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.

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

Dr. Karen Jaffe: Hi everyone, and thanks for joining us. I'm Dr. Karen Jaffe. I'm a member of The Michael J. Fox Foundation Patient Council, and I will be your moderator for today's webinar.

Dr. Karen Jaffe: I'm a proud co-founder of InMotion, which is an amazing wellness center for people with Parkinson's disease and their families in Cleveland. I was diagnosed with Parkinson's disease 14 years ago, in 2007.

Dr. Karen Jaffe: Today, we are going to discuss some of the physical, emotional, and social changes that we may notice if you're living with Parkinson's disease for some time. We'll cover some tips for managing these changes, and share with you some opportunities that you can take in your journey with Parkinson's disease.

Dr. Karen Jaffe: This webinar is brought to you with support from Acadia Pharmaceuticals. While their support makes this program possible, their donations do not influence webinar content perspective, or panel selection.

Dr. Karen Jaffe: So we've got a lot to discuss. So let's get started. Let me introduce our panelists.

Dr. Karen Jaffe: Dr. Veronica Bruno is a movement disorder specialist and clinical assistant professor of neurology at the University of Calgary in Alberta, Canada. Her area of special interest is pain and Parkinson's disease, a symptom many of us experience.

Dr. Karen Jaffe: Dr. Vikram Khurana is the attending neurologist and chief of the Division of Movement Disorders at Brigham and Women's Hospital and Harvard Medical School in Boston, Massachusetts.

Dr. Karen Jaffe: Henry Hansmann was with diagnosed with Parkinson's disease in 2009. He splits his time between New York City and New Haven, Connecticut, where he's a law professor at Yale University.

Dr. Karen Jaffe: And last but not least, writer, author, and PD research advocate, my husband, Marc Jaffe. Marc is also the co-founder of Shaking with Laughter, a nonprofit dedicated to raising funds for Parkinson's research.

Dr. Karen Jaffe: So to start our discussion, but paving a path with Parkinson's disease, I'd like to turn to Henry and Marc. Having more than a decade under your belt as either a person with Parkinson's or a care partner, briefly, what does your journey look like? And has the passage of time changed your perspective on how you see any of your Parkinson's challenges?

Dr. Karen Jaffe: Henry, I'll start with you.

Henry Hansmann: Okay, thank you. I was diagnosed, as you said, in 2009, 12 years ago, and for the first two years, it didn't affect my behavior very much at all, and my life very much. I continued being a full-time professor of law at Yale Law School, and the major change was in diet and exercise and sleep.

Henry Hansmann: I tried to get more sleep, I tried to get a lot more exercise, and I ate a Mediterranean diet. My wife is Italian, and is a heck of a cook, and that was pretty easy.

Henry Hansmann: So Yale Law School has a retirement plan, which if you give up your tenure, your academic tenure by the age of 73, it allows you to teach a little part-time for the next few years. It's kind of a phased retirement program, and I opted for that at the age of 73, which was the latest day I could do that, but it was time, and it was clearly time. I dropped my teaching load a bit and my writing commandments.

Henry Hansmann: Everything slowed down. With Parkinson's, everything just turns out to be slower. Everything takes more time, not to mention exercise and sleep.

Henry Hansmann: So as it is this year, I will be teaching one seminar. The normal course load would be two major, two large courses, and one seminar. I am not teaching any of these big courses. I'm teaching only a seminar, and I think that will be it for the rest of my life, as it were. I have a right to teach for the next 10 years, one seminar a year, and get paid for it rather generously, but I think I'm probably not going to take it. I'm going to probably, after this year or this year and another year, I will drop even the seminar-

Dr. Karen Jaffe: So can I ask-

Henry Hansmann: ... for the usual reasons. Symptoms are getting more pronounced.

Dr. Karen Jaffe: And Henry, if you were to look back at when you first got diagnosed, do you think that you could have imagined where you would be today, 12 years later?

Henry Hansmann: No, I was quite upset about it, as anybody would be when they get a diagnosis of Parkinson's disease, especially if you know nothing about it. I remember being quite afraid of it. I wouldn't tell anybody for the first two years. I didn't let it out beyond family and friends, close friends, which I think now was a silly policy to have followed, I should have let it out of the bag right away.

Henry Hansmann: I continued to live a relatively normal life, I would say, until three or four years ago, and at that point, the symptoms started getting more bothersome, and interfered more in my teaching and research for that matter.

Henry Hansmann: So I can go into detail on those symptoms, but let me just say, they're the normal things. Dyskinesia set in about two years ago in my right leg. It doesn't bother me much. I don't think about it very often, but it's there. You feel the mental, the cognitive effects. Terrible short-term memory. Mine was bad to begin with, and now it's really appalling and difficulty following a train of thought and so forth.

Dr. Karen Jaffe: Okay, well that gives an idea of how things have progressed for you.

Dr. Karen Jaffe: Marc, having never actually directly asked you this, I'm going to carefully listen to your response.

Marc Jaffe: You're right next to me, so it's hard not to.

Marc Jaffe: I think, as a care partner, you're thrown into this a whole new world upon diagnosis, which for us was about 14 years ago, and you are trying to look ahead and figure out everything, and how it might change your relationship and those things you don't know.

Marc Jaffe: After living with it for a few years, I think we've settled into, what I like to think of as a batting coach, is what I've become, to use the sports analogy. When the hitter, which would be you, isn't hitting as well as they should, it's my job to keep an eye and go, "Oh, well maybe she's holding her hands down a little lower, or her elbows not up, or something like that," and help my partner out, from a different point of view.

