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Speaker 2: 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.

Maggie Kuhl: Hello, thank you for joining us for this webinar. I'm Maggie Kuhl, vice president of patient engagement at The Michael J. Fox Foundation. Today, we're going to be talking about volunteering for research studies. We'll discuss how participating can benefit you and the Parkinson's community. We'll cover some things to consider when finding the right study for you right now. We've got a lot to discuss, so let's get started. Let me first introduce our panelists.

Lauren Traub is a nurse practitioner who was diagnosed with Parkinson's disease in 2018. She has volunteered for the online Fox Insight study, sharing information there on her disease journey and perspectives on Parkinson's research. Lauren, welcome.

Lauren Traub: Thank you, Maggie.

Maggie Kuhl: We also have Bret Parker. Bret is the executive director of the New York City Bar Association and co-chair of MJFF's Patient Council. He was diagnosed with Parkinson's in 2007. Bret has volunteered for multiple observational studies, and recently enrolled in his first interventional trial, testing a therapy for tremor. Thanks for joining us, Bret.

Bret Parker: Thanks for having me, Maggie.

Maggie Kuhl: And finally, we have Dr. Paulina Gonzalez Latapi. She's a movement disorder specialist and an assistant professor of neurology at Northwestern Medicine Feinberg School of Medicine in Illinois. She is involved in several research trials and leads the Hispanic Movement Disorders Clinic at Northwestern. Thanks for being here, Paulina.

Paulina Gonzalez Latapi, MD: Thanks for having me. Excited to be here.

Maggie Kuhl: Well, let's start with the why and the who of research. Each medication that makes your life with Parkinson's easier, every test for risk, onset, or progression, they started with research. Lab research into the biology of disease, surveys on what matters most to people with PD, and clinical trials, testing a treatment safety and efficacy. And when a cure is found, the first person to get it will be in a trial and it will be possible only with the input of thousands who before have raised their hands for research. Paulina, can you tell us who do we need to participate in research?

Paulina Gonzalez Latapi, MD: Well, the short answer is everyone. We need people who have been diagnosed with Parkinson's disease, people who may have a risk factor for Parkinson's disease, and particularly we need people who come from different backgrounds and different ethnic and racial backgrounds as well.

Maggie Kuhl: Can you talk to us more about that? Why do we need diversity in research, diversity in the participants who are joining us in these studies?

Paulina Gonzalez Latapi, MD: Certainly. I mean, as you mentioned, with research, we're trying to understand the disease better. We're also trying to understand how certain interventions and certain medications might help or might delay the progression of Parkinson's disease. If we only focus on just one type of population, so only people coming from certain areas or only people with certain backgrounds, then we're really only seeing one piece of the puzzle as opposed to seeing the whole picture. So, that's why it's really important to have a diversity in our clinical trials and our observational trials as well.

Maggie Kuhl: Absolutely, yeah. There was a notable breakthrough last year, for example, of a new variant in a gene, GBA1, that this variant was found to raise Parkinson's risk in people of African descent, which a lot of our basis of understanding on why Parkinson's occurs is based on people from European, Caucasian descent. So, that was a great example of why diversity in studies can really lead to new breakthroughs and hopefully one day more personalized treatments.

I wanted to call out before we move on the mention of care partners. And often, people who have a loved one with disease will enroll in studies as control volunteers, but there's often studies, especially learning about priorities and perspectives, that are solely asking people who caretaker love someone with PD for their perspective. So if that is you on this webinar, you are a valuable participant in studies as well, and we hope that you see that and will join us in those efforts.

On top of impact on science and how we're going to get to cures, there are a lot of reasons to join studies. Lauren and Bret, Lauren first, and Bret, I'll ask you to wait and share after, just share your own journey with research and what led you to raise your hand, what type of studies you've been involved in and why.

Lauren Traub: Absolutely. Absolutely. My journey, it started in 2018. I was 31 and I was expecting my first child and started developing some symptoms that many of our listeners probably likely have experienced with that twitching pinky finger. That led to a tremor, some gait troubles, and it led me on that journey of seeing multiple specialists getting misdiagnosed. But ultimately, I did land in the office of a movement disorder specialist and was given that Parkinson's diagnosis. As one can imagine, it's unexpected. It's a very emotional time. And for me, after that initial shock, it kind of sparked me into thinking, "What can I do next?" It led me to kind of reach out to the Parkinson's community, find individuals to connect to, and I ultimately did get connected with a member of the local team, Fox Detroit chapter here.

I was invited to a local research salon that they had put on, and I was able to get a first introduction into what the Michael J. Fox Foundation does. The researchers spoke about the current state of research and the future direction, and I was really inspired by that. I felt this call to action and really wanting to do my part and get involved in that, led me to enroll in the Fox Insight study, which is considered an observational study, and it really was the right fit for me at the time.

Maggie Kuhl: Bret.

