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

Speaker 1: 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.

Jimmy Choi: Hello friends. I hope everybody is doing well. I am Jimmy Choi. I am an advocate, a world record holding athlete, including six times competitor at American Ninja Warrior and I'm also a member of the Michael J. Fox Foundation's Patient Council. Now I was diagnosed with early onset Parkinson's in 2003. Last year I moderated a third Thursday webinar on medication management for Parkinson's, but there has been a number of new options to prove by the US Food and Drug Administration, so how to navigate finding the best treatments for you with your medical team as symptoms progress. And we're also going to dive into details about two of these new treatments. They're both under the skin 24 hour, seven days a week in fusion pumps. So let me introduce our panelists. First off, let me introduce Caitlyn Nagy. She's an author, she's an advocate and she hosts the Pretty Dope Women's Podcast and was diagnosed with early onset Parkinson's disease in 2014. She received support to cover her medication from the Ontario Trillium Drug Program and from AbbVie Care. Caitlyn, thank you for joining us.

Caitlyn Nagy: Jimmy Thank you so much for having me, Jimmy.

Choi: And next we have Dr. Jennifer Hui. She's a movement disorder specialist and an assistant professor of neurology at the School of Medicine at the University of Southern California. Thank you for being here, Dr. Hui.

Dr. Jennifer Hui: Thank you. Thrilled to be here.

Jimmy Choi: And finally we have Dr. Sanaz Attaripour. She's a movement disorder specialist and an associate professor of neurology at the University of California in Irvine. Welcome back, Dr. Attaripour.

Dr. Sanaz Attaripour: Thank you. It's a pleasure to be here.

Jimmy Choi: Now I want to get right into this. Caitlyn, I'm going to put you right into the spotlight and you've been living with Parkinson's for several years now. Tell our audience for you, what has changed over time for you?

Caitlyn Nagy: Okay, well in the Cliffs Notes short-term version of it, the first five years I went without medication solely because I was dedicated to wanting to have a baby and wanting to achieve that. When I had my daughter, my symptoms progressed significantly and so I had to go on medication at that point. I definitely noticed a big shift in terms of my personality and the way my body was moving and working with the drugs. It was really good in terms of the medication helping when I wanted it to, but I really, really struggled with the dyskinesia. I wouldn't be able to be sitting still like I am right now. And so I think that was the Coles Notes of how it's progressed into needing the pump for the sole need of the relief of dyskinesia.

Jimmy Choi: Yeah, it just blows my mind that for me, ironically the change in Parkinson's over time is just how consistent Parkinson's has been in terms of its progression, I mean, in way that I'm consistently having to adapt and change in not only how I communicate but how I move and how I plan my treatment regimen to maintain my own expectations of independence. It's definitely a challenge with this disease. Now, Dr. Attaripour, every journey with Parkinson's is different of course, but there are some common changes that you see when a person has lived with the disease for a few years. Can you tell us your thoughts on that?

Dr. Sanaz Attaripour: Thanks Jimmy. Absolutely. Parkinson's is different in everyone. I usually tell my patients your Parkinson's is yours. What happens in majority of the patients, usually the disease progresses as you noted, both in terms of motor symptoms and the non-motor symptoms. Motor symptoms when they progress, there may be some fluctuations, we call them motor fluctuations, which means more ups and downs. When a medication dose is taken, usually the patients experience some ups that can be dyskinesia as you guys mentioned, and it can be also more off time, which means that the medication wearing off faster than before. Other than that, there are non-motor symptoms that can progress. Like sleeping problems, like cognitive issues, like intellectual disorder, different aspects of non-motor symptoms of the disease. They also progress

Jimmy Choi: And since off times has been an ongoing battle for myself and I'm sure for you as well, Caitlyn, Dr. Hui, can you talk a little bit more about off time and tell our audience maybe help them understand a little bit more why they occur?

Dr. Jennifer Hui: Yeah, yeah. So I'm sure many of you are familiar with off time, which is basically the time where you're not getting symptomatic benefit from your medication and we contract that with on time during which your medications are working to control your symptoms. Over time our brain makes less and less dopamine, which is the pathophysiology of Parkinson's and we become more and more dependent on the medication to supplement dopaminergic levels. And so off time, initially there's very little off time because the oral medications typically treat the symptoms quite well, but as your brain is making less and less dopamine, there's less dopamine hanging around to kind of fill in between so to speak, your oral medication. And so patients start to feel the medications waning. The effect is less strong over time but also dose to dose.

