource List on your screen. Click on the link there and the document will open in a new browser window. You can save or print from there. I should mention that we had a little hiccup with our console as we were getting started, so if you don't see anything in your resource list, you can try refreshing or logging back in or even just checking back after the webinar and the resources will be there. Let's get into it and meet our panelists.

First, we have Ava from Tucson, Arizona. In 2017 Eva lost her husband of 25 years, Richard, who had Parkinson's and Lewy body dementia. Thanks for joining us, Ava.

Ava: Thank you. This is an important topic. Happy to be here.

Rachel: Totally agree. Dr. Katie Amodeo is assistant professor of Neurology and Psychiatry at the University of Rochester Medical Center and she's also an Edmond J. Safra fellow who graduated this year. We're really glad you're with us, Katie.

Dr. Katie Amodeo: Thank you. Yeah, I'm very happy to be here.

Rachel: Dr. Stephen Gomperts is assistant professor of Neurology at Massachusetts General Hospital. We're really happy to have you, Stephen.

Dr. Stephen Gomperts: Thank you. It's a pleasure to be here.

Rachel: Great. We've got a lot to cover and a lot of questions that have already been submitted and are already being submitted. Let's jump right into it.

The things that we're going to cover today on the next slide are what is cognition? What's the definition of cognition? We often talk about memory, but what else is involved in cognition? We'll think about how that changes with normal aging and also with memory. We'll talk about the experience of cognitive changes, how doctors evaluate and treat this symptom, strategies to potentially even prevent or manage cognitive changes, and what research is working to address this issue. All right, so Katie, can you get us started in talking basically about what cognition is? As I mentioned, people often think about memory when they talk about cognition, but we often don't think about the thinking part of cognition and all these other things that you see on this kind of busy slide here. Tell us sort of the basic definition of cognition and what it really involves.

Katie: Yeah. When we think about cognition and the way I always try to introduce it to my patients or if I'm giving a talk is that it really is all forms of thinking, and not necessarily just meaning memory. When we think about cognition, I think we equate that with memory. But when we talk about cognition, it's all the ways in which we process and respond and think about things in our environment and our everyday activities, the way that we're able to function from a cognitive perspective.

There are several domains, so there's more than just memory. There is executive function, which is really our ability to multitask, plan, problem solve, organize. There's attention which is the way we're able to focus. When somebody is coming in for evaluation for memory impairment, sometimes it's an attention issue because if you're not paying attention, you're not going to remember. Then there's visual spatial is another domain. The way that we can put things together around us and orient ourselves with our surroundings. Language is another important domain. Then the other one's on here as well. Social perception. When we talk about cognition, we're talking about all of these domains and when we talk about impairment, it can be in any one of these domains.

Rachel: That's a really helpful beginning. Stephen, I'd like you to not get into too much detail right now, but maybe just give us a little glimpse into what we're going to talk about a little bit later, but how are these affected in Parkinson's? What are the main ones that we often see affected in Parkinson's?

Stephen: Well, it turns out in Parkinson’s disease, many patients will develop subtle changes in the thinking. Sometimes they're not even aware of those changes but they can be identified on careful structure testing. The domains that are often involved in

Parkinson's disease are the executive function domain that we just heard about. Difficulty with multitasking and perhaps judgment, planning. It can be harder to perform more complex tasks like manipulate a computer, keep track of a complex medication regimen. We can also develop problems with visual spatial skills. We might start to find ourselves more dependent on GPS behind the wheel, getting lost more often than before. We can fill up some problems with memory as well, particularly short term memory. Although under careful scrutiny, it's different typically from the pattern of short term memory loss that arises in the other very common disease, Alzheimer's disease.

Rachel: That's really helpful. Ava, I'd to bring you in now to give us a little bit more context around what the real life experience around this is. We mentioned in the introduction that your husband Richard lived with Parkinson's and Lewy body dementia for several years and he had some of these cognitive changes and you experienced those as well with him. Can you tell us a little bit more about what those look like?

Ava: Sure. When he was diagnosed in 2010, I had no idea that any cognitive issues would be coming to play. So they all came as kind of a nasty surprise. Of course things evolved over time. Regarding executive function, for example, putting the dishes anywhere, not necessarily in the kitchen, the dirty ones, and cleaning them in a very random way. I would find dishes put dirty in the wrong area or an area that wouldn't even be in the kitchen. That was a bit of a surprise.

Getting dressed is difficult. For example, him trying to put his shirt on his legs, which just won't work no matter how much you try. He had a wonderful sense of direction, but got lost on familiar routes and also started to have trouble transferring money and doing simple things. Definitely having trouble finding words or completing sentences and keeping up with conversations. He could follow them but he couldn't keep up. Certainly forgetting. He forgot my name and his, not every day, but sometimes. Certainly everything on this page. We did not experience the social perception issue, but I do know that is very common.

Rachel: Again, we're going to get into this a little bit more later, but when you started to look at these things, how did you piece them together? Because oftentimes people say, "What's normal aging? I forget my keys. Is that normal, or is that Parkinson's, or is that dementia?" How did you start to piece together that all of these things were not a normal part of aging?