Bret Parker: My journey at the beginning was very similar. Back in 2007, I was 38, two young kids, barely noticed my symptoms, got diagnosed very quickly, and for the first five or so years, didn't do much about it, didn't really take any medication and didn't tell people about it. And then, my first foray into outing myself was to get involved with Team Fox and do some events. Research was not in my mind because I'm thinking to myself, "That's not for me. Why would I worry about research? I have such minor symptoms." And then over time, realized that I'm not a researcher, I'm not a scientist, I'm not a doctor, I don't have the big scientific brain, so maybe I could volunteer to do some research. And so, it seemed to be, "We'll talk more about it." It seems to be a way that I could help out and try to help find a cure.

Maggie Kuhl: Yeah, I think what I heard from both of you, Lauren, that question, what can I do, is something that a lot of people recently after a diagnosis ask and research is absolutely part of that answer. Some other benefits of joining research, and that middle one about access to specialists. Can you talk to us maybe about what the research experience might be that you're sitting and you're interacting with a team of specialists, who are not your individual Parkinson's care team, but do every day, in and out, see people with disease and really have perhaps the answers to some questions for folks?

Paulina Gonzalez Latapi, MD: Certainly. I mean, a lot of these research initiatives happen at academic centers and are led by movement disorder specialists. Again, people who are very tuned into the area of Parkinson's disease and what is the latest, what is coming down the pipeline. So, my experience, as an investigator in the PPMI initiative, for example, I see people who, some of them might be my own patients, but a lot of them are not. They actually come from outside of Chicago. It's always nice to have a conversation about what have we learned with PPMI, what other studies are we doing. Again, having that access to those specialists can also lead to further insight into what other research someone might be eligible for.

Also, we do the exam that someone might get when they see their movement disorder specialist or their neurologist, so it's also an insight into how they're doing, at least on that particular day that I see them. We also may talk about the medications that they're on, if it's a trial that allows them to be on medication. Again, it's also a chance to ask questions to a specialist.

Maggie Kuhl: And just to meet more doctors. Sometimes, finding the right doctor for you is a little bit like dating, taking some trial and error, might be things you like or don't like. And so, being in a research study, you just get exposed to other physicians versus just picking someone online or trusting your referring physicians. So, that

might be a benefit for enrolling in studies as well. Even if folks want to say yes to joining studies, though there could be real challenges to doing so, could be historical, personal, logistical. Paulina, could you talk to us a bit about some of the life or just feelings that might get in the way?

Paulina Gonzalez Latapi, MD: Of course. I mean, again, I think Lauren and Bret also touched upon some of the difficulties that might arise in joining a study. First of all, knowing about what studies are available and whether someone's symptoms are mild or whether they're eligible for a study. But there's certainly other logistics, especially people who are diagnosed at an early age. They're still working, so there's scheduling that might get in the way. There's also some studies require a little bit more involvement, require people to come to the hospital a little bit more frequently for some questions, for some tests.

And there's also some concerns about how data will be used, how the information that we collect will be used, whether people will know who is in the study, how do we preserve people's anonymity when they're in a study. Again, all of those are things that we certainly talk about and should be talked about when someone is thinking about participating in research.

Maggie Kuhl: Bret or Lauren, anything in your personal calculation or even if you said yes, something that made it difficult perhaps to comply or to continue in any studies?

Lauren Traub: Yeah, I think to echo what Paulina said, I think if you're someone that has a young family, you have to think about caregiving. There's the transportation. Can I be away from my home, my family? Can I even physically get to the center? So, those certainly are concerns that I would have as well. Further too, I think everyone has their own individual risk tolerance, if you will. I think maybe at this time in my life, I want something that's a little bit more of a low risk study and maybe that it certainly will likely change over time. So, I think that's a consideration too, those logistical factors, and then your own individual risk and what you're ready to do.

Bret Parker: Yeah, similar for me. I mean, the cost-benefit analysis, and early in my journey when my symptoms were very minor, I didn't want to risk taking a drug or doing a clinical trial where the side effects could be worse than the symptoms I was having, as we'll talk about is that my journey continued, that analysis changed a little bit. But at the beginning, side effects were a concern of mine and I didn't want to take a chance.

Maggie Kuhl: And it's absolutely a personal calculation, a conversation with your doctors and your loved ones. Just to share at the foundation, we are working in studies that we directly fund or support, or companies that we work with who are leading studies to really surface to them some of these challenges and how things, like paying for a caretaker for children or making sure that travel is not just reimbursed after it's been purchased by the participant but coordinated and paid for upfront, can perhaps address some of these. There's no perfect solution for everyone, but make it easier if those are some of your logistical challenges to be able to participate.

We got one question that I wanted to raise to you. How do you know if a study is legitimate? I, for example, in my recruitment work for some of our studies are using Facebook advertisements, and we're looking for ways to reach people where they are, be it through flyers or digital ads or such, but that means that it's sort of a faceless, nameless entity and it's not your position in front of you saying, "This is something that I am very aware of and I think you should do." So, if people are hearing about studies out in the world, how are they to know that this is a legitimate, approved, with all the right protections and such? Paulina, any green flags or red flags folks should look for?

