The Lewin Group
Diagnosis and Treatment of Parkinson's Disease
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Caroline Loeser: My name is Caroline Loeser, and I'm with the Lewin Group. This is the third webinar in the 2017 Geriatric-Competent Care webinar series. Today's session will include a 60-minute presenter-led discussion followed by 30 minutes of discussion among the presenters and participants. This session will be recorded in a video replay. The slide presentation, as well as the Q&A, will be available at https://www.resourcesforintegratedcare.com/GeriatricCompetentCare/2017_GCC_Webinar_Series/Parkinsons.

This webinar is presented in conjunction with the American Geriatrics Society (AGS) and the Lewin Group and supported through the Medicare-Medicaid Coordination Office (MMCO) at the Centers for Medicare and Medicaid Services (CMS). MMCO is developing technical assistance and actionable tools based on successful innovations in care models, such as this webinar series. To learn more about current efforts and resources, please visit our website or follow us on Twitter for more details. Our Twitter handle is @Integrate_Care.

At this time I'd like to introduce our moderator. Carol Regan has over 30 years of experience with national and state based public policy and healthcare advocacy organizations.

Carol Regan: Thanks so much, Caroline, and welcome to all the participants on today's call. We are so pleased to be doing this series with MMCO and the Lewin group. We've been doing this now for a few years. Community Catalyst, who I work for, and in particular The Center for Consumer Engagement, is committed to promoting models of care for older adults through education and advocacy. These webinars have been important in reaching out to a whole range of geriatric providers, provider networks and others who care for people with different conditions.

On the screen, I'll introduce today's faculty. Dr. Liana Rosenthal is an Assistant Professor in the Department of Neurology at Johns Hopkins University School of Medicine. The entire faculty we have today is from the Morris K. Udall Parkinson's disease Research Center housed in Johns Hopkins. Dr. Rosenthal completed medical school at Johns Hopkins, and she is board certified in psychiatry and neurology. She's the director of the Parkinson's disease clinical research specifically the longitudinal brain disease studies, which seek to improve our study of disease progression and the psychiatric and cognitive aspects of Parkinson's. Dr. Rosenthal supervises all day-to-day operations of the clinical research including patient recruitment and clinical assessments.

She's joined by Dr. Gregory Pontone, who is an Associate Professor in the Department of Psychiatry at Johns Hopkins University School of Medicine. After he completed a medicine internship and residency in psychiatry, he completed a two year fellowship in geriatric psychiatry, focusing on Parkinson's disease through this center. He's board certified by the American Board of Psychology and specializes in geriatric psychiatry. He's currently an attending psychiatrist where he treats patients with Parkinson's and Alzheimer's and other dementias and focuses on the behavioral disturbances from these.

Arita McCoy is a nurse practitioner at the Johns Hopkins Parkinsons disease and Movement Center. She's worked at Hopkins for ten years in multiple roles including community outreach, clinical research, and in the regular nursing care of patients with disorders and their families. Her experience has helped her gain fast knowledge in areas of Parkinson's disease from the initial diagnosis to the complex advanced stages.

She has a special interest in advanced treatment options for those with Parkinson's and other movement disorders.

Finally, we are so pleased to have Maryann Powderly with us. She's a family caregiver who cares for her husband, Mike, who has Parkinson's. She works full-time at Johns Hopkins, and her three adult children live nearby and also support Maryann and her husband. That's our wonderful faculty.

I'll quickly review the learning objectives for today's event. Upon completion, you'll be hopefully be able to identify the signs and symptoms of Parkinson's and demonstrate knowledge of the treatment options for Parkinson's disease.

Let's now jump right in and have Dr. Rosenthal start us off. Thanks so much.

Dr. Liana Rosenthal: Hello, thank you so much. It is my absolute pleasure to be here today to speak with all of you. First thing I want to do is give a definition of how we tend to think about our patients, and I want to talk about Parkinson's disease versus Parkinsonism. Parkinsonism is more of an umbrella term we use to define folks who have at least two out of the four following cardinal features. They have to have some bradykinesia, some slowness to their movement, some rigidity, a rest tremor and some balance problems, but not from any other cause. So if you have at least two of those four things, you have Parkinsonism.

Then about 75% of folks who have Parkinsonism have Parkinson's disease. Within Parkinson's disease, that needs to be a truly progressive neurodegenerative disease. The pathologic hallmark of that is going to be the Lewy Body. From our folks that have Parkinsonism, 75% of them have Parkinson's disease, and then that other 25%, have Parkinsonism from other causes. They can have it from medications, strokes, or from a number of different causes; this is what we call the atypical Parkinson's diseases. Those are the progressive supranuclear palsys (PST), the multiple system atrophies, and then a number of other diseases that are also neurodegenerative and share features similar to Parkinson's disease and share common treatments to Parkinson's disease because our treatments are not that specific yet, but are not exactly the same as PD. They also look and act a little bit different.

So I'm going to spend the rest of the time talking about Parkinson's disease, but keep in mind as I move from the diagnosis for Parkinson's disease, that a lot of times, one of our main goals is to differentiate PD from some of the atypical Parkinson's disorders I spoke off.

The topic is Parkinson's disease, and the key points of this is that the motor symptoms of Parkinson's disease are due to the loss of the dopamine cells in the substantia nigra. The reason that's important is because at this time, pretty much all of our symptomatic treatments are based on giving dopamine back.

The motor features of the disease are from the loss of dopamine, so the treatments are the ways we give dopamine back. In looking at the slide here, the brain on the left-hand side is a person with Parkinson's disease. You can see there aren't really any black dots there. Whereas the brain on the right-hand side in the area that's circled, there are a lot of black dots. Those black cells are the substantia nigra cells because the brain on the right-hand side is from someone who does not have Parkinson's disease. The brain on the left, where the substania nigra is pale, is someone who does have Parkinson's disease.

That is all I'm going to say about the physiology of Parkinson's. I'm happy to answer questions later, but the take home point is that it is due to the loss of dopamine cells. Specifically, the motor features of the disease, the movement part of the disease, is due to the loss of this dopamine cells.