Ava: Well, first of all, he passed away when he was 65, so he was pretty young. I mean I have normal senses of things like forgetting where my car keys are. It takes me longer to remember somebody's name. That was absolutely not what was happening here. You don't forget how to get home from the golf course you've been to 200 times. I mean that's just not normal. Or the executive functioning things. As an example, he used to take care of all of our finances and he was transferring money from one of our bank accounts to another, and he couldn't do it any more and said, "I used to be good at math. I don't understand why this is happening." That was just not a normal thing.

But it can be confusing, especially when signs are very small. But in my case, they were absolutely not normal. I just had no idea it was part of Parkinson's.

Rachel: Exactly. That's part of why we're having the conversation because people say that they weren't aware of this or they weren't sure how this happens or what it looks like. So that's part of this conversation for sure. Let's continue and expand on what we talked on a little bit. Stephen, on the next slide, we see that cognitive changes can happen in Parkinson's and they can happen to different degrees. We see a lot of these definitions that people make here thrown around as mild cognitive impairment or dementia and people often tend to say, "I don't want the medical definition of that. I want to know what it actually means in my life." We started the conversation with what cognition is and that this can change somewhat with aging, but take us through how it can change with aging, but then how it can change kind of across this spectrum we see on this slide and what those mean?

Stephen: Well, I'd be happy to. So that's right. Some cognitive changes really are expected with aging. We can become slower, and this can be detectable in our day to day function. But really our general visual spacial skills, our executive function, our short-term memory really remains quite good and we have a lot of data on what normal aging it looks like to compare against. We also have some cognitive changing arising in people with Parkinson's disease, as I've mentioned before, that can be detected with careful testing. But when it starts to get in the way, when people are noticing this, that's when we start to think about pathologic agent, and mild cognitive impairment is the first broad category that we think about. In this category of MCI, mild cognitive impairment, this is associated with a gradual decline in thinking abilities that people will notice, their loved ones might notice. That's also observed by the clinician, but the cognitive deficits are not severe enough to interfere significantly with functional independence like working or home activities, hobbies, chores and community functions.

This is mild cognitive impairment, and it's the loss of that that a functional independence that leads to a diagnosis of dementia and Parkinson's disease. The transition to a loss of the functional independence. Patients will now require assistance with their daily activities. It's important to point out that this is not due to their motor impairments, but due to their thinking difficulties. Using very crude criteria, we can differentiate those into three broad buckets of mild, moderate and severe dementia. In mild dementia, people can no longer work. They're going to have difficulty with problem solving and complex tasks. Judgment may no longer be sound, and it's going to be hard to, if not impossible, to safely balance a checkbook, manage the finances or a medication regimen. Difficulty organizing and expressing thoughts are often marked, and people might have difficulty following and participating in conversations, keeping track of where the conversation is going.

Even using something like a television remote control might become inaccessible. When these problems arise, memory for recent events can be increasingly impaired. People might forget the content of recent conversations, misplaced items around the home. With the transition to moderate dementia, all these problems can significantly worsen, markedly so. Patients will start to require help with some basic activities of daily living as well, such as dressing, using the bathroom and other self-care. This was really a marked worsening of function. The term severe dementia is really used for the late stage of the disease. At this point, people are quite impaired and will often lose the ability to communicate coherently. They'll often not make sense. People will now require total assistance with personal care including dressing, eating and toileting. People may become bed bound in this setting and may start to lose the ability even to swallow, putting them at risk for complications like pneumonia.

Rachel: Okay. That summary was really detailed and helpful. A couple questions coming through on this. Katie, can you tell us how people essentially go along this spectrum? Now, does having mild cognitive impairment mean that you will get mild dementia and then you will go along all the way to severe dementia, or how does this kind of happen in people?

Katie: Yeah. No, that's a great, great question. When we see individuals who are having deficits in one of these domains that we talked about, just like Stephen said, we kind of go through and ask more questions about, is there impact and function? In the early stages we might hear, "Oh, they're having trouble with one or two domains, but there's no impact in function." So we would call that mild cognitive impairment. Then that would then prompt the discussion of what does that mean? What I say, it can be an early stage or a part of that spectrum to progress to dementia. But not everybody will. So some individuals may stay along this mild cognitive impairment, and we follow them over time and there's really little change. Some individuals will convert over time. Of course that time can be very different for everybody.

In the context of Parkinson's, it can be over many years, so some people may not convert for 20 years. So it can be very variable and the timing of conversion from mild cognitive impairment to dementia. Then of course, we always are looking for, is the cognitive impairment due to something potentially reversible such as a medication change, such as maybe untreated depression? If that's the case and we can address those causes, then we can see actually individuals get better. That cognitive impairment wasn't due to part of the spectrum. I guess that's how I think about it.

Rachel: Fair to say kind of then in summary that if somebody has mild cognitive impairment, they could potentially progress to dementia but they could also stay the same or they could even get better depending on the person and depending on what else is going on.

Ava: Exactly.

Rachel: Okay, great. Then Steve, anything else to add on? A lot of people often ask, "When do cognitive changes happen in Parkinson's? When should I potentially be worried about these are looking for these or testing for them?"