Dr. Karen Jaffe: So what am I batting at this day?

Marc Jaffe: You're hitting at around 300, so you're definitely All Star. I don't know if you're Hall of Fame yet, but keep it going for a few more years.

Dr. Karen Jaffe: Okay. The more that we know about PD, it's clear that every person with Parkinson's has their own journey, and the path they take is unique to themselves. While each of us has a different rate of motor and non-motor manifestations. I'd like to ask our movements disorder panelists, to talk about what a personal practices might expect from a clinical perspective, your diagnosis. And is it typically different for a person who's diagnosed with young athletes versus really staying as much later in life?

Dr. Karen Jaffe: So let's start with talking about some motor symptom progression, and then Brian, you can address the non-motor component.

Dr. Vikram Khurana: Sure, I'd be happy to do that.

Dr. Vikram Khurana: At a high level, this, this is a progressive disease. I think we're increasingly recognizing that there are definable sub-types in the disease, and I'm going to be talking just about the motor symptoms. Veronica will chime in on the non-motor, but even with the motor symptoms, there are patients who have predominant tremor as asymmetric, it affects one side of their body, for example. There are other patients that will have more rigidity or imbalance from the beginning, more bilateral disease.

Dr. Vikram Khurana: So it's important to recognize that everyone's journey is different and that is the motor journey and the response to the medications, and so it's important to know that the relationship between patients and their physicians is very important, a good line of communication, and there aren't going to be periods of trial and error, as patients and their physicians get to learn about each other and find the best way to travel on this journey together.

Dr. Vikram Khurana: But in general, we expect the motor symptoms to worsen, and what does that mean? In general terms, that means that the dopamine reserves that we see in the brain are depleted over time, so a patient might find, for example, that in the beginning of the disease a lever doper or a dopamine agonist is very useful, but there's no clear on and off times at the beginning.

Dr. Vikram Khurana: And then maybe the nighttime. There's no need for medication, because there are reserves of dopamine that we have, but then over time, patients become more acutely aware of the need to have their medications. Those medications may need to be taken at increased frequency.

Dr. Vikram Khurana: We may need auxiliary medications that increase the length of which dopamine hangs around in the brain and that synapses in the brain. We may need to use combinations of medications. There may need to be more coverage at night. Patients may feel more dopamine-deprived when they wake up in the morning, after a long night of not having had medication.

Dr. Vikram Khurana: And so these are the kinds of changes qualitatively, and I'm happy to answer in more detail when we go through Q&A, but these are the kinds of changes that we expect to see, and I think that in general, and it's really hard to generalize because, as I say, every patient is different, but in general, patients who have early onset disease from their 20s to 50, for example, those patients will tend to, especially if they respond well to medication, which is a very important data point, tend to hold their course for a lot longer period, than patients who have the onset later in life. Those patients who tend to get the disease later will progress more quickly, both with respect to their motor symptoms and from motor to non-motor symptoms.

Dr. Vikram Khurana: But underline all of this by saying that this is an individual journey and that everyone is different.

Dr. Karen Jaffe: I think despite the fact that we know that it's individual, I meet a lot of people through the wellness center, Emotion, and you talk about how, when they first get diagnosed, they're so fearful about what's going to happen, because they don't really know about Parkinson's disease. But if I knew what I know today, back then, I think I would have been a different Parkinson's patient, because I wouldn't have had this worry, because my disease has, fortunately for me, has been a slow progression, and I think that most people I see, they don't wake up and have a big change over the course of a day or two. It's a slowly-progressing disease-

Dr. Vikram Khurana: That's absolutely right, and a point worth underscoring, and a disease for which there is so much available, and increasingly becoming available, not just for the treatment of symptoms, but many, many different avenues of approaches that we'll touch on later, for disease modification.

Dr. Karen Jaffe: Right, right, wonderful.

Dr. Vikram Khurana: I [crosstalk 00:12:48]

Dr. Karen Jaffe: Thank you. Okay, Veronica, how about non-motor symptoms?

Dr. Veronica Bruno: Well, this is usually after a few years from the diagnosis, is the time when we start noticing or seeing the non-motor symptoms emerging more clearly. Basically, when we talk about non-motor, we mean everything that happens in Parkinson's that is not related with movement ... it's not stiffness, tremor, or balance problems ... but it's related with some other parts of the body or some other [inaudible 00:13:16].

Dr. Veronica Bruno: So there are many non-motor symptoms, and you may feel that you have some of them. Many patients experience some of them and not others, so it's not that every single patient with Parkinson's, will have all the non-motor symptoms, but just to give you an idea, they're they can affect different spheres of, for instance, cognition, like memory problems, attention problems, as Henry was mentioning, feeling that the short-term memory is not working as well as before, mood disorders, like depression and anxiety are extremely common.

Dr. Veronica Bruno: And also for instance, sleep disturbances, like having very active dreams at night, or not being able to sleep well, or feeling extremely tired during the day, and having what we call excessive daytime sleepiness.

Dr. Veronica Bruno: There are a different set of symptoms that we call autonomic symptoms, and when we say that word, basically, we speaking about issues with your bowels, like severe constipation, issues with your bladder, like increased urinary frequency, and having to open the toilet many times during the day, but also at night, issues with your blood pressure, that may start to go down when you stand up and that may produce lightheadedness or dizziness, sexual dysfunction, and additional symptoms, such as fatigue or excessive sweating, or pain. That is my area of expertise.

