CENTERS FOR MEDICARE AND MEDICAID SERVICES

Medicare Evidence Development & Coverage Advisory Committee

Devices to Manage Tremors in Parkinson's Disease and Essential Tremor

June 25, 2025

Centers for Medicare and Medicaid Services
7500 Security Boulevard
Baltimore, Maryland

Panelists

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Vice-Chair

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Director, Coverage and Analysis Group

Tamara Syrek Jensen, JD

MEDCAC Coordinator

Tara Hall

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PANEL PROCEEDINGS

(The meeting was called to order at 10:00 a.m. EDT, Wednesday, June 25, 2025.

MS. HALL: Good morning and welcome, committee chairperson, vice chairperson, members and guests to our virtual MEDCAC meeting. I am Tara Hall, the Medicare Evidence Development and Coverage Advisory Committee coordinator.

The committee is here today to discuss the devices for management of tremor in patients with Parkinson's disease or essential tremor. The MEDCAC panel will examine which clinical endpoints in studies of devices to manage tremor in Parkinson's disease and essential tremor should be of interest to CMS. The MEDCAC panel will consider a review of the relevant clinical research and professional guidance literature, along with expert commentary.

By voting on specific questions and by their discussions, MEDCAC panel members will advise CMS about the ideal clinical endpoints and research studies of evidence to manage tremor in Parkinson's disease and essential

tremor, as well as appropriate measurement instruments and follow-up durations to help provide clarity and transparency of national coverage analysis.

The following announcement addresses conflicts of interest associated with this meeting and is made part of the record. The conflict of interest statutes prohibit special government employees from participating in matters that could affect their or their employer's financial interests. Each member will be asked to disclose any financial conflicts of interest during their introduction.

We ask in the interest of fairness that all persons making statements or presentations disclose if you or any member of your immediate family owns stock or has another formal financial interest in any company that is related to this topic of Parkinson's. This includes speaker fees, salaries, grants and other support. If you require a financial disclosure statement, please email Ruth McKesson so she can send you the form for completion. Her email is

ruth.mckesson@cms.hhs.gov, that is r-u-t-h dot m-c-k-e-s-s-o-n.

We ask that all presenters please adhere to their time limits. We have numerous presenters and a tight agenda; therefore, we cannot allow for extra time. During each presentation presenters will receive reminders informing them how much time they have remaining to help them stay within there allotted time. Presenters will receive a prompt two minutes prior to their speaking time to insure they are ready to present.

During the open public comments, attendees who wish to address the panel will have that opportunity on a first come basis. Please email Ruth McKesson if you want to address the panel by 11 a.m.

For the record, voting members present for today's meeting are Dr. Sanket Dhruva, Dr. Irene Chen, Dr. Robin Newman, Dr. Sally Stearns and Ms. Amy Goldsmith. Nonvoting panel members are Dr. Joseph Ross and Dr. Laura Mauri. A quorum is present and no one has been recused because of conflicts of interest.

The entire panel, including nonvoting

members, will participate in the voting discussion. The voting results will be available on our website following the meeting.

We ask that all speakers state their name each time they speak. Speak slow and concise so everyone can understand. Speak directly into your computer mic and do not use your speaker phone to help achieve best audio quality. Insure your devices are on mute if not speaking, and while speaking please place ringers on silent. Remove pets from your area and anything else that will minimize distractions and limit the background noises.

This meeting is being held virtually in addition to the transcriptionist. By your attendance, you are giving consent to the use and distribution of your name, likeness and voice during the meeting. You are also giving consent to the use and distribution of any personally identifiable information that you or others may disclose about you during today's meeting. Please do not disclose personal health information.

In the spirit of the Federal Advisory Committee Act and the Government in the

Sunshine Act, we ask that the advisory committee members take heed that their conversations about the topic at hand take place in the open forum of the meeting. We are aware that meeting attendees including the media are anxious to speak with the panel about these proceedings. However, CMS and the committee will refrain from discussing the details of this meeting with the media until its conclusion. Also, the committee is reminded to please refrain from discussing the meeting topics during the break.

And now I would like to turn the meeting over to Tamara Syrek Jensen, CAG director.

MS. JENSEN: Good morning. I'm Tamara Syrek Jensen, the director of the Coverage and Analysis Group. First off, I want to thank the MEDCAC panel for their time and sharing their expertise with CMS, and also thanking to everyone else that is participating today, including the CMS staff, to make this MEDCAC successful.