Stephen: Everyone's different, but the broad observations are that the longer a person has Parkinson's disease, the greater the risk of running into trouble with thinking in regular idiopathic Parkinson disease. Additional risk factors that we have no control over whatsoever for development, trouble thinking included, getting the illness at a later age or having atypical features that doctors would pick up on, like a lot of early postural balance problems, postural instability, not a lot of tremor. These would be sort of risk factor features. But I think that Katie's point about really emphasizing what the reversible contributions are to trouble thinking is going to be really important because in many people there are things we can do to help. The key is to look for doctors to team up with patients and look very carefully for reversible contributions.

Rachel: That's important. We'll get into that a little bit later more in the evaluation and the treatment. But again, Ava, just to bring you in, just to stress the importance of having a conversation with your loved one and your doctors. How do you talk to people about that now and caution them to have a conversation?

Ava: Well, a lot of times people feel embarrassed or shy about talking about cognitive issues, and that's not going to help you. I mean I would recommend very honest and respectful conversations with your person who's in this situation. I mean, they're not a child. They're a grown up with issues. So don't use child voices or talked about them in the third person. Be respectful of them, and be open with yourself, the person, your friends, your family, and your doctors, and be proactive. Doctors don't always, even in 2019, understand these issues very well. You do need to take the lead, I would say. In Richard's case, it's unusual for most people, his cognitive decline was extremely fast. We went through all of these phases in a year and a half, which was shocking. We just had to deal with in an open end, as I said, respectful way.

Rachel: Really great advice. Let's move into talking a little bit more specifically about Lewy body dementia, which is what Richard lived with, and some of the other kind of causes of dementia. One of the misconceptions, Katie, is that all dementia is Alzheimer's, right? Dementia is a disease that only has one cause. But actually that's not true. There are other potential diseases and conditions that can cause dementia. We were talking earlier about some of the reversible ones, but on this slide, we see listed the common terms that people may come across that can be really confusing. You hear Parkinson's disease, dementia and dementia with Lewy bodies and Lewy body dementia. It's hard to know what's what, but can you just briefly take us through this slide and what this means?

Katie: Yeah, yeah. Just like Rachel said, when we are making a diagnosis of dementia, which is an umbrella term that just means global changes in cognitive function. So across those domains we talked about that's impacting function with objective evidence of impairment on our testing. So that's an umbrella term. Often people, when they hear dementia, they think Alzheimer's, and that's understandable and that Alzheimer's is the most common cause of dementia. But it's important to know it's just one of the causes. But it's most common accounting for up to 80percent of the dementias. But then the second most common cause of neurodegenerative dementia are the Lewy body dementias, which is another umbrella term. Lewy body dementia is an umbrella term to include to match with Lewy bodies and Parkinson's disease with dementia. So sometimes in some individuals who have been diagnosed with Parkinson's, and then they start to see the cognitive changes, then they start to ask, so is this dementia with Lewy bodies? This is where I'll talk a little bit about that ... to distinguish Parkinson's with dementia and dementia with Lewy bodies, we do distinguish them.

Katie: Parkinson's disease with dementia and dementia with Lewy body. We do distinguish them, but some in the field consider them part of the spectrum. But the way to think about them are they're both neurodegenerative disorders that involve abnormal alpha-synuclein protein, this abnormal protein that forms Lewy body. So they both have that in common in their pathology. They both can have premotor or prodromal features like REM behavior disorder, anosmia, constipation. They both can have the Parkinsonian motor features, so the slowness of movement or bradykinesia, the rest tremor, the rigidity. And then as we're talking about today, they both can have cognitive and behavioral disturbances.

It's the timing of onset of the cognitive and behavioral changes in relation to the motor features, that's how we distinguish them. And so, traditionally with Parkinson's disease, it's people are presenting with the motor symptoms first, the rest tremor, the slowness of movement, and that it's not for years, and what we say is at least a year after the onset of the motor symptoms that we start to see cognitive changes.

So conversely in dementia with Lewy body, we see the motor symptoms occurring within a year of the onset of the cognitive. So the cognitive is occurring within a year of the motor symptoms. And that's how we distinguish them.

There's a note about these conditions can be accompanied with like a psychosis or hallucinations, delusions, depression and anxiety. And again, that can be in both, in Parkinson's disease with dementia or dementia with Lewy body. I guess it's also important to note that sometimes... I get the question of the hallucinations and depression, anxiety may not occur in the context of cognitive changes in Parkinson's. So you may see depression, anxiety, prodromal before the motor symptoms, and so there doesn't have to be cognitive changes to see these symptoms. But it's just an important note.

Rachel: And, Ava I'd like to bring you in here because you mentioned that Richard had some of these really bothersome symptoms. The hallucinations and delusions but also the depression and anxiety, and you shared how difficult those can be to manage. So tell us a little bit more about your experience with dementia with Lewy body.

Ava: Yeah, sure. And you know, building on what Katie said, Richard had all of those issues, hallucinations, delusions, depression, anxiety, and they were very difficult to manage. And some of them were showing up before even some of the physical symptoms. Getting a lot more depression and anxiety about things that we never had issues with before. Like flying, we flew a lot and suddenly he had a fear of flying. Things like that or delusions about me or people stealing money.