Dr. Veronica Bruno: All those may be there, before even the onset of the motor symptoms of Parkinson's, but it's usually after some years with the disease that patients become more aware, that they become a problem, or they start to affect quality of life, and there are two very important things related-

PART 1 OF 4 ENDS [00:15:04]

Dr. Veronica Bruno: Of life. And there are two very important things are related to non-motor symptoms. The first, is recognized because many people don't think that those non-motor symptoms are related with Parkinson's so they don't talk to the Neurologist about them. So talk to your Neurologist about every single symptom that you're experiencing and, don't assume that it's not related with Parkinson's.

Dr. Veronica Bruno: The second and very important point is that many of them respond well to different treatments. So maybe you assume that this is the way my disease behaves and there's no treatment or no solution, but may, we may have different strategies to tackle those non-motor symptoms, improving your quality of life, significantly. So be aware of their existence, talk to your Neurologist about them, and also know that there are many treatments that we can use even when the disease is advanced and you have been living with Parkinson's for many years. As a final point related to non-motor symptoms, you may feel that they are not related with your motor part, or your medications, but for instance, just to give you a short example, improving constipation will improve the way you solve your medication and hopefully improve your own periods.

Dr. Veronica Bruno: Improving hyperactive bladder will reduce the times you need to go to the toilet at night and that will improve your sleep so you will feel less tired during the day. So again, recognizing them is very important talking to your Neurologist and knowing that there are solutions for many of them.

Dr. Karen Jaffe: I find that as part of [inaudible 00:15:02], I speak to a lot of people with Parkinson's and they, they often tell the stories about symptoms that they'd had for many, many years before they got diagnosed, especially constipation, which is a problem I had for 20 years before my diagnosis. Why is it non-motor symptoms proceed before motor symptoms when we think of Parkinson's as a motoneuron disease, motor disease. Why would constipation bladder, things like that? What's the scientific rationale for that order of things to happen?

Dr. Veronica Bruno: We're trying to understand a little bit more about why that happens. We have a few theories. We know that for sure, for non-motor symptoms, constipation, depression, and anxiety, loss of sense of smell and sleep disorders, Like these very active dreams at night, usually occur before the onset of motor. And that may be related with the fact that the disease starts in the arias of the brain or the gut where the alpha-synuclein is deposited. We're learning more and more about it but, until recently it was not that clear that that was part of the disease but now we know that particularly with those symptoms combined, we, have a strong suspicion that these may be Parkinson's. So it's very important to recognize those.

Dr. Vikram Khurana: Underscore that, just for everyone to understand that there was this traditional view, especially because 50 years ago, we saw that there was a responsiveness to Dopa. There was a traditional view that Parkinson's disease is a motor disorder. These are the classic Parkinsonism is really a motor syndrome but, it really is worth everyone understanding this is a multi-system disease that does affect many different urinal population in the body. There are clear pathologies there, and that really reflects to these multiple symptoms [inaudible 00:15:02].

Dr. Veronica Bruno: Sorry, come in just quickly to answer to your question of the young onset Parkinson's disease. As Vik was mentioning, the disease has usually a slower progression for people with young onset Parkinson's and something similar happens with the non-motor symptoms. There are some that may be more frequent in young onset Parkinson's such as restless legs, but is mostly the same that late onset Parkinson's value with a little bit of a slower progression.

Dr. Karen Jaffe: So I'm getting a couple of questions about mild cognitive impairment. And let me just see, If I can, there's two questions here that I want to gather here, Veronica one is after the diagnosis with Mild cognitive impairment, how long does it take, usually take for Dementia to develop and then, they follow up question that is, they want to know is it true if we live long enough we will get PD Dementia. So can we talk a little bit about Mild cognitive impairment and Dementia and Parkinson's disease?

Dr. Veronica Bruno: Sure. And those are great questions and cognitive impairment and Dementia are usually concerned that one of the biggest concerns for patients with Parkinson's as I can see it in my clinic. So the first thing to recognize is Mild cognitive impairment is just a risk factor for Dementia. It doesn't mean that every single patient that has Mild cognitive impairment will develop Dementia with the years. So it's very hard to predict. And again, the journey is different for everybody, but it's not a 100 percent certainty that if you are diagnosed with Mild cognitive impairment, you will [inaudible 00:15:03] develop Dementia in the future. If it happens, it's usually a slow progression and we call Dementia what happens when you are not dependent, independent for your activity, they activities anymore. So it may take some years, and there are many things that we should, and we can do in order to reduce that speed and improve your cognitive status.

Dr. Veronica Bruno: So the first thing that I would always recommend, is check in on medications because many of the medications like Amantadine or dopamine agonist that we use in Parkinson's can produce some cognitive issues with time. A second one, that is extremely important is talk to your doctor and rule out the presence of depression, because depression can mimic Mild cognitive impairment, your attention is not great, and you cannot think properly or pay or remember things and maybe treating depression the cognition will get better. The third, and very important factor is reduced all the cardiovascular risk factors like hypertension, diabetes, and cholesterol, because those will add burden to the cognitive problems and exercise has shown to the late-onset of dementia and it's an important, extremely important thing to add to your routine. So again, it's a risk factor, it doesn't mean that everybody will develop Dementia and there are different strategies that we can use to try to reduce that speed and make it less burdensome for you.