Paulina Gonzalez Latapi, MD: Yeah. I mean, certainly studies that are sponsored by one of the Parkinson's bigger foundations that deal with Parkinson's, particularly The Michael J. Fox Foundation, that's a good way to confirm whether a study is valid, and that's a green flag for me. I know that The Michael J. Fox Foundation, their webpage has the wonderful trial finder, so that's a good way to find trials around the world. Certainly, any trial or any study that is presented to someone where they volunteer is not a volunteer but actually needs to pay for the chance to be in the study, that's a big red flag. Certainly, you shouldn't need to pay for the chance to participate in a study. So, huge red flag there.

I think other green flags, certainly you want to know that there's an oversight. We have, for all studies, whether observational or interventional, there's an institutional review board or IRB, which has the ethical and just the oversight committee for any study. You, as a volunteer, you always want to make sure that that's very clearly stated, and that there's also an informed consent so that you know what is expected of you as a volunteer, what are your rights. So, those are all green flags that a study should have.

I mentioned the trial finder. There's also another webpage called clinicaltrials.gov, which, again, most studies, particularly interventional studies, will be registered there. ,So that's another good way. Ultimately, I would advise anyone who's considering participating in research to also discuss it with their neurologist or movement disorder specialist. That's one of the reasons that we are here, and we're always happy to discuss the pros and cons of different studies.

Maggie Kuhl: All right. We're going to continue on in our conversation to leave time for lots of questions from the audience. We have alluded to the terms observational and interventional, and we want to define those a bit. So, an observational study is one that is not testing a new intervention, that can be a drug or another intervention, another strategy or tactic, like exercise or such. It is just learning about the individual and their disease. Where interventional is assessing the impact of some [inaudible 00:15:48]. We can talk a little bit more about that.

But, Lauren, you have been in observational studies, and Bret, you were in many and then have just transitioned into an interventional trial for the first time. Maybe you could talk a little bit about what that experience has been like, Lauren, filling out the surveys in Fox Insight. And then, Bret, what was your decision point or your sort of I'm ready to take that step and to try something new and experimental? Lauren first.

Lauren Traub: Yeah. As you mentioned, Maggie, I joined up for the Fox Insight study, and what I love about this study is that it's a patient-powered study where we get to really share our true lived experience with Parkinson's. It's something that you can do in the comfort of your own home. It's easy, it's low risk, it takes 15 to 20 minutes. We're responsible for quarterly visits, so it's not something that's overwhelming. It's easy to do just a few times a year. So, it's really been a great experience because you can really participate and work at your own pace. I find that it's been insightful for myself. It's been a bit of a symptom diary, and I've got to track my own progress over time. So, definitely very low risk, easy to do, and provides that sense of fulfillment to push things forward.

Maggie Kuhl: Great. Bret, how about you?

Bret Parker: I mean, similarly, I mean, the observational studies, and I started with the online ones where you just fill out information. And then over time, increased my engagement in observational studies. Some of them required that I make visits and give skin samples or do tests. What was helpful about that was, again, there was no downside of risk of side effects from taking medication. They were just observing me, and it made me more thoughtful at times about my symptoms. It was a way to do a check of how my symptoms are progressing and be aware of things which I might not think of when I'm sort of caught in the middle of being the patient, and so those are very helpful.

Observational studies can also require more engagement. The last observational study I did had a lumbar puncture similar to the PPMI study, and that actually was, as much as it seemed scary to do, it was actually easy to do, and in fact, easier than some of the other things that I've done. So, that was observational and also a good experience for me, and I'll talk a little bit about interventional in a second.

Maggie Kuhl: Yeah. Well, you did-

Bret Parker:

Maggie Kuhl: ... know that you did the lumbar punctures. What changed in your disease or your...

Bret Parker: I hit the point where my symptoms were progressing and one of the symptoms that bothered me the most was tremor. It was the one that I noticed more at work, when I'm concentrating or focused. So, I got contacted about an interventional study for a drug that was focused on just on tremor and signed up for it recently. In fact, all it requires that I do is take three capsules once a day in the morning. There's a weekly follow visit, but a lot of them are online or virtual. There's also, there's a great benefit to it. First of all, they do blood tests on me and they actually noticed that my HDL was a little high, which wasn't related to this, but it was. I got the benefit of this information for free. So far, it's been a great experience.

Now, I may have the placebo, I have a 50/50 chance of having a placebo, and it's double blind, so the people I interact with don't know either. It's early in the study, so I really can't tell either way. But at the end of it, I'll have the benefit of having access to the drug if it's found to be effective. To me, this is my first interventional study. I haven't had any side effects for me at least, and so it's been a good experience so far.

Maggie Kuhl: Paulina, we were chatting about a couple of days ago in preparation for this call, about the interrelationship between observational and interventional studies and how critical it is for us to learn about the disease, learn about what patients feel, care about, want, consider through observational studies to really inform what and how we do in driving toward new treatments with trials. Can you talk a little bit about the value of those and how you see them all feeding towards cures and new treatments?

Paulina Gonzalez Latapi, MD: Certainly. As you well pointed out, with observational trials, we're trying to understand the disease better. That means either understanding better how symptoms progress over time, understanding what blood markers or cerebral cerebrospinal fluid markers are correlated with different symptoms, correlated with disease progression. All of that ultimately fits into the interventional trials in different ways.