Hallucinations for him were very vivid. For a lot of people hallucinations are just some benign thing, like, oh there's a person sitting in my chair or there's a person in the trees or whatever. In his case, they were very fear-based. So you know, there were commandos outside and we have this beautiful totem pole and villages of people would live in the totem pole, would come out periodically. The plants would turn into children and the the white chairs by the pool turned into a bride and groom or there would be bands playing outside. I mean it was some very fearful and some just things to deal with.

My [inaudible 00:25:11] especially as things went on to try to correct him was not helpful. It was much better to just manage them. Sometimes I'd open the door for example and say, "Okay, you. Time for you to go out," and shoo them out the door.

Rachel: Yeah, you've had a lot of helpful tips and we've put a lot of these tips that you shared with me in our new guide on navigating cognitive changes in Parkinson's that you can find in your resource list, but a lot more of the information we're covering in this webinar, and also the tips like this, Ava, that you found were helpful with hallucinations and delusions when some of the other treatments just weren't enough or didn't cover the hallucinations and delusions.

Ava: Oh. I was just going to say that for me, this page was by far my most challenging for everybody.

Rachel: Could you clarify a little bit? This page meaning the...

Ava: The issues we're discussing on this page around hallucinations, delusions, anxiety were more difficult to manage than the cognitive issues. Although, those were pretty darn hard too.

Rachel: Mm-hmm (affirmative). And Steve, we often get questions about how many people with Parkinson's get dementia or cognitive changes, can I get Alzheimer's if I have Parkinson's? How do you answer those?

Stephen: There's a fair amount of good solid epidemiology data out there looking at those kinds of numbers and there's a broad range, but broadly speaking about approximately 30 percent people with Parkinson's have dementia. In terms of the transition from Parkinson's to a full blown dementia, it's on the order of 3 percent to 10 percent per year that people are transitioning to a full blown dementia. The risk of dementia in people with Parkinson's is actually about three-fold greater than in people without Parkinson's. So having Parkinson's really is a risk factor for developing trouble thinking and a full blown dementia.

Rachel: And let's talk a little bit more. Let's move to the next slide because diagnosing these conditions is really difficult and it's hard oftentimes to separate, as you mentioned Katie, which is which because we just use timing to separate Parkinson's disease dementia from Lewy body dementia and Alzheimer's and these sorts of things. So even maybe you can take us through this slide a little bit. If somebody talks to their doctor about cognitive changes, what are the next steps to that evaluation and then potentially treatment?

Stephen: Sure. Well, great question. I think the doctor has to work very carefully with the patient to try to get a sense of what might be going on. For example, Katie earlier mentioned depression and anxiety. These can impact cognition. A person who's really down and ruminating and is going to be busy thinking to themselves when someone else tells them something and then they'll be mad at themselves for having forgotten what was told them, when in fact the primary problem was one of depression. Anxiety likewise can really impact thinking in significant ways. So doctors have to think-

Rachel: And I'll just interrupt you there for one second because we're getting a question also about sleep which can be impacted in Parkinson's. Is that something that can also impact cognition?

Stepehn: It certainly can. Disrupted sleep can absolutely affect thinking, whether it's through Parkinson's or non-Parkinson's disease related illness. Severe obstructive sleep apnea starves the brain of oxygen, results in excessive daytime sleepiness and makes it really hard to think straight. And in general, sleep disorders can impact thinking. Some of the medicines we use to try to control our sleep problems can also affect thinking. So for example, the REM sleep behavioral disorder, the dream enactment associated with Parkinson's disease we'll often treat sometimes aggressively and that can lead the medicines we might use, the benzodiazepines, can also potentially have an effect on thinking as well.

Other things to think about of course for doctors will be other medications used to treat Parkinson's and just older people in the age group that gets Parkinson's are often on multiple medications and sometimes those medications alone are capable of causing trouble thinking, sometimes through interactions they can cause trouble thinking. And likewise, supplements or for example the use of marijuana or other experimental things, alcohol used socially as well.

So doctors have to review all of these medicines and exposures and to think of them as potentially toxic and many of the medicines we'll use to treat Parkinson's for example, trihexyphenidyl or Artane, which is quite good for tremor, is very good at causing trouble with thinking, trouble with memory, and even bringing out hallucinations in older patients with Parkinson disease. The dopamine agonists like Ropinirole, pramipexole, and rotigotine patch are also all very good at causing trouble thinking as well in bringing out hallucinations, and even amantadine also. So three broad classes of agents that we use aggressively and successfully to treat the problems with moving can cause trouble with thinking. So it's important for doctors to think about the medications and the dosing. carbidopa/levodopa, a really very successful work horse for treating Parkinson's motor problems at high dose also can be problematic, although at lower dose it's usually actually generally quite well tolerated.