So as Dr. Attaripour referenced, there's different kinds of off time, there's end of dose wearing off which is predictable off time towards the end of your oral dose cycle right before we take the next dose. There's also sudden off time, which is very, very quick wearing off, often over seconds to minutes. It can take people by surprise and often at unpredictable times, and then there's off time that happens because the medications just never kick in. So those are called failed doses where after you take a medication you think that you ought feel the effects of it, but then it never kicks in. So those are failed dose off times. So the presence of these off times with your Parkinson's is kind of what's driving these continuous pump therapies.

Jimmy Choi: I think it's important for our audience to hear that because sometimes I know, I've been living with the disease for a long time and initially when I was experiencing... Years ago when I was experiencing the first time where medication isn't working or the sudden off times I thought it was just me. But it's very important for everybody to know that this happens to a lot of people. Caitlyn, I'm sure you've had the same experience that I was talking about. Now, you mentioned that you're using the pump today. If you don't mind describing how does off time impact your day from two perspectives? Number one, what was it like before you started using the pump and if it's any different today, what's it like after the pump?

Caitlyn Nagy: Oh yeah, those are great questions and I think you might have to coach me through reminding me what I'm answering in the second half because I might go off on a train.

Jimmy Choi: No worries.

Caitlyn Nagy: Perfect example of what I am feeling with the drugs right now. So definitely in the beginning my off periods prior to the Vyalev pump were unpredictable, especially if triggered by food. Food was just a big trigger for me, but predictable in the sense that I could map when I was going to have my off days [inaudible 00:08:12] my cycle. And I have been tracking my cycle for I think over six years vigilantly, but tracking my cycle now and putting in points of what the off time is, what was the trigger? Noticing that in the past it was very triggered by absorption in the gut and that was just a big blocker. And obviously when the menstrual cycle hits and your body, that's... A woman's body naturally has trouble absorbing at those times.

So what I'm noticing it's not meeting is it's not meeting the challenge of women's physiology, like the natural physiology that we have. It's not up to snuff. That was really evident, but also stress has been a big indicator and that when I switched to the pump, everything just became much more clear. So in terms of I was able to predict and explain when the off periods were happening. So I still have off periods. I need to make that very clear. I've posted a lot of stuff like, "I'm feeling so strong and motor control is great." Yes, it is great during the on times, but during the off times when I naturally had off times before, it's still horrible. I can go six hours and I will be sobbing in tears because I just can't get any absorption.

So yeah, definitely off times and then also a big trigger for me now whereas before I wasn't able to link it so much to that. I think it's more precise because I'm able to monitor. I guess the way I would explain it is it more of a drastic drop now. It's so drastic that it can change my mood, I can flip on a dime and that's what I've had to be really careful about is just monitoring that like, okay, am I stressed out? What's irritating me? Is this a hormonal day? So I have to question everything.

Jimmy Choi: Yeah, I think it's very important. Two things that you point out. Number one is that women and men are going to experience different things and I think one of the things that we haven't done enough is do more... We as in the research and scientific side of Parkinson's research is we haven't done enough with women and the hormones and everything else. There's still so much more to learn there. I think that's very important.

So Caitlyn, when we're talking about, you mentioned going from before your pump going to the pump, what went through your mind as you were thinking about... What in your time with Parkinson's started make you think, "You know what, maybe I should think about different treatment plans, options and like that."? So what went through your mind during that period?

Caitlyn Nagy: So I have been very encouraged by my doctors to do DBS, but I am hesitant on that. So I stuck to the pills for a really long period, I think almost five years. What led to the ending of that was the wear off time wore down so much that I was maybe having an hour and then it was like 20 minutes of on time and then taking my pills every two hours but only getting 20 minutes of on time and then trying to juggle eating in between that and then I just lost so much weight and just trying to balance that was really, really hard.

Jimmy Choi: Yeah, so quick question, I'm just going to shift focus here for a second. Dr. Hui, what flags do you look for from the perspective of a movement disorder specialist that it's time for your patients to explore different options?

Dr. Jennifer Hui: Taking a good history and when you're at the doctor's office offering this history of what your off time is like and if you're having sudden off time or unpredictable off time or failed doses that's not covered by your oral medication, I think just having that conversation and bringing up those symptoms are really important flags in my clinic visit to explore other options to try and get a better, more even on-time coverage throughout the day. So as Caitlyn mentioned, different factors, sometimes factors that you don't even know about are affecting your medication absorption. Diet is one very consistent one. So we know that protein, for instance, compete with absorption of levodopa in the small intestine. So one of the easier things to do is to space protein away from your dosing.