In some cases, we might learn about different molecular pathways that are important or that are playing a role in the disease itself, and that can help us identify new avenues or new possible medications that could be used to treat or to modify the progression of the disease, so finding new pathways. It also may help us, again, by trying to find a blood marker or a cerebrospinal fluid marker may also help us when we design these interventional trials to think about what change are we looking for. Are we going to measure change and the efficacy of that medication that we're testing?

And then, of course, it's also, and something that has been a major focus recently has also been the patient experience. While we, of course, want to see a change in the exam that we do, in some of the blood markers or other biofluid markers, we also want to know the quality of life. And so, there has been, with observational trials, we've learned a lot about what is important to the person living with Parkinson's disease, what's important to their care partners, and that also we take into account when designing the interventional trials. So really, they're very, very interrelated. Again, they fit into each other in those ways.

Maggie Kuhl: I have a note, I like to play sort of translator or just make sure that as we talk about scientific topics and use certain terms, that everyone in our audience is coming along with us. We've used the term placebo in our conversation today. Just to define that, in trials, they want to know that the effects that they're seeing are truly for the drug and not because someone thinks, "I know that I'm receiving this intervention, and so things have changed, even just informed by that knowledge." And so, they try to mimic the experience of receiving a treatment with something called a placebo. If you're taking a pill, it might be a sugar pill. It's an inactive substance. It's not supposed to do anything related to the disease. It could be a saline infusion versus a therapeutic infusion. Sometimes in exercise

trials, for example, we ask people to just stay where they are, work as more of a control group. Trials try to work in a control or a placebo group to compare.

I will say that that is a concern for people in enrolling in studies. I don't want to go through all this if I'm going to get the placebo, like Bret was saying. Sometimes, the study will design so that even if you receive the placebo at first, you have the option to receive the therapy at some point. Or I was on some calls recently with groups that are looking to change the groups from one to one receiving therapy to placebo for two to one. So, you might have a greater chance, a greater likelihood of receiving the therapy. And so, studies again, are trying to make it easier for people to say yes, still maintaining the scientific integrity, but really more participant-informed, participant-friendly designs.

PPMI, we've referenced a couple of times, it's a longitudinal, that means we follow over time. Observational, observing the disease as it progresses or comes on. We are enrolling people who may be at risk of disease, people who do not have Parkinson's. Any age 18 or older can join us online. People 60 or older with certain factors may be invited to participate at a clinic. We cover travel and all the things I've been saying today about trying to make it as easy as possible. People who do have Parkinson's may also be eligible for the clinic population, and this is really the cornerstone of Parkinson's research. If you heard about the big biomarker breakthrough last year or the year before around alpha-synuclein, that Parkinson's protein that came from volunteers and PPMI contributing samples over time and us studying the disease. So, it has led to a lot of change in how we do research and what we are studying. You can be a part of it by going to michaeljfox.org/ppmi.

Now, we're going to talk a bit about choosing the right study for you. We've talked a lot about your readiness and some of the challenges that you may be thinking about, but really, okay, I would like to do this, now what? Paulina, you have mentioned some of these entities already, but if you were talking to a patient in your clinic, what would you say about how to find the right study for them?

Paulina Gonzalez Latapi, MD: Yeah, certainly. I think, first of all, understanding what are the different studies and those two big pockets, the observational studies, interventional studies. Something to take into consideration is whether a patient is already... If we're enrolling a patient, whether they're already taking medication or not. Because again, some studies might require someone to be medication naive, meaning they've never taken any medication. Something to consider is also what is expected of someone as a volunteer. What is the time? Does a study involve only one blood draw, or is it a every year visit? Is it every three months? That's important information to have. Again, for example, as Bret pointed out, there are certain studies that might be studying, trying to find a medication for specific symptoms. So certainly, if there's a symptom that is a major concern, then probably talking about those studies would be of use as well.

Maggie Kuhl: Bret, how did you find the studies that you've been in?

Bret Parker: At first, I used Fox Trial Finder just to get connected with my first studies, and then it turned out that some of the studies that I was being directed to were out of the hospital that my movement disorder specialist came out of. Literally, I feel like once they got to know me, they got to know me very well and they would keep their eyes out for other studies that were of interest to me, and so they would call me and say, "Hey, we've got a study on X. Would you be interested in participating in that?" I'd say yes or no.

So, a lot of it is you get connected with an institution, and then actually, what I've found is they asked for feedback from me on, "Well, if we had a study on this, would you participate then?" Sometimes, I think it's helped prompt them to create a study, and when it's patient-driven like that, it makes it even more meaningful. But that's how I found most of them. And they're not all from where my doctor's located. There's another hospital university that I work with.

Maggie Kuhl: Paulina, we have a couple questions from the audience on eligibility and how a medication that someone is taking or also DBS often might play into what studies people are eligible for. Can you talk a bit about eligibility criteria and how studies determine who they will enroll and how people can sort of navigate that based on their own treatment regimen?