And then outside of the Parkinson's medicines, it's just worth mentioning very common medicines that older patients will be exposed to that can cause trouble thinking as well. So sleep medicines like I touched upon, whether it's Tylenol PM which has Benadryl in it. These PM agents can really affect thinking significantly. Ambien, Ativan, lorazepam, these benzodiazepines are all potentially problematic.

Some bladder medications as well that are meant to just act from the bladder can cross the blood brain barrier and affect brain function as well. Some of the older antidepressants can have these problems as well. So I think it is important for doctors who work hard with patients and their caregivers to go through that and consider other medical conditions as well, thyroid disorder, B12 deficiencies which are common causes of trouble thinking as well as metabolic problems which might show up as a salt imbalance, electrolyte imbalance, liver function problems, kidney problems. And then doctors can quantify the... get a detailed assessment of cognitive function through detailed neuropsychological testing.

Neuropsychologists are trained to perform these careful tests to look at the strengths and weaknesses across the different domains of cognition that we touched upon earlier, and that can be quite useful to get a sense of what's strong, what's not strong both for diagnosis but also to get a sense of a baseline and level of severity across these domains that are sometimes hard to assess in the short time that doctors will have with their patients. With respect to treatments, once we've gotten rid of all the toxic agents we possibly can, including medications and the like, then it is time for doctors to start thinking about treatments. And just a quick word about diagnosis, I haven't touched upon brain imaging, but I do think it's important for doctors to get careful brain imaging to look at the contribution of vascular disease or other processes, some of which might even rarely on a rare occasion be reversible. But it's really important for brain imaging to be performed because you wouldn't want to miss something that's going to alter how we treat these illnesses and even the diagnosis we make.

But once that's all established, there are medications that have been proven to be effective both for Parkinson's dementia and for dementia with Lewy body. Most of these work by increasing a brain chemical called acetylcholine. The cells that make that brain chemical are damaged in both Parkinson's and dementia with Lewy body and so their loss definitely contributes to trouble thinking and we can increase acetylcholine using medicines like rivastigmine, known as Exelon in the US and also Donepezil is another one. There are multiple treatment trials in the US and internationally in support of those agents, both in Parkinson's dementia and in dementia with Lewy body.

In terms of mild cognitive impairment with Parkinson's disease, there's not as much data in support of treating medically, but it's worth mentioning that there are a few clinical trials that support, that show benefit or certainly a trend to benefit. These are smaller clinical trials but using the same strategy using medicines that increase acetylcholine in the brain.

There's another class of medicine called memantine, which has been used like these other agents in Alzheimer's disease for some time and in combination with medicines like rivastigmine or Donepezil, there appears to be some benefit in clinical trials, although modest on average, but everyone's different. Some might have a more significant benefit, while many will have no benefit, but it's often worth trying and then getting rid of the agent if it isn't beneficial.

In terms of non-medication strategies, I think it is worth talking about cognitive therapy as well as physical therapy and sort of exercise. It turns out there's actually a lot of data in support of exercise and thinking in Parkinson's disease and that's worth doing and very likely the same rules will apply in dementia with Lewy body, the sister illness. There, any exercise you can do that's more than you're doing already counts. So I think exercise is important. There are a number of ways to do that formally, plugging into Parkinson's resources for that purpose. In terms of cognitive therapy, people who aren't too cognitively impaired to benefit can benefit I think from cognitive therapy if they're seeing a good cognitive therapist focusing in on particular weaknesses they've got to help them practice. The problem with cognitive therapy that the research is out there suggests that if you get really good, say at Sudoku, that doesn't necessarily mean you'll be good at anything other than Sudoku.

And so we really want the cognitive therapy to focus in on the things that are actually causing a person trouble so they can benefit from those kinds of therapy strategies. And I think broadly speaking, it is valuable to take advantage of the expertise of movement disorder and cognitive specialists to help manage these symptoms and sometimes to work collaboratively together for this purpose. Some groups like ours in the Lewy body dementia unit do both, but there are many places where it's just a movement disorder unit or just a cognitive specialty group and it's nice to work together to make sure we're optimizing both movement and thinking in the same person.

Rachel: That's a lot to think about, but a lot that you can do with your doctor to look into these symptoms and these changes and potentially change around or reduce medications if that's safe for you or look at other medical conditions as you mentioned.

But Ava, there's a question about how can a loved one or a care partner bring up cognitive changes to their doctor if the person living with them doesn't want to discuss them or maybe doesn't even think there are changes? Do you have any advice there?

Ava: Yes, absolutely. And thanks for the question. As a care partner, you need to be proactive and if your doctor doesn't bring it up, you bring it up. Once again, be in a matter of fact way, giving as many examples as you can. And if your doctor is not paying attention, you may consider a different doctor. Not all neurologists and specialists are created equal and you need to find one that works for you, and I definitely want to build on Steven's point of creating a team. Find a team that's going to help you and your loved one.

Rachel: Yeah, it's very individualized and finding the right treatments that work for you and the right doctors who work with you. Katie or Steven, anything to add there on if you have a difference of opinion on what's going on or how people can bring it up. Is it safer to bring it up in a more objective way and just kind of asking, hey, are there cognitive changes or other symptoms that go along with Parkinson's? And then that kind of gives the doctor the window to open the conversation or ask more questions around that. Katie, maybe you would start.