Other strategies, not to discourage protein intake. I always have to include that because then everyone's [inaudible 00:12:45] protein and they need [inaudible 00:12:47].

Caitlyn Nagy: Yes.

Dr. Jennifer Hui: Don't cut out protein. That's not the advice. The advice is you can monitor your diet. Everyone's individual, I've had patients need to drink a diet Coke or something to get their medications to work, but in general, maybe trying space protein intake specifically a half hour, 45 minutes away from your levodopa dosing and then changing the spacing of your dosing, the timing of your dosing to dose maybe closer together. Those are some strategies and if those don't work, we can talk about these other adjunctive medications.

Jimmy Choi: And that's a very good point is you're trying various different timings and food combinations or just essentially lifestyle things to accommodate. Looking for better ways to fit your medication into your lifestyle. Dr. Attaripour, can you talk a little bit about weighing the benefits of when you're exploring the new drug or new treatment plan for your patients, how do you think about weighing benefits over side effects?

Dr. Sanaz Attaripour: Right, so I pretty much like Dr. Hui. I ask my patients what their goals are, what they want to do, what is a good day for them. I have patients who are retired, enjoying time, spending time with their children, with their pets. They want to have, for example, to be able to give a ride to the grandkids in the morning. So they want to have a good on time in the morning. I have patients who want to, the meaningful part of the day is getting together for dinner. They want to have a good on time, predictable on time for dinner time. I have patients who are actively working. I have patients who are surgeons, they spend seven, eight hours in the operating room. So it depends on everybody's lifestyle.

What I need my patients to tell me is what they want their life to look like. And of course the decision about moving to a different strategy depends on the risk profile every person has, like potential for developing side effects. Some people have a tendency to develop impulse control disorder. Some people absolutely cannot risk any amount of excessive daytime sleepiness. There are things that I would like to know if there is a history of them. And the next thing is a practical fit because if for example, I have a patient who is spending seven hours in the OR, I cannot really ask them to take medication every two hours. It's not practical for them. So then we have to talk, discuss. Sometimes it takes a lot of time and we do a shared decision making somehow at every single session. Something that we think works well for the next two, three months and then we can make the one change at a time and we track the results and then based on that we adjust the treatment plan again.

Jimmy Choi: No, and I think that's great in your process, right? Number one, I think everybody has to understand that your treatment plan has to fit in your lifestyle. That's why my treatment plan isn't going to work for somebody else and vice versa. So Dr. Hui, in addition to all the therapies available, the Food and Drug Administration have approved five therapies in this past last year alone. Can you walk the audience through those options quickly?

Dr. Jennifer Hui: Yeah, just a broad overview. I think today we'll talk about the infusion pumps more in detail, but Onapgo is a subcutaneous apomorphine, a continuous pump that's worn for up to 16 hours a day and taken off at night generally. Vyalev is subcutaneous. levodopa, so that's generally worn 24 hours a day and each of those, you change the infusion site regularly and you have to maintain the syringe. So there's some maintenance with those pumps on a daily basis. There's some surgical interventions that were FDA approved. So adaptive DBS is basically the traditional technology of D brain stimulation, but it's more of a software upgrade if you want to think of it that way. It allows the stimulation to adapt to certain electrical signals in the brain, but the actual surgery is identical to the previous DBS. Bilateral focus ultrasound is approved for Parkinson's and tremor and that is a relatively non-invasive way of via ultrasound. It doesn't involve surgery, but it's still [inaudible 00:17:58]. And finally, Crexont is the newest form of extended release of levodopa. It's oral.

Jimmy Choi: Thank you. And Dr. Attaripour, how are these different than what's already available before? Why is it such a big deal that FDA has to issue new approvals for these?

Dr. Sanaz Attaripour: Jimmy, if you notice, all of them have some tendency to give a continuous steady source of therapy to our patients, which becomes very valuable after the first stages of the disease when we have very good secure benefit from our oral doses of medication. They tend to give our patients less off time and more good on time, which is on time without troublesome dyskinesia. So dyskinesia is that dance-like flowing, sometimes jerking movements that happen because of excessive dopamine and at times they can be troublesome, they can cause falls or involuntary movements that can interfere with daily activities and these therapies tend to cause less of ups and downs.