Parkinson's disease is defined as having bradykinesia, slowness of movement, and at least one of the following: rigidity, rest tremor, and postural instability or balance problems but not from any other cause. One important point is about 25% of people with Parkinson's disease do not have a rest tremor. So certainly if a patient has one, that's very helpful in terms of diagnosis, but just because they do not have a tremor doesn't mean it's not Parkinson's.

It is common early in the disease for patients to talk about all of these things listed. They talk about how their handwriting is smaller, they will talk about slowness, they will talk about weakness, but it's more that their limb is not working well. It will be stiff and achy. They'll drag their legs, shuffle their walks, sludge over when they walk, have trouble getting out of chairs and rolling over in bed. A common complaint is getting out of the car. Their voice is softer or lower. There's a loss of sense of smell, dream enactment, constipation that usually predates the motor features of slowness by many years. Anxiety and depression is also very common, and you can also have a bit of a passiveness. They're not quite themselves. Things are just slower.

And some of these complaints, especially the loss of smell constipation, and the dream enactment, often come in years before they present to the doctor. At a certain point they may get the tremor, the slowness, the handwriting comes in and they reach out for more medical attention.

I want to point out that most of the time Parkinsonism is Parkinson's disease. You can tell on the pie charts, about 75% of Parkinsonism is Parkinson's disease. 25% is the other group I spoke about before. The people who have things like progressive supranuclear palsy (PSP), multiple system atrophy, medications, or strokes. However, we are going to focus on talking about Parkinson's disease.

So there is drug-induced Parkinsonism from drugs that reduce dopamine transition. Those drugs include haloperidol, metoclopramide, and risperidone. When folks have drug-induced Parkinsonism, it can be indistinguishable from PD. To manage it, we would reduce or discontinue the medication, but it could take months to resolve. For some patients, it's easy to take them off the medication. Only some patients with severe psychiatric illnesses, we're unable to change their antipsychotic. Dr. Pontone will talk about this. There are some antipsychotics that are less likely to cause Parkinson-like symptoms, so when patients have those diseases, we are able to switch them over to other antipsychotics. This involves a very close interaction between the managing neurologist and the managing psychiatrist to make sure the patient is on the best medication to manage their psychiatric illness and not cause any further problems with the side effects of their medication and with the movement disorder that's been developing.

One of the things that is important to point out is that Parkinson's disease is much more than the motor symptoms. In a study of more than a thousand Parkinson's patients, 99% of people reported non-motor symptoms, and the non-motor symptoms increased over time. Depression and apathy were the most frequently identified symptoms that had a determinant on quality of life. Motor function severity is of course also important in terms of health-related quality of life. Some other non-motor features patients talk about often include urinary urgency, fatigue, and sleep problems.

It is important when you're talking about treatments for patients with Parkinson's disease to discuss the non-pharmacologic therapies. I can't stress enough the importance of these non-pharmacologic treatments. Regular exercise is absolutely critical, and they need to be doing it all the time. There are a number of studies showing improved motor function for patients who exercise. Anecdotally, our patients who exercise do better than those who don't. A number of meta-analyses have shown this as well. Regular exercise programs are absolutely critical. They should be doing exercise that is challenging to them.

In addition, physical therapy is very important in order to restore their confidence and walking and maintaining balance. Sometimes they can use a cane or walker. Also an occupational therapist can help plan placement of assistive devices. I frequently send my patients to physical therapy, occupational therapy, speech therapy for swallowing issues and voice training, and these allied health treatments are critical to supporting the patient in terms of management of their disease.

Some of those non-motor symptoms are things that include psychiatric symptoms, sleep, and gastrointestinal issues; pain is a big problem along fatigue and urinary issues. In addition, cardiovascular dizziness comes up. Some of my patients are on anti-hypertensive medications to lower their blood pressure because prior to the development of Parkinson's disease they had blood pressure. Often times, we end up actually decreasing their anti-hypertensive medication, and sometimes, even taking them off the medication because the Parkinson's disease will lead to lower blood pressure. One of the primary medication treatments for Parkinson's disease can also lower their blood pressure.

On this slide, I have a list of some of the commonly used medications to treat Parkinson's disease. I'm not going to go over this in great detail, but I'm happy to answer any questions at the end. What I want to point out is that medication management for our patients can become very complex. Earlier in the disease, it's relatively simple. Patients are on one or two different medications, but as the disease progresses, the patients are often times on a whole host of medications taken multiple times a day.

The other thing I want to point out is that at the bottom of this slide, I have a list of medications that should never be used. If a patient with Parkinson's disease ends up in the emergency room, the hospital, or the assistive living, they should not be given Haloperidol, Aripiprazole, or any of the antipsychotics. Instead, if a patient needs it, they can be given Seroquel in small doses or Zofran for nausea. Those medications are unfortunately commonly used in the emergency room or in post-op cases, but it is important that for patients with Parkinson's disease, thought is given to taken the medication off the common order sets. Instead, nurses and care staff should be given options, if the patient needs it, for other medications, such as Zofran for their nausea.

There are some common complications that occur with Levodopa usually after four to six years of use. It is important to point out that these complications with Levodopa are complications from both the medication and the disease. While patients would not develop these complications if they were not taking the medication, the timing of the development of the complications is also related to the disease. There are patients who have not been on medications for 12 to 14 years, and they can develop these complications within one or two doses of getting the medication. It's the combination of the disease itself and the medication. Furthermore, it's important that we know that patients who take Levodopa do better than those who don't. Even though there are these complications, we should be aware of them and have patients on the lowest effective dose. Patients should not be afraid to take the medication, and they need to be encouraged to take the medication to adequately manage their symptoms to allow themselves to function well.

With that in mind, about 40% of people will develop dyskinesia after four to six years. These are the slow movements. Most people with dyskinesia do not get to the point of severity of Michael J. Fox, but rather experience small hand movements or swaying of the body. Risk factors for developing dyskinesia include a younger age of onset, higher Levodopa dosage, or a longer disease duration.