Dr. Karen Jaffe: Great. Do we, do we have an idea of what, what percentage of Parkinson's patients develop Dementia?

Dr. Veronica Bruno: So the numbers are different, but if with the years it's approximately 40 to 50 percent of patients, but with many, many years, there is a study that shows that after three years of their diagnosis of Mild cognitive impairment, only 20 percent of the patients so 2, every 10 patients will develop Dementia. So again, it's not a straight line and it's not a short, rapid progression usually if the diagnosis is Parkinson's disease dementia it's different if it's the Lewy Body Dementia or a different diagnosis.

Henry Hansmann: I do want to mention one aspect here that, that everyone have has different opinions out, but that is the genetic stratification is becoming more and more a part of our practice. And that is because we are starting to see the advent of therapeutic trials that are, that are directed at patients who carry specific mutations. But along with this knowledge of genetics, we are understanding that patients who have different genes associated with Parkinson's can have different manifestations or rates of progression. And so, there are a number of studies that have identified some clear genetic predisposition factors that will lead to a faster rate of motor to non-motor progression so, I want to underscore that, that's an important, it's important from the perspective of therapeutics and clinical trials, but also we are getting a little better every day at understanding prognosis based on genetics.

Dr. Karen Jaffe: Great, thanks. So this brings us to the very important topic of what can each of us do, some of the path in front of us. So what we don't have here yet, I do know this. We, can improve the quality of our lives living with Parkinson's disease. It might take hard work, commitment, patient support, and education, but we can't unpick our disease. Henry, I'd like to turn to you for a second. What lies in your arsenal of strategies to help with improving your day to day, feeling better, hearing good with living with Parkinson's disease?

Henry Hansmann: Sure. I would say the number one item is exercise. And, from my brief scanning of the literature, when I was diagnosed and from all the people told me, exercise was the only thing then available that might have a chance of slowing down the progression of the disease as opposed to just masking symptoms. So I went at it seriously and I, I had always kept in moderately decent physical shape through jogging and swimming and so forth. I did more of that, I did about an hour and a half a day, various forms of exercise, walking, running, trimming, working with resistance machines, you name it. And, and who knows what effect that's had, it makes me feel better anyway, and right after I do it. And, and I'm hopeful that it's doing something, any case I'm doing it on the mere probability that seems substantial that they're not substantial, it seems real, that it, it will do some good. Other than that, I've watched diet and weight, but nothing, nothing that that line has changed very much for me. And, I would say exercise a little more sleep than I used to get before.

Dr. Karen Jaffe: You mentioned that before you, you were hiding your Parkinson's disease and have you connected with the Parkinson's community at this point?

Henry Hansmann: No, I wasn't. My community of Parkinson's experts or friends is confined to several people on the faculty at Yale university who also had Parkinson's. I discovered it. And in both cases, just by looking at them and if you've got Parkinson's, you can see them. And the one of them, they had no, no right hand, no, no hand tremor, but her legs gave her away. So, so that's in my little community. I would talk to them, one of them has passed away only to heart problems, unrelated to barely to, to Parkinson's. But, but I haven't set out on a broader community. Most of my friends, all my friends, I think know that I got it. And they are, maybe too timid to raise a question or raised questions about it very often, but it is not [inaudible 00:15:03]. And, and so I haven't built a support group. I confess that I agreed with this meeting, this session, probably thinking that maybe they'd put me in contact with some people that I would find a couple to talk with.

Dr. Karen Jaffe: Great. Well, I hope that happens. I'm the start of that, I guess. Marc, do you have any advice on how as a care partner, you can be an integral part to the success of my well-being?

Marc Jaffe: Well, I hope I do. Been going at it a while. I think it's to, to go Henry. I think the social aspect of it is, is very important than maintaining, not just for the person with Parkinson's, but for the care partner on maintaining a social life and not just necessarily with people with Parkinson's, but your friends from before. And, it really, I think it has so many benefits, just the mental positive aspect. And, and I think you're seeing that to a great degree from the center, in motion center that is open here, which was initially done for exercise purposes, knowing the benefits of that but, we found that having the social life that exists because of it has added so much to our lives so, sometimes there's a resistance as Parkinson's patients in the beginning because they may be trying to hide it and later on because of the vagaries of the physical aspects of it to not engage socially but I think it's really important and as a care partner, I've tried to encourage that.

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Dr. Karen Jaffe: And I'll pick up a little bit on Marc's comments with emotion. You know, when I got diagnosed with Parkinson's disease, I really knew nothing about it but, when I went out to and I also kept it secret for several years as a Physician I was worried about my health of my career but, realizing that there were no resources really available, and I think that Parkinson's communities are bringing that to the forefront that we need to have exercise, but we also need, social context, we need education, we need support. And, I think that the Parkinson's communities are slowly but surely as I see through my advocacy work, the different communities are coming up and putting these together into one place where Parkinson's patients can build a community. So I think those are important changes that need to happen.

Dr. Karen Jaffe: Veronica as [inaudible 00:15:03] I'm sure you see a wide range of clinical presentations. What advice do you give to, to a person who has been struggling with their disease after years being diagnosed and here they are still struggling with, if they haven't really settled into owning this diagnosis? Well, how do you help them?

Dr. Veronica Bruno: I usually try to, to describe these, that the pathway or the treatment, or management of the disease as a team work. So where we have a very important role, because we can help with the medication understanding.