Paulina Gonzalez Latapi, MD: Yeah. Eligibility criteria, that's an important aspect of designing any trial. We want to make sure that we're choosing the right population, so that we increase our chances of success. That's where the eligibility criteria might include certain age or might include being at a certain stage in the disease. A lot of the trials that study a new drug or a new medication that could delay disease progression might require people to, again, have never taken any sort of treatment or they might exclude people who have undergone the brain stimulation, because again, that's a form of treatment in Parkinson's disease. The reason for this is that we want to make sure that this new medication that is being tested is truly producing the effect versus just being an effect that we see from the other medications or from the DBS. So, we're trying to make sure that if we're seeing an effect, it truly comes from the new medication that we're trying.

Now, something important to say is that while a lot of, again, this disease modifying or these trials where we're trying to look for a medication that will delay disease progression, they might require this. There are some studies that look at people who have already undergone DBS, and there are some studies that are focused on trying to figure out or answer the question about DBS settings. And there are also, more recently, some studies that might accept enrolling patients who are already on medication as long as it's been on a stable dose. So again, that's where having the conversation and really learning about the study is important. One shouldn't assume that just because they're on medication, they won't be able to enroll in any study. There might be studies out there for people who are already on medication or who have already undergone DBS.

Maggie Kuhl: And another plug for studies like Fox Insight or PPMI online that are really wide-reaching and want to understand the experience of people with varied disease experiences and treatments. A couple more questions in the same vein, Paulina, I'll start with you, but Bret and Lauren, please jump in. Can you be in multiple

studies at once? I think that that includes both interventional, but also if you're in an observational study, can you also be in an interventional trial testing a new therapy?

Paulina Gonzalez Latapi, MD: Usually, it's easier to be in both an observational study and an interventional study at once or in multiple observational studies, because again, with observational studies, we are not testing any new medication or exercise intervention or device. We're just learning more about the person's experience with their disease, with their symptoms. I would say most interventional studies, again, the ones where we are trying a new medication, new exercise regimen, a new device, those will ask the participants to be on one only, because again, otherwise, that [inaudible 00:30:57] the result that we're getting. We want to know which intervention was really the one that's causing the effect, if we're seeing an effect. Yeah, again, observational trials can potentially be combined with an interventional trials. We really would not recommend, and it's really usually not allowed, to be on two interventional trials at once.

Maggie Kuhl: Another question that we got was around early stage disease, more recently diagnosed stage disease versus later stage. It seems like a lot of these studies are recruiting people soon after they've been diagnosed. Bret, as you said, not many people may be really ready for that right after they've gotten a diagnosis. Or Lauren, as you were saying, "I've got a lot going on. It's hard for me to join a big interventional trial." Lauren, maybe you could talk a little bit about why that is and then also just maybe underscoring the fact that there are still many, many trials for people who are at different stages in the disease.

Paulina Gonzalez Latapi, MD: Certainly. Why is the focus on earlier stage? I think that the hypothesis or what we're thinking as investigators is that earlier intervention might make a difference. So, we're trying to catch the disease earlier in the stage. If we're testing a new medication, the thought is that that medication earlier where the symptoms are milder will have a greater chance of success. So, that's the reason that most or a lot of studies will focus on that earlier stage. Of course, again, there's the observational trials as well that someone might consider if they have been recently diagnosed and they might not be ready to enroll in an interventional trial. So, that's also very useful for us to know, to get the data when someone has just been diagnosed and see and then continue to learn throughout their journey.

But yeah, as you said, there's a lot of studies that are also looking at later stages and some of the symptoms that we see more commonly at later stages of the disease. That's also important to remember. Even if someone might have not chosen to participate in research at an earlier stage, later in the disease, they might still be eligible for a lot of observational and interventional trials.

Maggie Kuhl: Lauren or Bret, just as you peruse studies and you think about these things, what's right for me now, any thoughts about the types of trials that you see or what people should know about what's out there when they think about, "Well, I've had DBS," or, "Well, I'm three years in," et cetera, et cetera?

Lauren Traub: I think it's something that I would just echo is that if you are thinking about research and you're listening to this webinar, I think you've already made great steps. I think it's important to point out that if you are interested and you are early in the disease, to continue to look at these and use the resources available to you. That's something I was looking at, and certain age and eligibility did come into factor for me where I unfortunately was too young for them. And then, furthermore, the consideration of medication. It's a big decision about when you're ready to start medication, but I think it's important not to maybe ignore those kind of critical period where you may not need medication because it's a very important time where you might be able to get involved into a study that you might really benefit from or enjoy being in or learn a lot about.

So, I think that's the one thing I just wanted to point out to the listeners is that really do your research in that time period and use those resources to really look at it. The Fox Trial Finder is very important because you can stratify. Do you want to be in a phase two, a phase three trial? And each of those have... Maybe we can expand on later each have different risks and where the medication or intervention, what phase it's at, what they're trying to learn about. So, I just encourage people to really use that time period to reflect on their goals for research and get involved if they feel it's right for them.

Bret Parker: Yeah. I mean, I agree with that. When I started looking more closely at studies, scheduling was an issue and some of the logistics of it. I'm still working, I got a busy job, and so I needed studies that would be able to accommodate my schedule. I was able to ask questions about that, so that was a big important step for me. And also, many of the studies require, even the observation ones, at certain times to go on or off your medication. So, I had to make sure that I was comfortable those times and those days being on or off. When I'm on or off now, it's very different. My symptoms are very different. And so, being able to make sure that a study accommodated that.