A lot has been put into the management of these complications of Levodopa and management of patients who are in the more advanced stage. A PD patient who has mid-advanced PD, who has sustained good response to Levodopa and fluctuates with the Levodopa response often times have dyskinesia. By

fluctuate, I mean people who take their medication, feel good, and often times then develop dyskinesia. Another hour or two goes by, and the medication wears off. Then, they can't move as well. They take it again, and the same cycle continues. These patients are good candidates for Deep Brain Stimulation (DBS) surgery or Levodopa Intestinal gel. There are a number of other advanced surgical treatment or advanced medication trials that are coming along on the market, but these are the only two currently approved. However, there are number of research studies going on with the idea being that, for a lot of our patients, the biggest problem is the lack of predictability. When their Levodopa fluctuates on and off like that, their days are not predictable. The purpose of the DBS and Levodopa Intestinal gel is to smooth out their days and allow increased flexibility.

This is a picture of the Levodopa-Carbidopa Intestinal job. I put it up here because it's new and somewhat recently FDA approved. You can see the pump on the right-hand side and the Levodopa connects to what is a gastric porter or peg-tube. It goes into the stomach, then the intestines, and ends in the duodenum. It is a steady stream of Levodopa therefore getting away from the pharmacokinetics from all pills. That is when you take the pill, you get the peak dose, and it wears off. Whereas, the Levodopa Intestinal gel smooths things outs; similarly, DBS also smooths things out.

In summary, we diagnose Parkinson's disease based on the four cardinal features that I mentioned before: Bradykinesia, rigidity, rest tremor and balance issues. There are also a number of supporting issues patients may talk about in terms of their slowness of movements, handwriting changes, and the way their face looks. Today, I spoke about some new medications and surgical treatments. Everything still goes after that similar mechanism of action, which is replacing the dopamine that was lost in the cells that are making dopamine.

The main take-home points are that Parkinson patients can often have a complicated medication regimen, and they have many non-motor symptoms that interact with their medications and with other diseases. Also, many symptoms can be attributed to Parkinson's disease, so patients can have a host of changes that are absolutely attributed to PD. I want to warn everyone on the call, as much as we like to attribute it to Parkinson's disease, patients can have as many diseases as they damn well please. So I point that out as a take-home point as well.

Thank you very much. I'd like to turn it over to Gregory Pontone to talk about the neuropsychiatric symptoms associated with Parkinson's disease.

Dr. Gregory Pontone: Thank you, Liana. I'm going to start talking about the other side of Parkinson's disease, the non-motor symptoms and specifically the neuropsychiatric symptoms. When Dr. Parkinson first described the disease in 1817 in his “Essay on the Shaking Palsy,” he believed that the senses and intellects were uninjured. Even when things as severe as dementia were recognized in people who were suffering from Parkinson's disease, it felt it was an accessory symptom. This was an elderly cohort for the most part. That is when senile dementia occurred, so it was thought to be just a secondary process sort of like Hickman’s phrase, where he could have more than one disease. It wasn't until the end of the 19th century that people began to recognize that personality changes and other cognitive and emotional changes were part of the disease. Parkinson's itself was a sufficient cause for these changes, and you didn't need a second explanation.

Dr. Rosenthal mentioned the cardinal motor symptoms of Parkinson's disease, and she commented that around 25% of patients do not have a rest tremor despite it being one of the cardinal symptoms. Some of these non-motor symptoms are even more common than these cardinal symptoms. Loss of sense of smell is in more than 90% of people with Parkinson's disease, so there is a higher prevalence than even the

tremor. A dysfunction of the autonomic nervous system is also common, and often starts before the motor systems. This includes things like constipation, which is nonspecific but prevalent in Parkinson's, erectile dysfunction, and orthostatic hypotension where people feel faint from going from sitting to standing because they do not have the appropriate autonomic nervous system response to maintain blood pressure.

The things I'm going to focus on today are the mood, anxiety, and behavior changes that occur in at least half of people with Parkinson's at some point in the disease. These non-motor symptoms are responsible for changing the way we think of the disease. Traditionally, we thought of the disease onset at the time of diagnosis by motor symptom recognition. However, it is probable the disease is active for a decade or more before the motor symptoms begin, possibly in lower brainstem regions, causing things like REM sleep and behavior disturbance. Anxiety and depressive disorders have also been shown to occur a decade or more before the onset of motor symptoms.

Surprisingly, mild cognitive impairments, which may not interfere with functions, is recognized in 40% of people at the time of diagnosis. At least half of people will go onto a full dementia syndrome within ten years of motor symptom onset. If you continue to follow people until death, many, around 80% or more, will go on to develop a dementia syndrome.

I'll start with depressive disorders because they are the most recognized and most common of the psychiatric disorders that occur in Parkinson's. At least 40% of patients have a clinically significant depressive disturbance. There are several types, everything from a minor depressive disturbance all the way to major depression, which by definition interferes with daily functioning. Depression is a little bit misleading and often missed because you don't have to be sad. You don't necessarily have to endorse sadness or low mood, but what must be there is a decrease in interest and engagement in your usual activities. Usually people report not enjoying things they were passionate about.

Some of the other difficulties in recognizing depression in Parkinson's is the overlap in the loss of energy and motivation, which could be due to either Parkinson's or depressive disturbance. The same thing with sleep changes; insomnia is a symptom of depressive disturbance and is common in Parkinson's, but it turns out if we treat depression as a syndrome, we still do a good job recognizing it. For instance the commonly used depression scales, like the geriatric depression scale which is the one we recommend to use in Parkinson's because of the age range for most patients, is equally good at detecting depression in Parkinson's as it is in the aged population. Things like the Hamilton depression inventory also work. This construct of depression still holds up even though it might be influenced by Parkinson's disease. What is less clear is how often depressive episodes occur in Parkinson's. It is not clear if they occur frequently or less frequently in the general population or if they respond to the current treatment.

One thing that is clear is that depression in Parkinson's disease is commonly comorbid with anxiety disorders even more so than in the general population. The clinical message is that, if you recognize depression in someone, also look for anxiety.