Katie: Sure. I think as we've talked about... You know, I think it's becoming increasingly recognized that there are more than just motor features to Parkinson's. There are these non-motor features we mentioned, depression, anxiety, we mentioned potentially psychosis, and then of course we're talking about cognition. So I think whoever you're seeing for management of your Parkinson's, it's always good to be bringing up these other non-motor symptoms if your doctor isn't. Which, you know, we should be, but if not then just kind of running through a checklist of these other non-motor features. Because yes, it's important that it's brought up and it's talked about just like the motor symptoms.

I think one thing that we find to be helpful is I will often tell my patients to come with a list of things they want to talk about before the visit because that makes sure that things are being addressed. I think always having a care partner with you, like Ava mentioned, is very helpful to make sure that they're there to kind of bring up these things if they're not being brought up. And also I think in the office something more for providers is having these questionnaires. Like we use, for example, [inaudible 00:19:15]. It's a tool to kind of go through these non-motor features as well, so to make sure that they're getting as much attention as the motor features.

Rachel: That's really helpful.

Stephen: Oh, sorry, I just want to very quickly echo the value of having a caregiver present.

Rachel: Yeah.

Stephen: I just think that's super important and patients won't always have a whole lot of insight into some of the problems that they're having, and it's great to have someone else advocating for patients present for that purpose.

Rachel: Yeah, it's really helpful, especially the mood symptoms. Katie, you were mentioning, and Ava you mentioned that can go along with sometimes the people who are experiencing them don't recognize them or see them and the loved ones are the first ones to notice that there's a change there.

Katie, I'll ask you to kind of continue with us on the next slide because there's a question about what's the reason for even measuring cognitive change since we can't do anything about it. So is there also a myth that we can't do anything about cognitive change? What would you say to people in this situation? Why is it important to measure it and what can they do?

Katie: I think just as Steven said is that there are things we can do. So, unfortunately we don't have a cure. We're trying. I think the field is definitely trying, but we don't have a cure. But we do have ways that can help. I typically talk about this two-fold, just as Steven was saying, there's non-pharmacologic and pharmacologic approaches. And honestly, particularly in the mild cognitive stages where maybe there's a little bit less evidence, although as Steven said, sometimes it can be used with good benefit using those medicines, the acetylcholinesterase inhibitors, but typically we aren't recommending.

Katie: Typically we aren't recommending pharmacologic therapy in those stages because the evidence just isn't there. Or because maybe it's patient preference. The things that we can do non-pharmacologically that we know to be helpful are diet, exercise, socialization and strategies. Those are the big ones I talk about. When we think about exercise, I think there's the strongest data for that to help with both our motor and non-motor symptoms. So exercise. So I say try to get some cardio in, a mix of cardio and weight training, walking, be active. We know that that's helpful. Actually, it is disease modifying. It can slow the disease. So exercise. Socialization. Socialization is so important and it's because the worst thing we could do is isolate ourselves. So socialization because people are interesting. We learn from people. It helps with your cognition and neuroplasticity. So socialization is so important.

I love to hear when families, they're very close together, they have the grandkids over or maybe they have church groups or friend groups that they play cards with. I say keep doing that, keep doing that or start doing it. Then as far as diet, what I say for that, I think the best evidence in terms of cognition is for a Mediterranean diet. Thinking about, what are they eating in Tuscany tonight? So fish, fruits, vegetables, really things that is generally healthy for us for our cardiac health, but we know to be beneficial for cognition as well. Then with that, what I say is try to avoid inflammatory things. So sugar in general. Too much sugar can be harmful actually. So everything in moderation.

Then of course there are also strategies that can help. So Stephen already alluded to the fact that we should be looking for reversible causes. I'm always screening for depression, sleep problems, as the audience brought up, hearing issues. I think hearing problems can be overlooked. So making sure that that's being addressed, if that's something that could interfere with attention or memory. Then it's reducing demands on yourself. Simplifying, organizing, writing things down, delegating. These are things that I think sometimes we're hesitant to do but it is okay to do, and it can be very, very helpful and with your cognition.

Rachel: Important for your treatment plan. I like including those and thinking about how you can make a strategy with a cognitive therapist and with your doctor that's unique to you. So one size does not fit all for these kinds of strategies. Ava I'd like to ask you about some of the tips on the right hand side of the screen because you and the other care partners and family members who helped me put that guide together that I mentioned that's in our resource list, brought a lot of these tips to my attention about how to live with cognitive changes or live with a loved one who had cognitive changes. You mentioned also the importance of a support group, and that brings in also that socialization Katie was talking about. What would you tell families and loved ones of people who are living with cognitive changes?

Ava: Well, definitely your life has changed and will continue to change. To me, the most important thing is to remember is what we really were the most critical things in my life. Let's focus on our love for each other and being together, not all the other fluffy things that we could get rid of, so we could just focus on the most important. I would absolutely plan ahead. As I mentioned, Richard's decline was extremely fast. If we would not have had our living wills and things in order before this, there's no way that we could have done it after because you have to be of sound mind to sign documents.