I know there's some questions that we've done about travel and logistics. For the interventional study I'm in right now, they actually have a car service that picks me up in my apartment, brings me to the center, which is about 30 minutes, 20, 30 minutes away. And then when I leave, it drops me off either at my home or my office, whichever I wanted. So, that made a big difference for me. I didn't have to worry about getting to and from work, and that made it more easy, and I was able to ask those questions at the study center.

Maggie Kuhl: Just to address what you brought up, travel, we did receive a couple of questions. I think it really varies by studies. Some are online, which is great. Anyone can participate. For PPMI, for example, we pay for travel across the country for participants and a study companion. We have volunteers in Hawaii who travel to California, volunteers in Alaska. Some people just based on where the sites are that can really take them right now. I met a woman from Washington state who participates in Connecticut, and we fly her over there. So, I think it's really what you are willing to do and have the conversation.

My role at the foundation is often to try and think about these strategies and these approaches to get more people involved in studies, and we can't address the

challenges or the gaps unless we know what they are. So, we do a lot of, keyword of the day, research to find out what those gaps and challenges are, but we need people to tell us, "I would love to be in your study, but I live here and there's no academic medical center near me. So if you paid for travel, I would go." Or, "I care take for others, and so I can't take the time off." Or, "My pet is like my child and I won't travel without it." These are the things that there are full teams at foundations and companies to help think about and overcome, but we need your partnership. So, speak up about your needs to doctors and the coordinators and the study teams.

I want to go up one on this bulleted list and ask, Paulina, that you use the term informed consent. Can we talk a little bit about what that means and how participants can make sure that what they're signing, what they're consenting to is really informed and they know what they will and will not be asked to do or receive back, et cetera?

Paulina Gonzalez Latapi, MD: Yeah, yeah. Again, this informed consent. This is a document that should state what is the trial, what is being tested, what question are we trying to answer with this trial, what sort of information are we going to be asking of you. Whether it's just questionnaires, whether it involves, again, taking some blood samples or a lumbar puncture. That should be clearly stated in this informed consent. We should also state what are we going to do with that information. How are we going to store it, and how are we going to ensure your privacy? And that's something that I really want to stress. All of these studies, again, observational or interventional, that's a big area where we make sure to keep the information as de-identified, meaning that if you give a blood sample, that people won't be able to pinpoint, okay, this blood sample came from so-and-so. We try to keep the data anonymous. Also, this document should state how are we going to do that.

It should also state who is going to be the contact. So, who is in charge of the study, that's usually called the principal investigator, who is the team that you're going to be interacting with, and how, as a volunteer, how can you contact them if you have any further questions or if you have any concerns. Or particularly for the interventional trials, if you're noticing any symptoms and you're wondering are they due to the medication that's being tested, that should be very clear who you can contact. It also very clearly should state that at any point, if, as a volunteer, one changes their mind and decides that they can no longer participate in the trial, then it should state very clearly the right to just stop participating in the trial, and that it's not, again, it's a decision. And then, one is volunteering one's time. Those are sort of the information that you want to look for in this informed consent.

Maggie Kuhl: Bret and Lauren, you both talked about the different networks that you set up. Lauren, you were saying that you learned about Fox Insight and our organization through Team Fox Detroit, which is Team Fox is a community grassroots fundraising, but Team Fox Detroit has really grown into much more with lots of support and just really community building. Bret, you're sharing that the physicians and the research teams, you're a known entity now and so they come to you. But anything else in general that you want to share with those who are listening, who are thinking about research or how to get involved or how to find

the right study. We've got lots of questions, but just want to give you an opportunity to say anything that you feel like we should have touched upon that we have not yet.

Bret Parker: I mean, I would say, in some ways, once you do your first one, it becomes easier because you get more comfortable with the process of informed consent and asking the questions of whether the study meets your needs. I think once I did the first one, I was able to be more picky about which ones I could pick, and I said no to some and I said yes to others. The more you do, the more you know, the more you know. And then, I also got sort of better at asking for features of the trial or looking for features of the trial that would meet my schedule, like I mentioned, the transportation and whatnot.

I think having a couple of sources of trials is a good thing. I mean, I'm lucky that I'm in New York City where there's multiple sources. Not everybody lives in a metropolitan center where there's multiple places, so you may not be able to have as many choices. But I think, for me, being comfortable is the most important part.

Lauren Traub: I think one other way that you might start to think about research and get involved is even connecting through local support groups within the community itself. I mean, you learn a lot from your fellow Parkinson's community and learning where are they looking at trials, what trials are they in, what's working for them, what's not. So, I think that's important as well that you can learn from within your own community as well. And then, I think just continuing to... If you're not quite sure that now is the right time for you, I really urge individuals to just periodically look at the trials, go on the Fox Trial Finder, or speak with your movement disorder specialist, or even that standalone research facility and make contact with the research coordinators and nurses within those organizations.

Because I think Bret had echoed, you can start to tell these individuals what you want and the things you're looking for in a study. They can make it much easier for you to come to you and to present the things that they think you would be eligible and a good fit for. So, it doesn't have to be as intimidating as knowing which one's maybe the right one for me. Let your community and let the support team around you help you.