From a large clinical trial of neuro protective treatments in Parkinson's, there is some data about what the course of depression looks like in Parkinson's disease. Almost half of people suffering from a depressive episode in Parkinson's will remit within six months, and that's with or without treatment. One thing that is important is that even mild depressive symptoms predict a greater risk for developing more severe symptoms. The message there is that, if you recognize mild depressive symptoms, treat them because they put people at risk with more severe depressive disturbance. The risk factors for severity of the depressive symptoms are older age and longer duration of Parkinson's. They predict more treatment resistance for these depressive episodes in this Parkinson's study. Again, it looks like the pathology of Parkinson's is

contributing to the burden that people experience with depression. We are not sure of the exact mechanism, but these overlap. I will show you more evidence in the next few slides of how Parkinson's and depression overlap in a fundamental way.

Currently, the largest ongoing study of people with Parkinson's shows that depression has the biggest impact on quality of life. In fact, it impacts quality of life at least twice as much as the motor impairments that define the disease. Again, treating depression is an important clinical target because it can change people's overall quality of life.

I want to link depression and Parkinson's disease, the motor syndrome, even more directly. This is research from our longitudinal study of Parkinson's here at Hopkins, and basically, I'm going to show you a graph on the next slide that looks at activities of daily living, physical activity such as walking, hygiene, feeding yourself, dressing and talking and how depression affects those physical symptoms over time.

On this graph, the Y axis that vertical line, is the score on the northwestern disability scale with 40 being the highest level of functioning such as walking feeding and eating. The lower scores representing more disability. The X axis, or the horizontal line, from 0-6 is the number of years in our longitudinal study. There are three lines; the red and green overlap a bit. The blue line is people suffering from depression. You can see people suffering from depression physically function at a lower level at any time point than people who are not depressed.

The people on the green line are people who are never depressed and consistently functioning at a higher physical level. People on the red line are people who spontaneously experience depression or were treated by doctors and their depression improved. You can see that not only did their depression improve, which has a direct effect on quality of life, but their physical functioning improved simply by improving their depression. Clearly, these two symptoms are closely related.

Now transitioning to anxiety. Anxiety is at least as common as depression in Parkinson's. Half of patients will experience some type of clinically significant anxiety at some point of the disease though exactly how severe that anxiety is will vary from person to person. A third or more will have diagnostic and statistical caliber anxiety that require treatment. Certain types of anxiety are associated with the pathological process of Parkinson's and/or the dopaminergic treatment. The most common way we see it related to Parkinson's is in the on/off fluctuations in motor function where people take the medication, the motor symptoms improve and as it wears off, it gets worse. Anxiety comes as the motor physical symptoms return at the end of the dose. It turns out the generalized anxiety are more common than episodic anxiety in Parkinson's.

Anxiety at the level of the disorder is worry that is out of character compared to earlier times in their life. It's excessive worry that interferes with their ability to function on a daily basis. Sometimes, there can be physical symptoms of restlessness, butterflies in their stomach or other stomach complaints, and hot and cold flashes. In some cases, it could be severe episodes of panic-like anxiety that comes out of the blue and/or is triggered. In the case of fluctuation-associated anxiety, it comes on near the end of the dose. Once you establish that pattern, it might influence your treatment decision. Traditionally, we used antidepressants and serotonergic treatments for anxiety disorders, but if you recognize a pattern in anxiety related to the end of Parkinson's medication dozing, that might require a dopaminergic intervention. It's important to work with a neurologist to treat the specific type of anxiety you see.

Another common type of anxiety in Parkinson's is what we call anticipatory anxiety. This includes worrying excessively about an upcoming appointment or trip. We think that might be related, in cases, to

the executive function in Parkinson's because there is more trouble organizing sequencing and planning. It's harder to allay fears by running through the scenario before it happens in anticipating problems.

Similar to depression, the impact of anxiety is greater than the motor symptoms, and is an important clinical target. A higher level of caregiver distress is noticed in patients with anxiety. It's harder to take care of an anxious/depressed patient, even if the motor impairments are similar. If the anxiety is associated with on/off fluctuations, it is hard to say whether the anxiety might make on/off fluctuations more frequent or if it makes the anxiety more common. This is the same thing with freezing of gait. Sometimes people get anxious, and they freeze because of the anxiety, and sometimes they become anxious because they freeze. There appears to be a two-way association between anxiety and these motor complications.

In terms of how we treat anxiety disorders, there is limited literature on how to best treat them with medication. When I got my grant, we were the first one to systematically look at a pharmacologic treatment in Parkinson's. There is pretty good evidence that cognitive behavioral therapy is helpful for anxiety and depression in Parkinson's disease. In current clinical practice, what we use is the same for the general population, which includes, cognitive behavioral therapy, antidepressants, and in some patients, benzodiazepines. It's important to recognize that benzodiazepines, such as Valium and Ativan, have additional risks in Parkinson's, including increase risk in falls and cognitive impairment.

When considering treatments, you want to make sure their motor function is optimized. Certain types of anxiety are going to be linked to on /fluctuations and other problems with their motor symptoms.

Depression treatment is a little more advanced in Parkinson's. There have been good controlled trials of medications, and as I mentioned, there's good evidence that cognitive behavioral therapy helps. As Liana mentioned earlier, exercise seems to be an important intervention, not only potentially as a disease modifying intervention, but for both motor and non-motor symptoms. Staying active and exercising helps mood and anxiety as well.

There are a couple of systematic reviews in meta-analyses looking at drug and nondrug treatments for depression in Parkinson's disease. I want to give you the consensus of the current systematic reviews and meta-analyses. It appears that for both efficacy and safety, the selective serotonin reuptake inhibitors, things like Zoloft, Paxil, and Prozac, have the best evidence for treating depression in PD. They do so at the same doses used in the general population. Of course, cognitive behavioral therapy, alone and in conjunction with SSRIs, is also effective. There's also evidence that RTMS, Repetitive Transcranial Magnetic Stimulation, is effective for depression in Parkinson's disease and may even provide a secondary benefit for the motor symptoms. That might be another depression treatment to consider.