As many of you know, the Medicare Evidence Development and Coverage Advisory, or

the MEDCAC, was established to offer independent guidance and expert advice to CMS on specific clinical topics. Today's topic is devices managing Parkinson's disease and essential tremor. Terry Rogstad, she will be going through the clinical evidence report and explaining the basis for this particular MEDCAC, and then our MEDCAC panel will be discussing this topic and voting on specific questions.

Before we get to that, I wanted to go a little bit off script today and I wanted to announce that today is Dr. Joseph Ross' last MEDCAC. He has spent the last eight years on the MEDCAC, the majority of it as a cochair or the chairperson. I personally wanted to thank him for his guidance and his leadership for this MEDCAC. The MEDCAC is better because of his leadership and he has established a role model for our next chairperson, Dr. Sanket Dhruva. So thank you, Sanket, for taking on this role, we do appreciate that, and I am sure you will lead us well in the future as well.

As you will also hear, we do not have a cochair person to announce today, but

hopefully we will be announcing that in the near future.

So, thank you again for all of your time today. We do appreciate everything that you, the expertise that you are going to give us today. There are many devices coming to the market for managing Parkinson's disease and essential tremor, and this will help CMS make their decisions on all of those devices. Thank you.

Tara?

MS. HALL: We will call on Ms. Teresa Rogstad.

MS. ROGSTAD: Thank you. If someone will pull up the slides?

Good morning, everyone. My name is Teresa Rogstad and I am a senior advisor in the Coverage and Analysis Report. As was reported earlier, I am going to review the CER report that CMS commissioned, and review the background information from this report that is the focus of today's meeting.

Could we go to slide number three please? Next slide.

So, the objective of this report was

to identify the most common clinical endpoints for clinical studies of medical devices for the management or treatment of medication refractory Parkinson's disease and essential tremor, with a focus on tremor and motor symptoms. A secondary objective was to identify the instruments or tools commonly used to assess those endpoints and to identify definitions of clinically meaningful differences for each instrument where possible. Next slide.

So Parkinson's disease is, involves the progressive loss of dopaminergic and other kinds of brainstem neurons which leads to impaired motor function. These clinical signs include slowness of movement, muscle rigidity and tremor, which is worse during rest. Some non-motor symptoms are also characteristic of this disease.

First line treatment is pharmaceutical, beginning with levodopa and other dopaminergic drugs. They stimulate the dopamine receptors of the brain, but long-term use can lead to what are called motor complications. These come in two forms. One

is motor fluctuations, which refers to variable effectiveness or treatment efficacy wearing off. The other kind of motor complication is drug-induced dyskinesia, which involves involuntary erratic movements. And as we'll see later, professional guidance documents stress tracking the motor complications in patients who have Parkinson's.

So because of these complications, nonpharmacologic treatments, mainly devices, have been developed. Next slide please.

Essential tremor is also a progressive disorder, but the tremor that characterizes this disorder occurs during voluntary movement, in contrast to Parkinson's disease tremors. Non-motor symptoms also occur with essential tremor. Next slide.

So the goal of nonpharmacologic treatment is to improve motor symptoms, including tremor and/or to reduce motor complications in Parkinson's. Examples of nonpharmacological treatments include various types of stimulation or surgery, as well as external devices. Next slide.

So the CER report began with a

systematic search of the published literature beginning in January 2008 and going up through August of 2023. The gray literature was also searched. The review authors collected systematic reviews of any device that was used to treat tremor associated with Parkinson's or essential tremor. The report also collected professional guidance documents. These could be consensus statements regarding clinical endpoints for studies of any treatment for these disorders, or it could be practice guidelines on the management of these disorders.

The authors of the CER consulted with a neurologist with expertise in movement disorders at the beginning of the report, and that neurologist also reviewed the first draft of the report. Next slide please.

The report reviewed 30 systematic reviews and abstracted all the clinical endpoints that were reported for the included studies in each review. This list of clinical endpoints was then subjected to a prioritization rule that was based on a certain threshold of citation volume.

The report selected five professional guidance documents and extracted the clinical endpoints that were emphasized in those documents either through implication or by explicit recommendation. In today's discussion we will focus on the endpoints that were implied or recommended by at least two of these five documents. Next slide please.