Maggie Kuhl: Okay. Well, we have got lots of questions to get through, so we're going to transition to those. But I first want to start with a couple definitions. Like I said, I like to make sure everyone's on the same page, and we got a couple questions on things that we referenced. One is, what is the denotation of a recently diagnosed that many trials look for? Paulina, correct me if I'm wrong, many studies that are looking to stop or slow the early progression, say about two to three years.

We are getting better at that because I think a lot of people who've recently been diagnosed know that two, three years in, one individual may look a lot different than another individual with PD. That's our big... If you've met one person with Parkinson's, you met one person with Parkinson's. So, through biomarkers like the synuclein biomarker and others that we are looking at, we hope to get to a spot where it is not time-based because how long does it take for you to even get

to that diagnosis, but really more biological and more staged to the individual's disease rather than their healthcare experience. But currently it's about two to three years.

The other thing that I wanted to define was phases. Lauren, you said there's difference between a phase two and a phase three trial. There's four phases of studies. Phase one, two, three, and four is often after approval. It's more how is the drug doing on the market and testing in more people and for a longer time. Phase one is very small. It's often actually in people without disease. Purely safety. Can we give this to humans? It's already been tested on other species to try and make sure that it's safe to give to humans, but safety.

Then, we invite some more people and say, "Let's keep on with the safety, but let's also maybe look for a couple markers of does this thing do what we think it does in the body, does it actually help solve what we're trying to solve." If that's strong enough signal, we go to hundreds of individuals and we, again, make sure that it's safe, always has to be safe, but then we're really testing. Is this better than our standard of care? Are we going to ask people to take this ,and Medicare and insurers are going to pay for it? We have to make sure that it's actually improving symptoms or slowing disease, et cetera. As, Paulina, you were saying before, not just biologically, but having a real functional impact on improving quality of life. Those are [inaudible 00:45:32], those are phases.

Now, let's get to some of the meatier questions. We all said study teams. Study teams are great resources. Paulina, sometimes people will reach out about studies and then they won't hear anything back. I think study coordinators are some of the most overworked, overburdened individuals. They are often on many studies, they're juggling so much. But what to say to someone if they say, "I've called, I show interest, I email, and no one's contacting me back"? What would you say and what should folks in that situation do?

Paulina Gonzalez Latapi, MD: Yeah. I mean, that's tough because of course we would not want that to happen. But the reality is, particularly the number of research coordinators that might be on a team might differ from site to site. So, one thing to consider is if this is a trial that is ongoing where you're being seen as a patient, something to talk about with your movement disorder specialist and neurologist. They might have a way to notch the research team. Certainly, also to continue to try to reach out. I know that might seem frustrating, but again, the research coordinators will eventually get back to you. It's just they might have a long list of participants to have reached out, and so they just have to... There's so many hours in a day to reach out.

And there's different ways to reach out. Usually, for example, in our center, we do have a phone number that people can call for if they're interested in some of the research we're doing. There's also email information. Certainly, also making sure that the contact that one has is the most updated contact, because, of course, sometimes, the staff changes and the research coordinators might move on to other positions. Usually, also confirming with the webpages of the site that you're trying to reach, that you actually have the most updated contact.

Maggie Kuhl: So, advice is to be your own advocate, which we say a lot in healthcare and extends to research too, really continuing to press. We know it's frustrating and we try to give as many resources, but the nature of so much activity, which is a positive thing, but often just a lot of juggling priorities. Staying on the topic of hearing back or return, Bret, you were referencing in one study that you were told a result that wasn't tied to the disease, but the study team felt that you needed to know from what they found in the study testing. Can you maybe talk about, in observational studies or trials or [inaudible 00:48:16] as well, just how you feel about getting back either your personal results or the impact of your contributions on science overall? I have a couple other things to share there too, but how important is that to you and what have you seen done well in the studies that you've been in?

Bret Parker: Yeah. Anytime I'm in a study, I know there's going to be any sort of testing, a blood test, a urine test, a scan. I wasn't good at this at the beginning, but I always ask, "Is there an ability for me to get any of that data back?" Sometimes the answer is no. They specifically don't have the data tied to one person because it's supposed to be across the whole population. But sometimes, they do have my particular data back, a particular scan back or test result back. So, to the extent they're willing and able to send that back to me, it's not a prerequisite for me to be in the study, but it's sort of a bonus. It's an extra sort of a bonus and an added benefit to being in the study.

Yeah, recently, this interventional study, they did a blood test and they noticed that, I think it was my LDL or one of the LDL subcategories, the nurse noticed that it was slightly high and out of range. They said, "Look, you're not at super high risk, but you're out of the range. We just wanted to flag that." I said, "Oh." I said, "Could you send me my entire blood test result?" And so, they provided that to me, and that's just a great thing for me to have just as a health record to keep track of. But they would've only mentioned that one piece, I had to ask for all my blood test results and then I could see it. So, that's been an extra benefit. Sometimes they provide it and sometimes they can't.