Jimmy Choi: So that's one of the things that for our audience who are newly diagnosed and haven't experienced dyskinesia, for those of you who are wondering, the movements that you see me make is dyskinesia. So I just want to point that out there. The movements that I'm... Right now I'm in a little bit of a dopamine surplus, but that's kind of what dyskinesia looked like. So Dr. Attaripour, thank you for that. I really appreciate it. I do want to mention that we're getting a lot of questions from our audience about DBS and the focus ultrasound since that was mentioned. Just so everybody knows that we're going to get into that in much more detail in our next month's webinar. So click in the calendar icon at the bottom of your screen to register for that. But moving forward today we're going to focus more on some of the other therapies that are available today. So Caitlyn, just real quickly, from your perspective as a patient person living with Parkinson's now, why is it important to have these options available?

Caitlyn Nagy: Oh, I think that we have to start looking at Parkinson's like we look at any other major disease, even like cancer, there's different types of Parkinson's and there's different types of people. Like an ADHD brain or a neurotypical brain is going to respond differently than a neurodivergent brain to Parkinson's, and I think that we have to be really aware of the differences. When we're starting to dissect what treatment plans are needed, we have to look at the patient in terms of what their environmental history has been growing up in terms of what traumas they've been through and things like that. I think that all has a major effect.

Jimmy Choi: Yeah, absolutely. And Dr. Hui, now you already mentioned the two pumps that are available, they're newly approved, they're both different in terms of the medication that it's delivering. Can you clarify that a little bit? One is the still carbidopa levodopa, so what's the difference between the two?

Dr. Jennifer Hui: Yeah, there are several key differences. So NFO is subcutaneous apomorphine. It's not morphine, it's not a narcotic, don't be confused by that name. But apomorphine is a fast-acting dopamine agonist and it is when met in the clinical trial can be given with your other medication for Parkinson's. So there's an injection pen that was approved earlier with apomorphine, but this is the continuous pump. In the clinical trial patients with motor fluctuations, which is wearing off and dyskinesia. So they had to have about three hours of off time to meet criteria for the clinical trial. They wore this pump for up to 16 hours at a time. They were titrated to an adequate dose and if they develop dyskinesias or other side effects related to over medication, the first thing that was done was to reduce the oral medication and try to have the pump carry more of the weight in terms of controlling symptoms.

So again, one of the three differences I usually outline is a smaller size of the pump. It's also worn up to 16 hours a day, so it's not a 24-hour a day therapy. And finally you are taking concurrent Parkinson's medication with the Onapgo. The Vyalev pump is subcutaneous levodopa, so it actually is levodopa and so this is able to replace all of your oral levodopa. So you do not need to take any version of generic Sinemet, carbidopa, levodopa or your Rytary or Crexont. It replaces all those oral medications, oral versions of levodopa, and you're just basically switching to the Vyalev pump gel version of... It's a pro-drug. So focsarbidopa, foslevodopa, which can get converted to levodopa. Again, the differences here are the 24 hour a day it replaces your oral levodopa completely and the larger size. So those are the three differences that I typically go over with patients.

Jimmy Choi: I think that's important because I think we talked about how treatment should fit into your lifestyle and all three of those are going to play a role into that. So Dr. Attaripour, can you tell us how would you decide when the patient comes to see you? How do you decide whether or not one pump is right versus the other? What are the differences that would make you change your recommendation to your patients?

Dr. Sanaz Attaripour: Jimmy, that's a difficult question still because we do not have head-to-head studies of two options, but as Dr. Hui mentioned, Onapgo, we added to current medication treatment plan that we have. So you imagine that patients who have a lot of difficulty because of the current treatment plan, they probably don't like it. They want the medication to be as less as possible or even they want to transition to a different method. In those cases, Vyalev is absolutely a better idea because it'll be a substitute for oral therapy. If you have a patient that you are dealing with GI system not absorbing the medication because that's a consideration when people have failed doses or they do not respond to medication as much as expected, they may have some difficulty with absorption, then you need to think of parenteral, means outside GI system way of managing their symptoms. Vyalev will be a better option because it'll be a substitute for medication.

On the other hand, there are some side effects that are a little more likely to happen with Onapgo and that is essentially because the main mechanism of action of apomorphine as Dr. Hui said, that doesn't have anything to do with opioids. The morphine here, it is not the morphine opioid, it's just the molecule that is similar but doesn't have any opioid features. Apomorphine is the main mechanism of action is dopamine agonism, means that it acts like dopamine, it tricks the dopamine receptors of the brain and activates them. There are some likelihood of having some side effects more in the Onapgo group. For example, nausea is something that happens more with Onapgo group. That's why FDA now has recommendations specifically for the Onapgo group, how to manage nausea. Even sometimes we have to pre-medicate our patients and give them the medication and then start the pump.