PART 2 OF 4 ENDS [00:30:04]

Dr. Veronica Bruno: ...your role because we can help with the medication, understanding how it works, how to dose it, what are the side effects, but the patient itself, or the people with Parkinson's themselves have a huge responsibility and work to do. Basically getting connected with a disease. That is going to be a very slowly progressive disease in most of the cases. So it's going to be with them for the next 20, 30 years. And then it's very important to learn how to live with it and finding your normality that may not be exactly the same that you were experiencing before the diagnosis, but doesn't need to stop you're living a pretty normal life.

Dr. Veronica Bruno: So all the strategies that are on this screen are extremely important, even sometimes more important than medication. As Marc was mentioning social interactions, try to stay active. Recognize the limitations, so you don't feel upset or embarrassed if something doesn't work exactly as it used to work, but try not to stop doing what you love, because that is extremely important for dopamine, for the brain and for moving and thinking power and for Parkinson's... The one that is in charge of your Parkinson's disease.

Dr. Veronica Bruno: And again, recognize the non-motor symptoms. Talk to your neurologist about them, and also planning ahead. I think that's a very important aspect because learning and talking to other patients, knowing how the pathway may be, will help you decide what you want to do and how you want to leave your life, and that I find it's extremely important. In the particular case of pain, that is very important aspirations. I want to mention a few words, sometimes because patients with Parkinson's can be in their seventies, eighties, everybody thinks that all pain is osteoarthritis and it may limit your activities, may limit your exercise. Many patients say I would love to exercise, but I have pain. So learn that Parkinson's disease can hurt and talk to your doctor because we may have strategies in terms of adjusting medications, adding new medications, manage painkillers that may help you gain that...Reduce the pain so you can feel better and you can exercise more and get more engaged with your exercise.

Dr. Karen Jaffe: I think that all those things that you say are so important, I feel that as a Parkinson's advocate, I try to talk to patients about self advocacy, that they need to own their disease and control it. But we're also talking about a group of people who are 60, 70, 80. It's hard to make an old dog learn a new trick. You know, we can say eat healthy, or exercise, but trying to get that to happen is difficult. But I do want to send the message that these things do make a difference in your quality of life. And if you're sitting at home and you're not moving, you're going to find that you have more pain, more troubles. Some of this is all masked though, by something called apathy. And that's a hard one. I mean, it's a hard one to know exactly what is causing it or whether it's part of the disease or whether there's another reason for it.

Dr. Karen Jaffe: But apathy is the big reason that people fall through with it, with some of these suggestions, would you agree?

Dr. Veronica Bruno: Yeah, exactly. Apathy is one of the symptoms that challenges us the most because we don't know how it happens. It can or not happen, it can happen at any point in the course of the disease and we don't have a very good approach to it. We don't have a particular treatment. I would say my suggestion to my patients I notice, or they notice that they are feeling less engaged with things, not enjoying things as usual. They don't want, don't feel like going out. Don't feel like seeing family or friends. Try to find the support of someone like Marc, like a care partner, like a friend, like have Parkinson's body. Someone that can tell you, "I know that you don't feel like going out, but we're going to do it anyway." And after that, you're going to feel much better. And everybody, most of the people confirmed that after they pass that barrier, even if they feel that they don't want to do something, they feel much better after. And they say, "yeah, you are right, you know I enjoyed this so much and you really helped me feel much better."

Dr. Vikram Khurana: Underscore one aspect of that. And that is that there are just so many great group programs that are out there increasing all the time at the community level. And I've found that my patients in general really love that. You know, when they're part of a program and that collective energy is really important.

Dr. Karen Jaffe: Right. And then a lot of people are worried about going to a group because they're worried that they're going to see somebody who's more advanced than themselves, but it doesn't really work that way. I mean, most people look well who are out and about, and they feel well. And I think it's very encouraging to see people who have been living with the disease for many, many years. Vik, how much impact can a medication adjustment have in the management of people's changing symptoms? And in that respect, do you have a comment that you can make about work delay and using carbidopa-levodopa because of worry about dyskinesia?

Dr. Vikram Khurana: I'm so glad you brought up that question. So I think medication dosage, as I mentioned, right at the beginning, working closely with your physician adjustments, these are really important. It's really important to know that something that works at one period of time in a year or two may not be the most effective strategy for you. This is, a moving target and it's constantly evolving. So I would say, this dialogue is really important. Keeping logs of your symptoms, actually getting some quantitative data. It can really help your physician work with you as a team. Increasingly, we're going to see biometrics out there in the community, the use of cell phones so that we can track our movements in an objective way. And this kind of data can be helpful for your physicians. So adjusting medications, changing medications. In general, thinking about changing and dosage or changing a frequency. These are the things that we need to think about and sometimes changing a formulation.

Dr. Vikram Khurana: At some point you might need to switch from a medication that's an immediate release, to a controlled release or a combination of an immediate and controlled release. These are all things that you should be considering as this evolves. And finally, this really critical question that you raise of being sparing of levodopa. I think that the long-term data would suggest that really our patients should do everything they can to treat their symptoms and improve their quality of life. The concept that if you try to spare yourself from levodopa, you will somehow have a better disease outcome or be able to use it for longer later, has generally not been born out in any long-term studies. And in fact, some of the most interesting studies have related to populations, such as in Africa where patients have not had exposure to levodopa for a long time and their illness, and then have had exposure, and it turns out that the effects like dyskinesia and other things are really no different in patients that are exposed long-term to levodopa or not.