Maggie Kuhl: Lauren, in Fox Insight, you tried to give more aggregate results of you participated in a survey and here's everything that we learned in a survey or here's how researchers are using your data. Often now, a lot of sets are sort of open access where they're not tying your data to you as an individual, but they're looking across the dataset, and more scientists are able to glean more insights from what participants share. What does that mean to you to really know I'm making a difference?

Lauren Traub: Yeah. I think it's great to know that what part you're doing is having a direct impact on driving the strategy for study, whether it's the target, the design, and I think that's really rewarding. I've already learned just by even keeping up through press releases from The Michael J. Fox Foundation or even local researchers in my area, they have explicitly said a lot of the... PPMI data or from Fox Insight, and I think getting that feedback periodically really helps keep you motivated. It's certainly something that I would look for going forward in studies, and I think that's a good sign of good research when it allows from an ethical consideration.

Maggie Kuhl: So, more researchers are trying to do this. I just want to talk through a couple sometimes challenges that folks should understand. Often in interventional trials, they're not able to give you personal results while the study is going on. That's part of testing and keeping everything blinded. But more companies are considering maybe at the end of the trial giving you a full personal report, or at the beginning, your screening data where you haven't taken anything yet but they're just looking at your eligibility.

In PPMI, we're starting to return some individual personal results. There are logistical challenges to giving everything. We really want people to feel informed about what they mean, and that can sometimes be a challenge when we're creating research tests where they don't perhaps have any impact on your clinical care yet. So, really telling someone not just a result but what that means for them and their disease is something that we're waiting into now, but we're doing it with participant partners and we hope to learn more.

Also, open access reporting. If your data is used in a study that is published in a journal, the participants should not have to pay to access the outcomes of that. So, that's something that the Fox Foundation pays for in all of our granted studies. We pay for open access for any papers that come out of that research, and we encourage others to do the same.

I want to just get to a couple more questions. One we got, sometimes it's not so great if everyone has your personal data from research. We got a question about people who are in studies, they don't have Parkinson's yet. Will their insurance companies be given data from the study? And could that be concerning if they do show signs of Parkinson's that that's a preexisting condition? Paulina, could you take that one?

Paulina Gonzalez Latapi MD: Of course. Well, I mean, again, that's where we go back to the concern of data privacy. Again, for most of these studies, the information is de-identified. So again, one should not be able to link specific information to a specific individual. Again, we're looking more at groups of people, and certainly this is being researched data. It's not really data that we are sharing with insurance companies. It's also generally not data that is going to be available or uploaded into the medical record. Again, other than the internal, the research team itself, no one else is going to have access to that raw data. That's, again, something that I would question to ask the research team for anyone who's interested in research. How is my data being protected, and who is my data being shared with or not shared with? Those, again, are two important questions to ask if someone is considering participating in research.

Maggie Kuhl: Exactly, yes. Just reinforcing, have those conversations, ask those questions. We're almost at time, and I want to end with a question that I understand, but also I think we could say a lot about. Someone said, we are still using the same therapy to treat Parkinson's that we did 50 plus years ago. What difference does research participation really make? Paulina, as someone who treats Parkinson's patients every day, Bret and Lauren, you're living with PD, you do participate in research. What does it mean to you to participate in research? What impact do

you think it has, and what do you hope for the future due to volunteers raising their hands joining trials? Paulina, why don't you go first?

Paulina Gonzalez Latapi, MD: Of course. Yes, we still use levodopa, which of course we've had for a long time. But the research that has been ongoing for several years now in Parkinson's disease has also led to the discovery of some other medications. For example, the dopamine agonist or other medications that can help improve the control of symptoms in Parkinson's disease. Again, that's a very clear area where without research, we wouldn't have this long list of medications we have right now to treat the symptoms. Maggie, you alluded to it earlier, really that biomarker, the potential biomarker that we have now found with the synuclein assay, that alpha-synuclein the cerebrospinal fluid, that will also change the way that we think about Parkinson's disease and the way that we design our trials.

Of course, research takes time. We all wish that we could move a little bit faster, but it's also good to move a little bit slower because that means we're really being very careful to make sure that what we are finding is a true finding and that it will truly make a difference in people's lives. Again, I think it's a very hopeful time to be involved in research in Parkinson's disease. We are seeing the area and our understanding of the disease really move at great strides, particularly in the last couple of years with the finding of this biomarker. So, I think we have very exciting things to come in the next few years.

Maggie Kuhl: Bret, any comments on that question?

Bret Parker: If we're not willing to take the chance to participate in a trial, who would? So, I think taking that first step is really important, and I'm glad I've done it.

Maggie Kuhl: Lauren, last word's yours.

Lauren Traub: Yeah, I agree. I think to echo what Bret said is that we're the ones that are going to drive the progress. The patients with Parkinson's, we hold the answer. It's within us, and the scientific community needs us to participate because we are the ones and we are the key. I am very hopeful with the progress that has already been made, the biomarker and even new therapeutics that are coming out. Everything is a step towards that final answer and final goal, and I really feel hopeful that we're close and I'm excited to be a part of it.

Maggie Kuhl: Very well said. Thank you for the three of you for sharing your time and expertise and experience today. Thank you, listeners, for being part of our community and for joining us. We hope you found today's discussion helpful. Thank you, and have a great day.

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