Another thing is impulse control disorder. In patients who already have some history of, for example, gambling too much or having some behavior that is hard to control for them, usually carbidopa levodopa, which is now Vyalev, is the prodrug of carbidopa levodopa. The post carbidopa plus levodopa will be converted into carbidopa levodopa in the body is safer in patients who you have some known history of impulse control disorder. So another thing is the risk profile. I care about the possibility of side effects. Other than that, very important, still it's a reality in our world that insurances have some... Sometimes they should be taken into consideration depending on what our patient might get. Of course that affects our decision.

Jimmy Choi: I want to thank you for highlighting some of the side effects of both of these options and one of the things that I just want to make sure the audience knows is that for a complete list, of course you guys can go and using the resources, find more information, exactly what side effects and complete list of those side effects, and of course talk to your cure team about that. Now Caitlyn, you've chosen the Vyalev pump. Can you tell us exactly why you and your doctor picked that one? And you've already started telling us what your summaries of experience are, but maybe give us a little bit more for the audience.

Caitlyn Nagy: Yeah, definitely. We don't actually have the Onapgo available in Canada, so Vyalev pump is the only one available in Canada. It was also a coverage thing. I was waiting for I think Ontario Health to approve the coverage and I specifically, I worked with my doctor on this. I didn't want to do DBS. I would like to see more research with women and DBS first.

I wanted to do the Vyalev pump because I felt like it was the right fit for me that I knew that I was needing some type of more consistency and I was seeing real inconsistencies with the Sinemet, the levodopa that I was on, and I was just losing so much power where I initially started on the levodopa Sinemet pills, I was think every four hours and then it was down to every two hours and sometimes hour to hour, which means you can't even eat. It just became impossible for me. And the Vyalav pump was the one thing I was praying for that I would be able to try. I saw other people's responses on it and I wanted to try it for myself because I felt like it would be a really good fit.

Jimmy Choi: Your experience of course is very unique to yourself and I think one thing that I want to highlight in your response is that you're in Canada, so it's going to be a little bit different than other countries, especially here in the United States. But overall, I think once again, this is a fit into your lifestyle at the moment. Not just lack of options but to treat it too. But I think it's important that you found that it does fit your lifestyle. So switching gears a little bit to the topic of the Onapgo pump, Dr. Hiu, you've had more experience with that pump. What are your patients reporting?

Dr. Jennifer Hui: Yeah, I mean I think overall the goal is, as Caitlyn said, is to smooth over the off time. So in both of the clinical trials, the outcome was about two hours more on time. And in the case of Vyalev, it was on time without dyskinesias. So they were both FDA approved and showing significant benefit in improving up to two to three hours of on time average in patients per day. So I should emphasize there is and always will be a wide range in how patients respond to these therapies and everyone's experience is very different. I do want to speak a little bit about side effects. I think in terms of what's the most common side effects for both of these pumps? The most common side effect is skin reaction.

So as that you might think being very consistent with the way these medications work. For Onapgo, most commonly patients experience little nodules, which are very, little bit firm areas where the catheter is inserted. Generally they didn't really progress further than nodules, but they would last for several days maybe up to a week. So you can just feel them on your abdomen or wherever you're inserting.

For Vyalev, it's a little bit more common. So skin reactions were a little bit more common. So another thing to keep in mind in terms of keeping the area clean for both pumps, but in particular for the Vyalev, we really want to be careful about cleanliness. There was more in the way of skin reactions with the Vyalev that not only caused nodules but also a little bit of inflammation and cellulitis. Aside from... And Caitlyn, I would love to hear your experience with that too. And then finally after skin reactions were both the most common in both devices, things like nausea, which was more common in the Onapgo and drowsiness was more common in the Vyalev. So I just wanted to point out the skin reactions and the major side effects for both.

Jimmy Choi: No, thank you. And since Dr. Hui posed the question to you, Caitlyn...

Caitlyn Nagy: Yes, because I'm very much like, yes, there's skin reactions. I'm a redhead, I don't tan, I have pale skin, I'm very sensitive. I will say that I've been lucky in the sense that I've only had one infection and sometimes I have to change my sight up to three times a day. The reason why I'm noticing with my skin and my body and my hormone shifts is that anytime it's a hormone day, I will get those edemas. So where the site is located, it will swell to a ball and won't absorb and that can be quite painful having to rip it off and then start a new site because the burn that you feel when you have to put a new site in is excruciating. For me, I found it hard to avoid getting the burn and also having a burn sensation where you just ripped off the site, especially if there's an edema, it can be quite painful having to rip off the injection site there.