After the CER report was completed, it was sent to three subject matter experts in academia for additional clinical perspective. They included one neurosurgeon and two neurologists who were different from the neurologist involved in the development of the report. The version that these subject matter experts responded to is the same version that was posted on the website prior to this meeting, so their input has not been incorporated into that report but it is reflected in my slide presentation today. Next slide please.

In the following tables I'm going to be reviewing the key findings from the CER report, and these same tables appear in more detail in a Word document with the file name

PD/ET CER Summary, and this is available on the website for today's meeting under other materials in a ZIP folder labeled comments. So please keep that handy to refer to during the discussion that follows my presentation. Next slide please.

So most of the endpoints that were determined to be important by the CER report and the external reviewers fell into the domain of clinician-assessed health outcomes, and by clinician assessed we mean endpoints that were either directly measured by a clinician or assessed in the context of an instrument that the clinician administered with or without patient-reported information.

The black font in this table shows the clinical endpoints that met that prioritization threshold in the CER report. The red font shows the clinical endpoints that were added to this list by the hits three external reviewers.

I'd like to comment a bit on activities of daily living, which you see down close to the bottom of this slide. These are not the same activities of daily living that are used to assess general function, they are

disease specific activities that are affected by Parkinson's disease, often referred to in the literature as experiences of daily living. Next slide please.

In the patient-reported outcomes domain, quality of life and sleep quality were determined to be important and both of them are, can be measured by disease specific scales.

The CER report did not find safety outcomes to be frequently cited. This is probably because the report focused on systematic reviews, which don't normally cover a wide range of outcomes. But our three expert reviewers were very helpful in this regard and identified some potentially serious adverse events on the left-hand side of this slide. The external devices are usually not accompanied by anything very serious. Next slide please.

I would like to comment on the United Parkinson's Rating Scale. This was by far the most common instrument used in the clinical research literature and the most frequently recommended by our external reviewers. The

current version is a revision that was published in 2008 by the Movement Disorders Society. The scale consists of four parts, each of which has been separately validated and paired with a definition of a minimal clinically important difference. Next slide please.

With regard to essential tremor, only a handful of endpoints were identified and not surprisingly, they all relate to tremor. The instruments that we use to measure these outcomes on the right-hand side, none of these instruments were found to have definitions of MCID, at least as far as we could tell. The device-related outcomes are the same as those that were supplied by the expert reviewers for Parkinson's disease. Next slide please.

Among the professional guidance documents that are covered in the CER report or practice guidelines, one is number two on this slide, is a set of expert recommendations on measures that can be used to, measures that can make use of the data provided by wearable sensor devices, and these clinical endpoints can be use in clinical practice, also in

clinical reserve. Next slide please.

So the most comprehensive of these professional guidance documents was a set of guidelines from two European organizations. The checkmarks on this slide show us the clinical endpoints that were identified as important either in the CER report itself or by the three expert reviewers. So you can see that all of the outcomes that were considered by the European guidelines to be critical were also important according to out CER report or the expert reviewers, and some of the outcomes listed as important in the guidelines were also considered important in our original sources, so there's quite a clear amount of emphasis there. Next slide please.

The CER report was not able to provide helpful information on follow-up duration because that wasn't reported in systematic reviews, but our three external reviewers expressed their opinions on this issue. They recommended followup from three months to one or two years depending on the type of clinical endpoint. One of the reviewers differentiated between the type of followup or the duration of

followup that would be appropriate for different types of devices. Next slide please.

We always request that there be a section on applicability to Medicare beneficiaries in our CER reports. Applicability is another term for generalizability. In the systematic reviews that were collected, none of them focused on older adults. However, the mean age across the studies represented by those reviews was 54 to 77 years, so they represent a population that includes a healthy percentage of older adults. The studies were also representative of a mix of disease severity. However, there was insufficient information in the reviews on other patient characteristics.

One of the external reviewers pointed out that two endpoints are especially important to assessing older adults. The first is the assessment of gait and related measures of physical function. The other would be any cognitive decline or mood changes that occur as adverse events of treatment. Next slide please.

As I said before, additional detail

can be found in the CER summary Word document, and I thank you for your attention.

DR. ROSS: Thank you, Terry. So, my name is Joe Ross, I'm the committee chair for today's meeting. I'm a professor of medicine and public health at Yale.