Now, I want to talk about Parkinson's disease psychosis. Currently, the best criteria to use in recognizing psychosis in Parkinson's is the NINDS criteria, the National Institute of Neurologic Disorder and Stroke. Basically, that requires at least one of the following symptoms to be present: illusions, false sense of presence, such as feeling that someone is in the room when no one is, hallucinations and delusions. The symptoms of psychosis need to be related to Parkinson's. If they're preexisting, they are due to another phenomenon. They should be continuous for a month. Basically, you want to make sure you exclude alternate causes of Parkinson's disease psychosis.

Psychosis can mean a lot of things, but overall, it consists of perceptional disturbances, illusions, and thought disturbances or delusions. The key difference between illusions and hallucination is that illusions require that there's an external stimulus in in the environment that is being misperceived. Whereas,

hallucinations can occur with an absence of an external stimulus. For instance, if you see a man in the corner of your room and you turn on the light and it is a coat rack; that is an illusion. If you see a little girl on the bed and you flip the light and nothing is there, that's a hallucination because there is nothing to be misperceived.

Delusions are disorders of thought, and they're false, fixed, idiosyncratic beliefs. They can be bizarre, but they could also be about mundane topics. It can take a while to recognize a delusional belief because it might be plausible. The other problem with delusions is they can't be reasoned with. I worked with many caregivers and families that were frustrated by delusions because they can't provide insight to their loved one, and they can't talk them out of these beliefs no matter how problematic they might be. While we don't necessarily say that it is inappropriate to try to provide insight, it might not be effective and it's not going to be fruitful to argue with people with delusions. They're going to require, in most cases, medication treatment.

One of the most important clinical distinctions, whether it is perceptional disturbances like illusions, hallucinations, or delusions, is whether or not the patient has insight or not. Do they recognize that these experiences are unreal or do they have some idea that these are not real?

I want to give you two examples that illustrate this important point because both can result in adverse outcomes, depending on the level of insight. Take a patient who sees a bunch of people entering his home at night, and they look aggressive, so he gets his firearm, loads them and gets ready to defend his house. He has no insight that these people aren't real. Everybody would agree that's clearly a dangerous situation, but let me give you an example of a non-distressing hallucination that might be equally as dangerous.

Here's a patient whose brother goes to work every day, so he is home alone. He sees a parade of three foot wooden puppets. He enjoys these because they're entertaining, and he's bored. The problem comes one day when he needs a snack during the parade. He tries to cross the hall to the kitchen to make a sandwich, but has to step over the parade and falls and breaks his hip. This resulted in a pretty bad adverse outcome. The mortality is high with hip fractures in Parkinson's. Here's an illustration of the lack of insight even in non-distressing hallucinations making them dangerous. If you're deciding how to aggressively treat psychosis, this distinction of with and without insight is important.

Another important type of phenomenon, which might not be fully psychotic, is vivid dreaming that occur in waking from sleep or going to sleep. Vivid dreaming is when people have dreams that feel real that upon waking, they may think it was real. This is sometimes responsible for people wandering and having adverse outcomes. If this comes to light, you definitely let your physicians know even though it might not be fully in the full spectrum of psychosis.

Again, just like anxiety, depression, and the psychiatric problems, psychosis worsens quality of life. It's one of the major reasons for lowering or discontinuing dopaminergic drugs that help with motor symptoms, which is an unfavorable trade off. You're worsening their movement in order to control their psychosis. It's one of the leading cause of hospitalization and institutionalization more so than their motor disabilities. People don't wind up in nursing homes because of their motor impairment whereas they may because of the psychosis. It also increases risk of mortality.

When managing Parkinson's disease psychosis, you want to treat any underlying medical illnesses. Sometimes you'll get lucky. You'll recognize an infection or something else triggering the psychosis. Urinary tract infections are common. Another common cause is medications; anticholinergic medications, for bladders symptoms, and pain medications, such as opiate pain medications, can be a problem. The

reason that anticholinergic medications are important, is because they are over-the-counter. Caregivers will get over-the-counter sleep aids that may be anticholinergic; these can trigger psychotic episodes, so be sure to check if any of these medications are introduced. If Parkinson's medications, specifically dopaminergic-medications, have been added or increased recently, that is an important thing to recognize and may be adjusted.

Using antipsychotics is important as well. Some evidence shows that cognitive medications/inhibitors might indirectly lessen the burden of psychosis.

If people are experiencing hallucinations, especially if they're happening more toward the evening or at night, you want to add night lights or make the house better lit. Discuss this with the patient, so they don't panic and provide education. Visual techniques such as looking away from the hallucination can sometimes help. Interacting with people seems to decrease the frequency, so isolation is another risk factor for this.

I'll turn this over to Arita McCoy, so she can talk about patient and family support for Parkinson's disease.

Arita McCoy: Thanks, Dr. Pontone. I'm going to briefly talk about how to best manage and support patients and families with this disease. Those needs evolve as time progresses with Parkinson's, so early in the disease, we want to make sure that individuals have good education on what Parkinson's is and how to best manage it, so they can educate themselves, families, coworkers, and other loved ones about the disease.

We want to start controlling their symptoms. We really don't need aggressive treatment, but mainly mild symptom control as Dr. Rosenthal went over. We will also discuss being proactive in developing ways to manage Parkinson's early. That includes exercise, nutrition, staying socially engaged, and developing the healthcare team, which we'll talk about.

During the mid-stage of Parkinson's, we're doing more with symptom control, focusing on specific problems and maybe a little bit more aggressive treatment at that time. We're also using our specialty care. Depending on how many problems that patient may have, we may need to send them out on referrals.

The advanced stages of Parkinson's includes more cognitive problems and managing those and maybe assistance with activities of daily living and other things that come up as the disease progresses.

One of the things that we are pretty big advocates of is education, so support groups have been a strong part of managing Parkinson's disease and developing community around the disease. It's an extension of the doctor's office visit where you're learning more about your disease and specific problems that can come up. Support groups are often present in certain cities or counties or maybe even regions, depending on the area. These usually span over a multitude of different topics that patients and families may have questions about. It allows them to become their own self-advocates, and find community resources in their own local network that might be helpful for them.