I mean the burning is the number one thing, my pet peeve about it. The other one I wanted to mention is that in the beginning when I started the levodopa, I was actually getting rashes on my face. Sorry, when I started the Vyalev. I was getting rashes on my face like a mask of red. And that would happen on the days that I was having trouble absorbing and I was bumping every hour and by bumping I mean if this is my pump here, I'm going to hit the top button to say I want an extra dose because I can control that. I can only do it every hour. Unfortunately on those days where I'm not absorbing, it's like you're bumping and you're not getting anything and that can cause my body to be more inflamed the next day. It can also cause more risk of impulse behavior the day after because you've retained too much of the drug. So that is also why I really want to see more research with women and this response.

Jimmy Choi: We're getting some questions about why I personally don't use the pump and it all goes back to lifestyle. I'm a very, very active person and that includes spending time in the waters, includes spending a lot of time under stress and a lot of different various activities with the things that I do in terms of my athletic goals. So because of that, the mechanisms themselves are not waterproof and I would have to take them on and off all the time anyways and supplement with oral medication. So at this time in my own lifestyle it just is not a fit, but that's the only reason. So I want to get into, now that we've learned a little bit about these pumps, how accessible are they in terms of, are they covered by insurance or by Medicare? Dr. Attaripour, can you tell us your experience in terms of coverage?

Dr. Sanaz Attaripour: It's getting easier and easier. They are both covered by most insurances. Right now, I think Vyalev is considered durable medical equipment, a DFE, so it's for Medicare patients, it's on their Medicare part B and Onapgo is, I think it's part D, and there is a platform for pre-authorization. The paperwork is usually done by your care team, so you can wait until they get the paperwork done. Either they started covering it or they are in the process. I think realistically over the past months or so, I haven't had any rejections unlike earlier last... When they got FDA approved, which we got a lot of rejections from all the insurances. So it's becoming more and more available.

Jimmy Choi: That's great news that it's becoming more and more available. One of the things that Caitlyn mentioned is about changing the sites for these patches on your skin. Dr. Hui, can you talk about more about maintenance on this? And I can also imagine a lot of times when if I'm off or if I'm experiencing a lot of dyskinesia, it'd be kind of difficult for me to change these patches out. What should people know about maintenance and also perhaps maybe assisting with these placements?

Dr. Jennifer Hui: Yeah, yeah, so like I said, the pumps do require daily maintenance. They come each with a vial. I think in the picture there you can see the Onapgo vial in the plastic, but they do require a change out of the vial once you drain the medication from the vial. And the rate at which you need to change vials does depend on the rate at which you're getting the medication. So of course if you're getting more medication you need to change up the vial more frequently. I think they're both designed generally to last one vial per day, but as everyone's needs are different, if you have a higher need, you might end up needing to change a vial multiple times per day or at least once.

You do need to change the injection site. And I've been telling my patients now to change it daily. I think the package labeling may stretch it out to every two to three days, but the longer you leave a needle in or the catheter in a site, the greater chance of infection or skin reaction. So like Caitlyn says, I mean she changes it many times a day sometimes, and that does require assistance, especially if you're off and having trouble with fine motor movements or conversely, if you're on and having a little dyskinesia, also difficult to control fine motor movements. So the pieces are somewhat small and might require some dexterity.

Jimmy Choi: Caitlyn, you and I had a discussion off site and I think this is very important, that's why I want to bring it up, but I do think this is important because you and I talked about this just a couple of days ago, right? You mentioned a story of needing help. Can you talk about that a little bit? I think it's important for our audience.

Caitlyn Nagy: Yeah, so I think one thing I want to say is that when I have a drastic off time, when I go into a drastic off, I need help right away and I need to change my site right away. And I would say it's really important. Now that I've learned this, it's really important that the people that are with you know how to change the site for you. So that is important. I got stuck in a situation this summer where I had to ask one of my nieces to do the change for me and she is a babysitter, she's got her first aid and CPR. She's a very, very smart girl and she was able to sit there and go through the whole map and do it for me and stay calm and that is exactly what I needed. Now I was worried that, "Oh my gosh, I'm asking a minor to help me change my site. Is this a bad thing to be promoting?"

I'm not promoting that. I'm just saying that we need to make sure that everybody that is with you, whether you're going out for the night or whether they're with you for the weekend, if it's a new scenario that you're going into, you need to educate people on how to change your pump because I do, I have to have people help me sometimes. If I'm either off or dyskinetic or I might be in so much pain from the drastic off, it would be more like a mental logical pain that I have to deal with. So just heads up about that.