It takes a village. Don't be a martyr. Don't think I can do this on my own because you would not be of this Earth if that were the case. Look for your support system and build upon it before you're at a breaking point. I would say there's a lot to learn. I mean I learned things I didn't want to know, but I'm happy I did. I feel like I'm a better person for what I went through even though it was darn tough. So look for the balance of what are you learning and what's important versus, oh my goodness, what the heck is going on? And keep learning.

Rachel: Important tips for all of us. I would like to continue on to the research, and Katie you mentioned this already, that there are so many treatments in the pipeline that could potentially help with a lot of these symptoms we've been talking about but also slow or stop the progression of dementia. We're also really working to better understand what causes it and also measure it so that we can better predict and test the therapies that are in the clinical trials. I'll stop with just that brief overview and get to questions because we're getting so many of them. Back to Katie. You gave us that great overview of Parkinson's disease, dementia and dementia with Lewy bodies and how they both fall under that umbrella term of Lewy body dementia. But why is it important to even put them in a different category or diagnose them differently? Do we treat them differently?

Katie: Oh, that's a great question. I think we are moving toward putting them under this umbrella, Lewy body dementia, when there is dementia involved with Parkinson's. Because we really do at that point treat them very similarly, and clinically, patients can look very similar when there's dementia with Parkinson's. They can look very similar to those with dementia with Lewy bodies. Just like Stephen said, acetylcholinesterase inhibitor like rivastigmine or donepezil can be used in both, in both Parkinson's dementia and dementia with Lewy bodies. So in the Lewy body dementias. When we are talking about managing the psychosis or the hallucinations or delusions, we can use agents like ... Well actually the most evidence is in Parkinson's dementia. The new agent is pimavanserin where that can be used. But off label people may use it in dementia with Lewy bodies.

Clozaril is used with good effect in both Parkinson's dementia and dementia with Lewy bodies. Then Seroquel is the other agent that we use. In both, so in the Lewy body dementia broadly, and then Parkinson's disease with dementia and dementia with Lewy bodies, we have to be careful to know that other dopamine blocking agents or other anti-psychotics should be avoided in both. The three that we use safely are Clozaril, pimavanserin or Seroquel or clotiapine.

In terms of when we're thinking about dopaminergic therapy, so the motor symptoms, this may be where they vary a little bit. So in Parkinson's, like I said earlier, individuals are presenting with the motor features. So often they're being treated with dopaminergic therapy or anti Parkinsonian meds, I should say, more broadly. So levodopa or the other agents like dopamine agonist or amantadine. Generally in the beginning, it's generally responsive. They're typically well tolerated, and we don't start to see maybe some drug induced affects like psychosis or hallucinations until later stages. Where in dementia with Lewy bodies, when there's the motor features in the setting of cognitive, it's a little bit more tricky there because if the motor features are to the point that maybe they're causing falls, it may be reasonable to have levadopa on board. There is some suggestion in the literature that maybe these individuals are less responsive to dopamine. But I think a lot of us clinically see that they are responsive. We often maybe will use a low dose, but of course there's the concern for limited tolerability in these patients once there ... So if it is dementia with Lewy bodies or Parkinson's with dementia, it could exacerbate psychosis or confusion. You have to be more careful. I think in terms of when we're thinking about treating the motor features, that's where they differ. But in terms of treating the cognitive and psychosis, we actually address them similarly.

Rachel: The treatment strategies are pretty similar, but it's helpful to have a diagnosis, especially of Lewy body dementia or dementia with Lewy bodies because of the potential progression and being able to plan ahead and those sorts of things. Would you say that's fair?

Katie: Yeah, exactly. I think that that's fair because we do think ... because we already said that the cognitive symptoms occur very early with dementia with Lewy bodies. I think having that diagnosis has obviously a different prognosis, so it can be helpful.

Rachel: Steve, a question for you about deep brain stimulation and cognitive changes. Does it help or harm them or have any effects on them at all?

Stephen: Well, that's an interesting question. Deep brain stimulation is a surgery, and neurosurgeons are putting in electrodes sometimes bilaterally, sometimes on one side, to improve the motor function in Parkinson's disease. That reliably, when successful, can reduce the requirement for the dopamine medications that patients are on. By reducing some of those medications, thinking it could theoretically even improve a bit if it's not quite perfect upfront. A lot depends on where the electrodes are placed and because it's a procedure, there's some variability from patient to patient even on the order of millimeters. Most patients don't have any cognitive problems from the DBS placement, although occasionally it can happen. It's unusual. People will work hard to come up with their doctors with a stimulation paradigm that works without causing trouble thinking, and sometimes that does require some tweaking to work. It's unusual for thinking to improve purely on the basis of DBS per se.

One question that's come up in the past is whether or not patients with trouble thinking in Parkinson's should get DBS, deep brain stimulation. There's been a matter of have some debates. Because in general, patients who have dementia tend to do worse with deep brain stimulation than patients that don't. Many facilities will not do DPS in patients who are having a lot of trouble thinking because of that. That said, it's still an act of research question and it's not quite settled yet.