The next slide shows an example of support groups that we support at Johns Hopkins in Baltimore Maryland. In 14 counties of the state, we have about 29 support groups. There are three counties where you'll see purple stars; those are groups that we help manage and coordinate within our center. The red stars are groups that are run by local community leaders and natural leaders in general. That shows you

how support groups are something that people appreciate and take upon themselves to continue. We try to be a liaison for them, but it's a very important part of extending care beyond the doctor's office.

We talked a little bit about therapies in the beginning, but physical therapy, occupational therapy and speech therapy are a big part of the support network. With physical therapy, there are special trainings that are available for therapists, and those are the groups we tend to refer to the most. There is the Lee Silverman Voice Technique (LVST) that extends not only with speech therapy but also with physical and occupational therapy. The BIG program is something that physical therapists can become certified in. They're specializing in balance disorders, gait problems, allowing patients to retrain themselves on how their natural body instincts change as Parkinson's changes and forcing the movement in other ways. PWR (Parkinson's Wellness Recovery) is also a specialty PT program. You can find these therapists through their online systems and search for one in patients' areas. Balancing and gait training can be a focus for a center or a specific therapist. Occupational therapists are excellent because they can specialize in the BIG program, but they can also help with activities of daily living and other issues that come up as Parkinson's progresses.

OT's are also great at doing home assessments. They can recommend home modifications such as grab bars or assistance with their shoes or buttoning buttons. They are great at talking patients through those motor symptoms and providing assistive devices and other ways that they can help with walkers or canes or other modifiers.

We see issues with speech commonly, so we pull in the speech therapy team. The LSVT team provides the LOUD training, but also swallow evaluation and cognitive training are helpful for patients with Parkinson's when we're talking about the disease progressing.

We also have community exercise programs. Dr. Rosenthal and Dr. Pontone both talked about the importance of exercise. There are special Parkinson-specific programs like Rock Steady boxing and also dance for Parkinson's disease. There are also exercise courses that have been developed by special trainers who have taken time to get training in PWR or other modalities. They may focus on balance or stiffness. Yoga, Tai Chi, and other modalities can be helpful and hone in on different parts of the disease and strengthening those areas. There's a ton of these classes; there is cycling for Parkinson's and many others that patients can do. We tell them to do what they are going to continue doing over a long period of time. Finding things they enjoy and keeping up with them is very important.

I'm going to talk about the networks we want patients to develop early in the disease so they can have a comprehensive care team. The first person that's very important in that plan is the neurologist. Often times, when people are diagnosed with Parkinson's disease, it is with a neurologist, but it could be a primary care doctor. We want to make sure patients understand, that it is important to seek neurology care. This would be the primary person treating Parkinson's disease but could also refer out for specialty care including PT, OT, psychiatry care, and urology. Gastrointestinal and also sleep disturbances may be referred out to specialty care. Neurologists can refer out to deal with those specific problems as they need to.

The neurologist should also know about medication changes. We talked about medication interactions; that is an important part of this puzzle as well. Movement disorder specialists are actually neurologists who received specialty training in movement disorders. If patients are questioning their diagnosis or aren't sure whether or not they're receiving the best care, they should be able to consult with a movement disorder specialist. This could be their primary neurologist or someone they consult with once a year if they're not living near a movement disorder specialist, but it is an important part of the puzzle that

patients should consider as they're being diagnosed with PD. The most important thing is they feel the neurologist is competent, accessible and communication is good between the patient and the neurologist. Making sure the disease is managed the best way.

It is important to know that it's okay to get second opinions in order to make sure the disease is being managed the best. A comprehensive care team is an important part of managing this disease over time.

The primary care physician is also an important part of family support. The primary care is the hub for all of the medical issues or problems, not just Parkinson's disease, but all the other things that can occur as a part of the aging process. This person should be the primary tie to all the specialty care folks that Parkinson's patients are interacting with on a regular basis. We request that patients send all of their records to their primary care doctor. Geriatric internists are great in Parkinson's disease because they end up also being able to specialize in comorbidities and dealing with those medication interactions that can come from polypharmacy and other issues that arise in the aging population. We want this to be a trustworthy relationship, and we want the primary care doctor to be accessible and local and someone they are comfortable with. There are some acute issues that can come up with Parkinson's. We want to make sure that patients can get worked up for those right away.

Another important point that I want to discuss briefly is about hospitalization in Parkinson's disease. This is an important concept because when our patients are hospitalized, they end up having a lot of other issues and problems that come up during their hospital stay that they may not have had when they went into the hospital. Most often, patients are presenting in the emergency room or going to the hospital overnight for infections; that can be urinary tract, which is the most common. Dr. Pontone talked about delirium that can send people to the ER right away. Falls and injuries could be a part of hospitalization needs and also scheduled procedures. Overall, we find that people with Parkinson's are hospitalized 50% more than their peers.

That is part of the process we should be educating patients about. Worsening of the disease can happen because medications can be given off schedule. There is an hour before or after window for medication timing; this is a problem when we talk about the rigid complicated medication schedules that can come with Parkinson's disease. Dr. Rosenthal talked about contraindicated drugs. We see that in acute hospital settings, that is where a lot of those drugs end up being administered. The therapies that patients need including physical therapy and speech therapy may be delayed or not as effective if the medication cycle is not done correctly.

I want everyone to be aware that the National Parkinson's Foundation has developed an Aware and Care kit. This is an excellent resource that is consolidated to one bag for patients when they are hospitalized. This is important because we've got a list of all the medications that patients with Parkinson's should avoid during hospital stays, and it also gives guidelines for safe medications that can be given for the same indications.

If you flip to the next slide, you'll see what that sheet looks like. There is a photo further down on the page. On the back, there are the contraindicated medications and the safe ones to give for people with Parkinson's disease. They can put the medication inside the kit. These kits are available on http://www.parkinson.org/find-help/aware-in-care-kit. Anyone can order them and have them available.