Jimmy Choi: The reason why I want you to share that story and so important is that again, this is something that needs to be considered when you're thinking about new treatments. One thing that I do want to point out is that we are getting a lot of questions about new treatments that we haven't mentioned yet, like stem cells and about other treatments that will slow and stop the progression of the disease. Just so you guys, the audience know that the last two Third Thursday webinars were on these topics. So if you're interested in that, please go back and visit MichaelJFox.org/webinars and you're able to watch the last two Third Thursday webinars and you can find more information on those subjects.

So speaking of these new treatments, one of the things that moves these new treatments forward is getting people involved in clinical trials. Dr. Attaripour, can you tell how people can get involved in trials? Especially for those who have had the disease for a few years and are already on medication. If you're not on medication, it's easier for you to get into trials. But what if you are, what should people do?

Dr. Sanaz Attaripour: One very easy answer is to ask your movement disorder specialist. They are usually aware of the clinical trials in their center and around you, but also the trial finder on Michael J. Fox Foundation website is amazing. It walks you through the right clinical trial for you. So please do that because none of this is possible without everybody's help. We need both Parkinson's patients and healthy volunteers for all those studies.

Jimmy Choi: Yeah, personally I've been involved in many clinical trials earlier in my diagnosis and even throughout later in life. It's harder for me to get qualified now just because of how long I've lived with the disease and the medications that I take. But I want to encourage everybody to get involved and even if you don't have Parkinson's. So I think it's a good time to mention that the foundation itself has a landmark study that Parkinson's Progression Marker initiative, which is also known as PPMI. It's always recruiting volunteers, people from all backgrounds with or without Parkinson's can get involved. And just by participating in this online research and signing up, it's just changing everything in terms of the research and you can help that. We've got about 10 minutes left and we got a lot of questions and I just want to really get it into those. So let's go ahead and get into some questions that we've received. So a question for Caitlyn, is it difficult to sleep with the pump?

Caitlyn Nagy: It was definitely an adjustment period. So I will say I was a little bit awake and a little bit more agitated for the first six weeks. I needed to give myself that time to get comfortable. Also, the other thing that I would love to request is a more automated system where you can tell if you're going to sleep or not because it's your job to lower your dosage. I fall asleep, I don't even know when I fall asleep. So sometimes I forget to lower the dosage at nighttime and that is frustrating because then I'll wake up, I will probably wake up in the middle of the night forgetting that I've changed my dosage like in having a high heart rate, being more agitated because I've just been lying down with that pump at high level. So we need solutions for making that more automated because Parkinson's people, we don't have time to remember all this stuff. We need support with that.

Jimmy Choi: And Dr. Attaripour, in terms of placement on the skin, where exactly are these patches placed?

Dr. Sanaz Attaripour: So the manufacturer prefers the abdomen around the belly button. Actually there is an M shape and a W shape that they recommend you to move around and don't stay in one place to prevent all the skin reactions that Dr. Hui mentioned. But there is possibility if people cannot really tolerate that in this area and less encouraged, but it is possible to use it in upper arm and upper thigh as well. The catheter will go in that area, but there is a tube, Caitlyn knows much better than me, that is about I think a fit. And then you can carry the pump in a different location. For example, some people wear a vest and put the pump inside the vest or sometimes a fanny bag so people choose their own way of carrying it.

Jimmy Choi: Dr. Hui, who are these treatments best tailored for? And we mentioned that already something in our discussion. Is there a typical audience for this?

Dr. Jennifer Hui: Nothing is typical in Parkinson's. [inaudible 00:44:06] one thing to keep in mind. I would recommend for patients who are having motor fluctuations, like I said. So this is you're already on oral therapy and not getting a consistent or predictable on time with your oral therapy. And this is also kind of despite doing all the other adjunctive oral medications and changing the timing of your medications and identifying triggers of off time. So those things should all occur concurrently trying to optimize your on time. But if you're not having adequate on time despite all those measures, it's time to consider these continuous therapies. And usually the discussion is centered around should I do a pump or should I do surgery or focus ultrasound or some interventional therapy like that. So it's definitely a question for your mood disorder specialist. And there's different things that push people in either direction.

Like Caitlyn said, some patients are not interested in surgery or are not surgical candidates due to other medical comorbidities. And those patients might be better served by the pump that's less invasive. Also reversible, easily reversible, you can just stop using the pump if you're having issues with it or it doesn't fit your lifestyle, it's much harder to reverse a surgery that's already been done and you have an implant. So those things, lifestyle, as Jimmy mentioned, I mean with the implant, you implant it and you really don't have to think about it. There's not that much of a maintenance unless you choose a rechargeable battery, in which case you do, you just have to recharge it. So lifestyle questions and factors and talk it over with your neurologist, but generally for patients with motor fluctuations, it's the best candidate for these therapies.