Dr. Vikram Khurana: And so while there are different, there are different pieces of data behind this in general, my philosophy certainly, and I think this is philosophy of the field now. Is to treat our patients most effectively. And if medicines are not as effective as levodopa, there's no compelling reason to spare oneself from using levodopa. Treat yourself. These are not altering the course of the disease one way or another is our consensus right now.

Dr. Karen Jaffe: Great. Thanks. Well, regardless of how many years I've had Parkinson's disease, one of the most pressing issues for me is what is happening with PD research that is helping us to manage the symptoms of Parkinson's that is also getting us closer to a cure. All right, let's start with some trials focusing on improving life with PD.

Dr. Veronica Bruno: Yes and this is a very important part, I know that you're all waiting for me to tell us about stem cells or disease modifying treatments, but it happens to patients that have some years with the disease that they sometimes are frustrated because after so many years, "I cannot be part of the biomarkers or the early diagnosis trials. So what can I do for research? There's no place for me." And that's not true because there are many different trials going on right now. Trying to improve your quality of life. So trials that are focusing on improving the [inaudible 00:38:39] parturition, reduce these [inaudible 00:38:42]. Trials that focus on new medications to make the on periods last longer, reducing the fluctuations, the ups and downs that you may experience during the day. There are new trials also improving the use of intestinal [inaudible 00:38:59] levodopa.

Dr. Veronica Bruno: So in terms of the motor symptoms, there are many things going on. Trying to, until we get a cure, making the management of your symptoms and your medications much better. But there are also many trials trying to tackle those non-motor symptoms that I mentioned before. So there are a few new compounds that have been tested in places like London, Ontario, and Canada, or California, searching for treatments for dementia and Parkinson's, these are experimental, but they're already been tried in humans. There are also some trials trying to use medications that have been shown to delay the onset of dementia and Alzheimer's in Parkinson's disease. And there are different trials trying to find mood solutions for mood disorders, pain. Myself, I have many trials trying to treat pain in different ways. And what I found, it's very exciting, is that now we're not focused on medications all the time, but there are now trials to show what we just mentioned, that there is evidence for exercise, for acupuncture, for probiotics, for Mediterranean diet.

Dr. Veronica Bruno: We're trying to understand the role of cannabis, because this is a very important topic these days. So there's a very long list of trials that you can find using the Fox Trial Finder tool or the clinical trials, that gov website. If you want to ask someone in your family to help explore those resources, but the most important thing is talk to your doctor and ask, and don't feel that because you have had 10 years of disease, you are not a good candidate for research anymore. We really need you. We cannot find treatments or solutions without you. So feel free to contact your community and ask because there may be a trial that you may benefit from, but also help us understand all these symptoms a little bit better.

Dr. Karen Jaffe: Thanks. Okay Vik, everybody's asking me questions about this. Can you talk about your work using stem cells and other disease monitoring approaches used to slow establishment?

Dr. Vikram Khurana: Sure. I'm happy to. Rather than focus on my work, maybe I'm just going to give some pointers about how to think about what's out there in the field right now, and I can answer any more detailed questions. So I'm going to put disease modifying therapies in their first big category. And what do we mean by that? We've talked about Parkinson's being a multi-symptom disease. Critical to the disease is a protein alpha-synuclein, which many of you will have heard of. This is the protein that aggregates in many different cell types of the brain, not just dopamine neurons, but cortical neurons that relates to cognitive dysfunction, autonomic neurons relating to bowel, bladder, sexual dysfunction, and so forth. This protein is very involved in the disease. And so if we're thinking about disease modification we're basically saying, "can we intervene in a way, that alters the outcome aggression rate." This transmission from motor to non-motor symptoms in this multi-system disease.

Dr. Vikram Khurana: And I'm going to describe three categories for simplicity. The first is that a small number of patients right now have well-defined genetic mutations that relate to their disease. Patients who, for example, carry the mutations in a GBA or LRRK2, also known as LRRK2. There are active trials that are specifically be provided for patients with Parkinson's, who carry changes in these genes. So that's one category, genetic related. This is the big category relates to therapeutics that are really directed at alpha-synuclein themselves. And I'm going to talk really about a couple of approaches. The first major approach is decreasing alpha-synuclein. And so antisense oligonucleotides are a genetic approach to decrease alpha-synuclein. There are small molecule drugs that are being tried to decrease alpha-synuclein. There are antibodies that are being tried to let's say, soak up alpha-synuclein and reduce its levels. And then there are companies that are looking at the downstream, what happens after alpha-synuclein clumps up in neurons, what the downstream effects of that are and using either molecules or genetic therapies to reverse that.

Dr. Vikram Khurana: So these are different ways of thinking about alpha-synuclein. So genetics was the first bucket, alpha-synuclein directed is the second bucket. Then I'm going to broadly talk about other types of therapies that look at the reaction of the brain or the metabolic state of the brain. And there are a number of different types of medications directed at metabolic state into unrelated signaling, for example, that are being advanced to trial. We're learning a lot more about the interaction of inflammation and which is the response in the brain and the microbiome, for example. So this is a very active area of, of research.

Dr. Vikram Khurana: Could we change something in the gut of Parkinson's patients to alter the disease course in the brain? So these are, this is not an exhaustive list, but this is just a way for you to think about classifying them. And finally, we come to stem cell transplantation therapy. So there are two different ways people think of stem cells. So for example, in my lab, I generate human stem cells from my patients in order to develop an understanding of the patient's disease and to develop drugs and other therapies in the dish when I make the stem cells or even mini brains now from our patients. But other advances relate to transplanting stem cells back in the brain.