We also want to make sure we are taking care of the caregiver. Part of this is making sure that when additional help is needed, we are able to talk with the caregiver about those additional needs and make sure that we are guiding them appropriately.

One of the things that we often do is have caregivers fill out a caregiver strain index, which goes over different parts of caring and being a caregiver. That questionnaire can highlight many of the issue that's we want to avoid when caring is too stressful.

We also know that if there are safety issues, we need to pull additional help. We are talking about more falls, more problems with mobility, walking eating or daily activities or balance problems. We also know we may pull in additional help if there are cognitive problems or if there are hallucinations or delusions causing behavioral trouble.

When that additional help is needed, we know that we need to pull in the care team. So more than caregivers, we're also talking about family and the friend network, supporting your neighborhood and your faith community. Moving is something that we often have to talk about with patients and their families especially if there are safety issues with steps or tight spaces, which tend to be difficult for Parkinson's mobility. It's a difficult decision for both parties but continuing care in retired communities are great options where you can benefit from things that are great for aging but can also benefit from the transition of care if that's needed.

We often tell patients and families, it's not a failure of either the patient or the caregiver that they're not able to stay in their homes. It's more of a realization that there are other medical issues beyond what the family or the care partner can provide. The caregiver role doesn't change; it stays the same, but the level of care and type of care just changes as the disease progresses. The caregiving role becomes more of an advocate role or overseer of care to make sure there are appropriate things that are happening and can be honed in had on as the disease progresses.

Okay, so with that, I will introduce Maryann Powderly who is an amazing family caregiver of a spouse who has Parkinson's disease.

Maryann Powderly: Thank you, Arita. Good afternoon to all. Thank you to all of the presenters today, some of which are part of my husband's team. My husband Mike was diagnosed with Parkinson's disease around 2002 when he was 42-years-old. We lived in Long Island at the time with our three sons; our middle son has special needs. About the time of Mike's diagnosis, I had eight years earlier gone through Hodgkin’s. We thought we had our hands full prior to that.

At the time, Michael had been working in Manhattan and been going into the city on the Long Island Railroad for about 20 years. Walking up was the favorite part of his day until Parkinson's because getting to Penn station and around crowds became more difficult.

We slowly noticed his arm swinging and some other motor symptoms, and then he was eventually diagnosed by a local neurologist. In 2004, we decided to move to Maryland; Mike’s brothers moved down here, his company had an office here, and it was difficult for him to keep up with the pace of Manhattan.

It was a difficult decision to tell the people at work he had Parkinson’s. We went back and forth on that decision a lot, but he was in sales doing presentations, and he was a little shaky. His voice was not as strong, so he was afraid people would think he was losing his edge or drinking at work.

In 2006, after much research and prayer, Mike had DBS surgery. It was life altering and helped him a great deal. I know that he still has a lot of other symptoms and difficulties, but the actual tremor is greatly helped by having the surgery.

We had hoped at the time it would allow him to work a little longer, but he went out on disability in 2010 full-time. We felt all the pressure of him; his position was putting a strain on his disease and the symptoms, so we decided at that time that was a good time for him.

We did go on COBRA insurance. It was difficult because he had to go on Medicare. I had to have insurance for myself and my kids and all the premium costs of insurance.

Now that I've given you the history, I want to mention a few points that I think are important to managing his care over the years and really trying to keep our family intact.

In Maryland, we are blessed with great hospitals, many which take a team approach. I can't say enough about the continuity of care. A few months ago, Mike was struggling with an increased tremor. We found out several of his doctors took a team approach on how to handle it. The surgeons and neurologists came together to decide on next steps. Did they want to do a different type of DBS or change medication? Between that and the electronic health record, keeping track of everything as a caretaker is really important.

I think another point to mention as a family member is the challenge that the entire family goes through with the diagnosis of this kind. Obviously for Mike, it's been a challenge to face the physical and cognitive changes. He can't just get up and jump out of bed, and this was a man that was a New York City marathon runner, but you know it goes deeper than just the patient. We have three kids, and they walk-the-walk. Their dad has fallen numerous times, and the brain surgery was scary for them. Our youngest was only 10-years-old at the time. We moved from New York to Maryland, and our youngest son can't remember his dad not having a limp. There were difficulties there. The pro is that they are nurturing. Even though they don't live at home, they spend a lot of time supporting us.

Being a caregiver is not always easy. While we continue to have a great relationship, it is a different relationship than the way it was. Sometimes it is like parenting with coordinating multiple doctor’s appointment and reminding him to sit up while he is eating, so he doesn’t choke. He is starting to have increased cognitive difficulties, so it's hard to be patient all the time on my end and that brings guilt to me.

The other important thing to mention is remembering the difference between the young-onset, at 42, compared to an older patient. There are so many different things that go on. The challenges that an older patient faces are different. Most likely, a person with young-onset is still working and may feel embarrassed at work.

People at work probably already know something is wrong. Deciding to go out on disability is another problem for people with young onset. Do you go out when you can't do the job or get fired? Also, you still have a young family at home, and the busy schedule is hard to keep up with. Like us, if your family moves and changes jobs, how will that affect you? Lastly, Michael will be taking these medications longer than someone whose diagnosed later in life.

In closing I want to say, even with these challenges we feel blessed. We have a great life and family. We try to provide care with love, but the disease affects the whole family; it affects where we live and the job choices, so we can have insurance. I started working at Hopkins a year and a half ago mostly because I needed insurance that the local doctor that I used to work for could not provide.

Thank you for letting me share my story. I hope it helps you understand the needs of your patients and family. If you're caring for someone, I hope this helps a little bit. Thank you.

Caroline Loeser: Great. Thank you so much, Maryann, and thanks to all of our speakers, Dr. Rosenthal, Dr. Pontone, and Ms. McCoy.

We have a few minutes now for questions from the audience. We have a couple that came in throughout the course of the presentation.

I'll start with the question we got during Dr. Rosenthal's portion. It was specifically about what Lewy Bodies look like. I know we don't have a slide to show, but if you would go into detail, that would be helpful.