Rachel: Before you would get DBS, you would have a baseline cognitive testing to understand what you're thinking and memory, where they could, and if they would potentially change before deep brain stimulation. Is that right?

Stephen: That's right. You'll get very careful evaluation to assess both your baseline function and also your candidacy as to whether it would make sense to proceed. There are situations where people can do great with DBS and be a very effective treatment for the motor problems with Parkinson's, but it certainly doesn't appear to alter the course of thinking in Parkinson's disease. In so far as you're stimulating brain cells to improve moving circuit function. You're driving circuits in the brain that help with moving. We wouldn't expect to alter the proteins that accumulate in the brain and contribute to trouble thinking and Parkinson disease like alpha-synuclein in particular but others as well. There's little reason to think that this would actually alter the course of cognition in Parkinson's.

Rachel: Great. Katie, another question, we touched on this earlier about if and when cognitive changes happen in Parkinson's and who would they happen to, but there's a question about, does this only happen in older people? Does it happen in young onset Parkinson's or earlier onset Parkinson's which can happen under the age of 50? Anything to add there?

Katie: I think, even kind of touched on this a little earlier, we know that firstly not everybody with Parkinson's disease will have cognitive changes. When we look at the epidemiological studies, we know that there can be mild cognitive impairment in about 40 percent of individuals at disease onset. But just like Stephen said, this tends to be in certain individuals, so individuals who are older at onset, individuals who have more postural instability or even early orthostatic changes, so where there's changes in their blood pressure with standing. There are certain individuals who are more at increased risk. Actually it's more likely in those with older onset.

Rachel: Question, Steve, on what are the early signs of memory problems? We talked a little bit about how memory can be affected in Parkinson's and even with age, but what would you say to that?

Stephen: Early signs of memory problems that are getting in the way might be forgetting the content of conversations. Your loved ones might find that you're asking them the same question twice for getting plans and events such as a visit to see family or to the doctor. Increased reliance on notes or a calendar compared to baseline, like a significant change there. Some of us just tend to use notes, but a real change there would be significant, and an increased reliance on family members. In addition, to a tendency to start losing things around the home more, watch, wallet, that sort of thing also would be clues. All of us experience problems finding our car in the parking lot coming out of the the grocery store, for example, on occasion. That by itself should not be alarming to anybody. It's when it's starting to get in the way, when it's changing, that's when we start to pay attention and then I think it's worthwhile getting your doctor involved.

Rachel: Ava, a question for you on sundowning. I don't know if you're familiar with that exact term, but this could be when somebody gets worse at night. Tell us a little bit more maybe about your experience with that and what you would tell people who are potentially living with that change.

Ava: Yeah. Sundowning is obviously when the sun goes down, being not as functional in the afternoon or an evening versus in the morning. It was definitely a factor for us. We found that the change of the light increased hallucinations because the trees looked different. The wind can change. Certainly even the full moon or not made a difference. I would say just be very a patient with that and know that it can happen and absolutely do not schedule things for the end of the day. Go when your loved one and you are at your best, which for most people are the morning.

Rachel: Really helpful. We are already at the end of the hour. I can't believe it. I know we had so many more questions than we could get to, but I will give each of our panelists just a couple of seconds to give a last word on this important topic. Katie, I'll start with you.

Katie: Yeah. I think this is a very important topic that I think is often unfortunately maybe under-recognized. I've just encouraged that it's something that we talk about with each other as the provider and patient relationship and care partners so that we can recognize it and then talk about treatment and even get involved in early research because I think there's a lot of exciting research for those with cognitive impairment in the pipeline.

Rachel: Absolutely. Steve?

Stephen: Well, I completely agree. I think these are important problems that people are experiencing. The important thing is for us all to cue into them and engage with our physicians and our teams and do everything we can to mitigate them. I think there are a lot of useful strategies even now that can be helpful. We can't stop the progression of these diseases yet, but there's a lot of research going on to that end. But what we can do is provide symptomatic benefit and get rid of all the complicating factors that could actually be making things a whole lot worse than they otherwise would be. My expectation based upon the really significant similarities between Parkinson's disease and dementia with Lewy bodies, looking under the brain, they have the same process going on. My expectation is that a cure for one will be a cure for both.

Katie: Right, right, right.

Rachel: Super helpful. Ava, the last word is yours.

Ava: Oh, thank you. Thank you to you, Rachel, and to the Michael J. Fox Foundation for this and for the guide that you put together. It's so important to understand the cognitive issues and to treat them just like physical issues and not like something that you talk about in whispered tones or in some kind of shameful way. It's important and there's so much more to learn. I'm really happy to have had the opportunity to be here with you today.

Rachel: Well, thank you again to you and to our other panelists for sharing your expertise. Thank you everyone who joined and asked such thoughtful and insightful questions. We'll be sending a link to the webinar on demand to listen again, or just share as you'd like. Mark your calendars for our next webinar on October 17th where we'll discuss a very popular topic of complimentary and alternative approaches to Parkinson's care, including medical marijuana. We'll have staff behind the scenes again to answer your questions live. We'll talk to you then. Have a great night.

Katie: Thank you.

Stephen: Thank you so much.