PART 3 OF 4 ENDS [00:45:04]

Dr. Vikram Khurana: ...this relate to transplanting stem cells back in the brain and I think this is inactive. A lot of you will have active questions about this because we know that different companies now, and academic groups around the world, are advancing these types of stem cell therapies. I'm happy to answer questions in detail about them. They are all a little different. Some trials seek to make a off the shelf stem cell product that is transplanted into the patient. Other smaller scale efforts, actually using a skin biopsy, for example, can make a patient's own stem cells from themselves, these are the kinds of techniques I use in my lab all the time and then make their dopamine neurons and transplant those back. So these are called allogeneic, either off the shelf or autologous from oneself, stem cell therapies.

Dr. Vikram Khurana: And so these are the different types of approaches that are out there. And whether or not stem cell therapies are disease modifying is still a very open question. In general, the field probably considers them as a way to replace dopamine in a physiologic way, maybe a little more naturally than using deep brain stimulation to alter circuits, but just like deep brain stimulation, not obviously expected to change the course of the disease. That's a complex question, but generally, we put stem cells in the symptomatic therapy group and not disease modifying, but really time will tell. We have a lot to learn about those kinds of therapies. Happy to answer any more detailed questions.

Dr. Karen Jaffe: Oh boy, it sounds like the pipeline, the research pipelines, for Parkinson's is pretty robust. In the interest of time, I'm going to direct you, in terms of DBS and that you see on the slide there, to a recent webinar and a Fox Foundation guide that details the latest research in DBS.

Dr. Vikram Khurana: I'll just make one more minor point on DBS that could be important for people to hear, that DBS is really a therapy for patients who respond to dopamine. They may have side effects from dopamine, but DBS is not considered for patients who really aren't good responders to dopamine. That's one point I just want to make there.

Dr. Karen Jaffe: Thanks, Vik. Thanks. So this discussion about research is a great segue for me to talk a bit about the foundation's landmark study, PPMI, and its new recruiting efforts. The Parkinson's Progression Markers Initiative, also known as PPMI, is the study that could change everything about how Parkinson's is diagnosed, managed, and treated. Right now, the study needs parents, brothers, and sisters, adult, children of people with Parkinson's to take a short survey. You can even get started right now by clicking the get started tab in the Take Action box on your screen. The study is also recruiting people diagnosed with Parkinson's in the last two years, who are not taking medications yet. You can learn about the PPMI by clicking the link in the resource list and help spread the word about the PPMI. The link to share is michaeljfox.org/ppmi, that's michaeljfox.org/ppmi. So Marc, I'm going to have you kick this segment off and hit because of your recent participation in the PPMI and helping not only me, but the Parkinson's community abroad.

Marc Jaffe: Well, as a care partner, one of the things that is so frustrating is that you feel like you can't do anything for your partner, in terms of making the disease go away. But there is, in a way, I realized after we were in it for a while, and that is participating in clinical trials. And I was fortunate that when the time was right for us and I was available, that the PPMI had just opened up and was looking for not just people with Parkinson's in control, which they are again. So I signed up and it's been very helpful to me to know that I'm benefiting the Parkinson's community and hopefully one day to find a cure from this.

Marc Jaffe: And the study has been amazing. I don't know how many billions of downloads there have been of all the data and of all the vitals that people have given, but it's been a lot and it's done amazing things to this point. I've been in it for about seven years and they're now opening it up again to a whole new consort of people who are participating and just being a part of something that, hopefully one day, will lead us to a cure is very rewarding.

Dr. Karen Jaffe: And we all appreciate it. So any of our other panelists, Henry, Vik, Veronica, have any words of wisdom for the Parkinson's community who are watching this today and how they can get involved to make a difference in how Parkinson's disease is treated and managed and dealt with?

Henry Hansmann: I confess, I have nothing special to add at this point. I haven't participated in any of the studies. Largely in due time and location problems, I commute back and forth between New York and New Haven, but my life is now opened up so that I can really do it. And I need to participate if I can.

Dr. Karen Jaffe: Well, there's a great study that likes to tell people about it, it's an online study that the Fox foundation does called Fox Insight. And it is collecting information from people with Parkinson's, as well as care partners, regarding living with Parkinson's disease. You don't have to leave your home, it's done right on the computer. Quarterly, they send you a series of questions that you answer and they're collecting this data from tens of thousands of Parkinson's patients in order to direct their research efforts, not only in the lab, but in the clinic. It's our opportunity to share with the Fox Foundation and researchers what it's like living with Parkinson's disease and what should they be looking at, in terms of research, that can improve our situation. So, that's Fox Insight and anybody can sign up for that. Like I said, you don't have to leave your home, it's just done quarterly on the computer.

Marc Jaffe: That's also for people without Parkinson's as well.

Dr. Karen Jaffe: Right.

Dr. Veronica Bruno: I think it's an important point to remark that we are moving through something that is called patient-oriented outcomes in research. So we want your opinion. We want your feedback. We want to know what you think is more important, where should we focus? What are the areas that you found are more challenging? So if you stay at home and you don't get in contact with the community, it's very hard for us to know, but if you approach us, we will be happy to learn more. The world community, the global community, we're all very open to learn more from you so we can find the cure, but also the best way to manage Parkinson's all together.