Dr. Liana Rosenthal: Sure, the Lewy Bodies are a glob of proteins that are inside the neuron. You can probably do a nice Google search for the Lewy Body features. That should show you that it is this abnormal, circular area within the neuron. Depending on the type of stain you are using on the pathology of the tissue, it will be a different color, but basically, look for a circular thing within the neuron. Lewy Body is both in the substantia nigra, where the dopamine making cells are, and in the cortex, which is where we believe the cognitive changes come from.

You can also see the protein that makes up the Lewy Bodies, alpha-synuclein. They found abnormal alpha-synuclein cells in tissues and skin biopsies. The direct answer is that they look like abnormal globs of protein.

Caroline Loeser: Thank you, Dr. Rosenthal. We'll move onto the next question. This is directed to Dr. Pontone. Is the PHQ2 and PHQ9 equally effective screening in measuring depression severity with patients in Parkinson's disease?

Dr. Gregory Pontone: I would not recommend the PHQs. I would recommend a more depression specific scale. As I mentioned, there have been studies of which scales to use. For the most part, the geriatric depression scale looks the best. You can also use self-inventories, such as the Beck Depression Inventory, the Hamilton Depression Rating Scale, or the Montgomery-Asberg Depression Scale. There are a number of options, but I would say, use the ones that are depression-specific, the ones that measure other non-motor symptoms or quality of life can be tricky because they're not sensitive or specific enough.

Caroline Loeser: Great, thank you. Ms. McCoy, we have a question for you that came up during your portion of the presentation. The question is, how can we best improve provider collaboration in treating Parkinson's patients?

Arita McCoy: That's a great question. I think provider collaboration is one of those things that is a sensitive topic for some. It is best to reach out personally to the healthcare team. I've reached out to primary care teams and hospital care teams, and that direct connection provider-to-provider seems to be a pretty collegial relationship. I think it's more difficult to try to navigate around getting notes and other things when you haven't actually made that direct connection. Talking one colleague to the other is a helpful relationship.

Same thing with our therapists, PT, OT, SOP; we love for them to reach out and talk directly to one another. I think that's the best way to facilitate that communication. It takes a little bit of effort and work, but once that connection happens, it tends to be advantageous to the patient.

Caroline Loeser: Great. Thank you for your response. Dr. Pontone, I'm going to move to another question for you. What do we know about the interaction of opiate given for pain management in Parkinson's disease?

Dr. Gregory Pontone: Opiate pain medications, similar to the benzodiazepines, potentially increase the risk of falls in Parkinson's because of decreased attentional resources. Opiates, even in non-Parkinson's conditions, are infamous for causing confusion, and is more likely to happen in neurodegenerative disorders. So, you want to be caution about using them. Now, sometimes it's inevitable. For instance, if you break your hip, for a short period of time, you're going to require the heavy duty medications. At that point, you do your best to use the least amount possible to control the pain, and do things like keeping the area where the person is well-lit and keep them engaged to decrease the risk of hallucinations and confusion to the extent that you can.

Caroline Loeser: Thanks for your response. I'll open up this next question to our panel. Can you comment more on sexually inappropriate behavior related to sentiment? Also, there's a follow-up question that asks, how can you tell the difference between Parkinson's disease and Lewy Body disease?

Dr. Gregory Pontone: I'll take the one about sexually inappropriate behavior, and I assume that's probably related to dopaminergic medications. One scenario that I see with sexually inappropriate behaviors in Parkinson’s patients is an impulse control disorder, which has been associated with dopamine agonists and sometimes, but less frequently, to Sinemet where that dopamine agonist triggers something that revs up normal drive. People require or request an increased frequency of sex or even have sexual behaviors that are outside of their characteristic appetites.

And so, when you recognize something like that, it is important to take a history that looks for new medications introduced or a change in medications especially if there are dopamine-containing medications. Try to bring that to the attention of a doctor as soon as possible because sometimes when there's one behavioral problem, like sexual changes, there could be other behavioral problems that you might be missing or hiding in the shadows.

The second scenario where I see sexually inappropriate behaviors is with a major mental illness occurring in Parkinson's. One would be a bipolar illness which is fairly rare, but it can cause mania, which can have hypersexual behaviors. The other one that's unfortunately fairly common is when people start to develop cognitive impairment and dementia, they can be disinhibited and they might perform sexually inappropriate behaviors or make sexually inappropriate comments in inappropriate social contexts. That may be another scenario, and obviously that has a different set of management demands.

Caroline Loeser: Thank you, so much. Dr. Rosenthal, are you able to address the question about how you can tell the difference between Parkinson's disease and Lewy Body disease?

Dr. Liana Rosenthal: Absolutely. The pathology of Parkinson's disease are these Lewy Bodies, and the pathology of Lewy Body dementia is also these Lewy Bodies. Most of us believe that dementia with Lewy Bodies and Parkinson’s disease with dementia are actually a continuum. For most of our patients, we think about it in terms of which features are more prominent. So dementia with Lewy Body patients often have early in their disease hallucinations, significant fluctuation and moderate to severe cognitive

impairment in addition to Parkinsonism. The official definition, are patients who have moderate to severe cognitive impairment within one year of onset of the motor features of Parkinsonism. Those people have dementia with Lewy Bodies.

People who develop significant or moderate cognitive impairment more than one year after developing motor problems, those people have Parkinson's disease with dementia. It is more of a continuum, and we think about it as patients who have clusters of hallucinations and rapid motor day-to-day fluctuations versus those patients who have more of an insidious course of dementia that develop over time. The official cut offs are the one year mark, but that relies on patient history, which in some patient is very good and in some patients isn't quite as clear.

Caroline Loeser: Great. Thank you, Dr. Rosenthal. At this time we're going to go ahead and close the presentation. I know there are a questions that weren't addressed, so we will type it up in a Q&A document and post it on our website. If you have additional questions for our speakers or comments you'd like to make, you can go ahead and email us at RIC@Lewin.com. The slides for today's presentation and recording and the transcript are going to be available shortly.

Thanks again to all of our speakers. Have a wonderful afternoon, and thanks so much for your participation.