Jimmy Choi: Thank you. Dr. Hui. Got a question for Caitlyn in terms of the Vyalev pump. What about exercise or other daily tasks? Does it get in the way, the tubing, the pump itself? What's your experience?

Caitlyn Nagy: Yeah, well it is going to get in the way. It's there, it's big, but what you have to do is kind of be okay with it and be willing to work with being exploratory in terms of how you're going to get it to support you on your body. And I mean try and find a fanny pack that is comfortable that maybe has an elastic band. I find the packs that they give you, I think there's a sleep one that is elastic and that is really great because if you need to go tighter or make an adjustment, if you're going to be doing jump up and downs, you need to go tighter with the pack so that it stays firmly to your body.

I think I have a few pants that I have side pockets that I can slide it in or if I'm baking I can stick it in my apron pocket. I love that. So it is cumbersome, but I can still exercise. Swimming, like you mentioned Jimmy, swimming is kind of off the table unfortunately unless I'm like, "Okay, I'm going to go for a swim now. I'm going to take it off and I can be in the pool for 30 minutes." So that was okay. I wanted the motor function the most and that is what it has given me for sure. I'd love to add with exercise, you perform better the more you exercise and you really, really see that. You really see that.

Jimmy Choi: I'm a big proponent of that. I think medication that helps you perform better in your exercises that then help you build your base, so to speak, so that your body itself can better handle the effects of Parkinson's over time. Dr. Hui, these are the first pumps that are available. How might this change in the future? So what's coming next in terms of these pumps?

Dr. Jennifer Hui: Yeah, I think Caitlyn was alluding to there's improvements that could occur with the design of these pumps. So I think design improvements always occur with multiple iterations. Certainly the customizable features of maybe an automated or an easier way to program. The catheter length has already changed. I think with the Vyalev pump now, at least in the US, they're recommending starting with the nine millimeter over the six millimeter just because there's maybe a fewer less of a chance skin reaction with the longer millimeter catheter. So just slight modifications like that. I'm not aware of any drug modifications at this time that they're working on, but these companies are always trying to vie for the next best thing to market their product. So I'm sure some new devices will come out with better features.

Jimmy Choi: Thank you. And Dr. Attaripour, these pumps, are they just for helping with motor symptoms or does it help with some non-motor symptoms as well?

Dr. Sanaz Attaripour: The medication itself, the levodopa helps with some non-motor symptoms. For example, sleep and mood are among them. So whatever you expect to get better with your regular carbidopa levodopa, you should expect to get better with pump as well. For example, everything that gets better during a good on time, for example, if you have freezing of gaits and your freezing of gaits responds to carbidopa levodopa, it'll respond to the pump, Vyalev pump as well. Freezing of gait is motor, but I mean if your mood is better during your on time. If your pain, you have some pain that is better during your on time, that will respond to the pump as well.

Jimmy Choi: And we have time for one last question. Caitlyn, we opened with you and we're going to close with you. What are some tips and tricks that you think you can share with the audience in using the pump?

Caitlyn Nagy: I would say the number one for me is when you're doing the change, when you're doing your pump change, just remember to stay really relaxed. For me, I put music on in the background so that I can just stay focused and do the change. And now I'm so good at it, I can do it really quickly. So I think in the beginning this drug felt very overwhelming for me. It was like, oh my god, this is new and I'm going to do it wrong and oh my God, and I'm going to get an infection. Just take your time, your body going to create those new neural networks to remember how to do it.

What I love about this medicine is that when I am on, I'm creating new neural pathways of what it feels like to be on, so it's easier for me to be off. So if I'm off, I know that I can get back to my on. So it's not so much of a... I have the capacity to handle the stress of being off, if that explains things. One other tip I would say is watch your cats. They can bite through the line. If you have animals in your house, it happened really fast. I didn't get an infection, but it happened in seconds.

Jimmy Choi: That's something that I certainly would've never thought of. So thank you very much, much and thank you guys. I want to thank everybody for being a part of this community and for joining us today. And thank you to our panelists, of course.

Dr. Sanaz Attaripour: Thank you.

Jimmy Choi: [inaudible 00:51:13].

Dr. Jennifer Hui: J Thank you.

immy Choi: [inaudible 00:51:15] webinar. We hope you found today's session very helpful. Thank you everybody, and have a great day.

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