Dr. Vikram Khurana: On the research perspective, I would just add that we have so many, as you said, the pipeline is so strong, but there is a huge challenge in translating great insights from the lab into an effective clinical trial. This is a really major challenge. We don't fully understand how to match a patient to the right treatment. We're in our infancy of understanding that and efforts like the PPMI, and other efforts that track patients longitudinally over time, are so important for us to be able to diagnose the disease early, or if it's during the course, to understand how we can classify patients and watch them more appropriately for the right kind of therapeutic trial. So we won't be able to do that without gaining the kind of information that the PPMI study is really trying to elicit. And I can tell you, I use the PPMI study daily. It's a very, very well run study. And for researchers like me, it's been very pivotal not to design hypothesis and then test them in the lab.

Dr. Karen Jaffe: Thank you, I agree. Well, again, I want to acknowledge that this webinar is brought to you with the support of Acadia Pharmaceuticals. We have received a lot of questions and you can still submit them. So let me start reviewing some of the questions that we have before we close up here. Some questions on genetics, do I need to get tested after diagnosis? Can family members get tested? What can it tell me? Does it impact treatment? That's a big question. If somebody wants to give a distinct answer to that question about genetics and who should be tested.

Dr. Vikram Khurana: Yes. I think in general, we test patients these days who have strong family histories or early onset cases. The bottom line is genetic testing is much more widely available, especially in major research centers and is much more covered now by Medicare and insurance companies. So it's much easier to obtain and there are good studies that allow also completely free testing. So talk to your doctor about that.

Dr. Karen Jaffe: Great. Veronica, somebody is asking, are there recommended drugs to treat mild cognitive impairment?

Dr. Veronica Bruno: Yeah. So the truth is that the trials that have tried different medications for mild cognitive impairment in Parkinson's didn't show significant benefit. There are some drugs that we can use when there is a diagnosis of dementia, but not for mild cognitive impairment, in terms of medication. However, we know again, that treating mood disorders that may be masking or worsen in mild cognitive impairment, reduce some of the Parkinson's medications, such as dopamine agonists, or amantadine. And exercising, as well as controlling the risk factors for the cardiovascular risk factors as hypertension, diabetes, high cholesterol, all those can help reduce the progression of mild cognitive impairment to dementia.

Dr. Karen Jaffe: And do either one of you want to answer the question, how close are we to a cure?

Dr. Vikram Khurana: Closer every day, closer every day. It's a robust pipeline, please participate. This is a partnership between researchers, clinicians, and patients, and we need your involvement. It's so exciting what's out there right now, but we're going to need to work as a team.

Dr. Veronica Bruno: We are facing an extremely exciting time in terms of new mechanisms of potential therapies. So hopefully, for sure, we are much closer than ten years ago, and we have some of the brightest brains in the world thinking up a cure for Parkinson's. So hopefully it's much closer than what we think.

Dr. Karen Jaffe: It depends on how you define a cure. If somebody told me that they could stop my Parkinson's where it was, but not go back to normal, I would consider that a cure. And I think many people who think that would be a cure to be able to just stop the Parkinson's where it was at. I think that you were both young and so you probably worked when you got into medicine and into neurology, didn't have to see how it used to be, but 30 years ago, I think the life with Parkinson's was very different than it is today. And I've met lots of people with Parkinson's disease and they're living well, and they're working hard at living well and being self advocates and really taking away a lot of the stigma that's associated with Parkinson's disease and working with it and continuing to be well and living well with Parkinson's disease.

Dr. Veronica Bruno: And, sorry, short comment. We have witnessed this with other diseases, like multiple sclerosis, when in five years many therapies, modified therapies, for the disease appear and the management changed completely. So there is a lot of hope out there and a lot of science going on. So let's keep working to reach that point together.

Dr. Vikram Khurana: And the time at which a good idea can get into the clinic is becoming shorter and shorter. Of course, it's still team effort, but it used to be 10 or 12 years before something in the lab could get out into clinical trial. That is reduced considerably now, both at the regulatory level and because of the pace of science, we're seeing early ideas getting out into the clinic within a few years for the first time ever. So I think these are all really promising signs.

Dr. Karen Jaffe: Well then it must be also a sign that we have more people who are willing to participate in research. I know that 80 percent of clinical trials get slowed down because of poor enrollment and 30 percent get stopped because there's not a single enroll. They don't have enough enrollees to keep going. So there's a lot of research that's probably worthwhile and it's sitting on a shelf waiting for somebody to participate in it. And so it's important that we take that on as ourselves. We've only gotten to where we are in Parkinson's disease today because of people before us who were willing to do the research and to be participating in research. So I encourage people, not only is it important, but it makes you feel good because you really feel like you're helping the Parkinson's community enlarge, and you are.

Dr. Karen Jaffe: So Fox Trial Finder, as they mentioned earlier, is the place to find clinical trials that are related to Parkinson's disease and you can just go to The Michael J. Fox Foundation website to find both Fox Trial Finder and Fox Insight. And those are two good ways for you to help advance the cure that we're getting right now, so. Okay, well, I think we are close to out of time. I wanted to thank my panelists for participating in this discussion. I think there is probably a lot of questions that can be still answered. And I think that the Fox Foundation will look over your questions that you submitted, and hopefully we can find a way to answer those questions for you. But thank you all for joining us and I'm going to end here and wish you all a great day.

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PART 4 OF 4 ENDS [00:59:53]