And I just want to remind people who are in attendance today for the first time that what's different about the clinical endpoint review program that we're taking on is we're not talking about a specific device or service in making a decision on whether it's reasonable and necessary for Medicare to cover. We're talking about the evidence that Medicare, CMS should be looking for when it's making those decisions, and providing our advice on which are the endpoints that are of greatest importance and should be prioritized in an evaluation of these devices in a particular subset, so today we're talking about obviously devices that are used for Parkinson's disease and essential tremor.

Since Terry's finished her presentation, I want to give an opportunity for those members of the committee to ask any

clarifying questions based on the evidence review before we go forward with the rest of the meeting. Any specific questions? Okay. That's great.

So just before we go to the discussion, just a reminder to the members of the committee, what we will be asked to do in our deliberations and the voting is to review which of the domains that the endpoints sit in are going to be of greatest importance, and talk about the scales or measures that are being used in that domain, and whether we think there is a relationship and those types of questions. You will have the voting materials in front of you. As Terry outlined, the vast majority of them in Parkinson's are clinician-assessed health outcomes but there are also some patient-reported outcomes, especially in the domain safety domain.

So Terry, the one question that I had for you is as you reviewed the literature, one of the challenges I think with clinician-assessed outcomes is trying to understand how reliably they reflect the experience of the patient and what the patient

experiences as a burden or a functional impairment. Did you read or see in the evidence review very much around specific measures and how they were calibrated against patient experience in their development?

MS. ROGSTAD: That's a good point. Actually, clinician assessed is maybe not an entirely accurate description, so the measures that we put into that domain are assessed by instruments that are administered by a clinician but not necessarily without patient-reported input. So there are some questions, for instance in the United Parkinson's Disease Rating Scale that are answered entirely by the patient with the physician present. There are other questions where the physician makes an assessment based on patient comments and his or her own observations, so it's a bit of a mix.

Obviously thing like gait function and posture, and amplitude of the tremor, those kinds of things are directly measured by the clinician.

DR. ROSS: The only other question that I had if people don't have more, is when I

was reading materials in preparation for the meeting is that one of the other measures that came up in the comments that were submitted were diaries around symptoms, both sleep and otherwise, and I was wondering if those came up at all in the evidence review.

MS. ROGSTAD: One of the expert reviewers recommended a scale for assessing sleep, and right offhand I don't know whether that's -- oh, that was patient reported, yes. And then the quality of life of Parkinson's disease was, the survey results were patient reported, so that's the United Parkinson's Disease Rating Scale was patient reported.

The diary that you probably noticed, the diary that I recall is a diary of motor complications so those motor, those fluctuations in treatment effectiveness and dyskinesia, there's a diary for that.

DR. ROSS: Okay. Other questions from the committee members?

MS. NEWMAN: Can I just ask one?

DR. ROSS: Of course. But Robin, please just state your name.

MS. NEWMAN: Sorry. I'm Robin Newman,

I'm a faculty member in the department of occupational therapy here at Boston University.

Just a quick question about some of the function oriented components of what was happening in the physician's office. So for example, I can appreciate gait is observable. When they were asking questions about activities of daily living, was it the patient, someone with the patient answering these questions, how was that information collected, do you know?

MS. ROGSTAD: That could be either patient reported or caregiver reported. And at least within the United Parkinson's Disease Rating Scale there is a specific list of things that are difficult to do related to tremor.

MS. NEWMAN: Okay.

DR. ROSS: Any other clarifying questions from the committee members? Okay. Well, Terry, we reserve the right to ask questions later as they come back up.

MS. ROGSTAD: Certainly.

DR. ROSS: Tara, should we turn now to the scheduled public comments?

MS. HALL: We're going to go to the

first presenter, which is Dr. Kelly Lyons.

DR. ROSS: Great. Will you keep the time or do you want me to keep the time?

MS. HALL: I will keep the time.

DR. ROSS: Okay. And just for the presenters, we will hear all the public speaker presentations and at the end we'll ask clarifying questions, as opposed to asking them after each presentation.

DR. LYONS: Are you ready for me to begin?

MS. HALL: Yes.

DR. LYONS: Okay. Good morning and thank you for allowing the International Essential Tremor Foundation, or IETF, to provide information on this important topic. You can go to the next slide please.

I am Dr. Kelly Lyons, I've been involved with the IETF for over 30 years, and I am the current president of the organization, a position I've held since 2008. I'm also a research professor of neurology and director of research and education for the Parkinson's Disease and Movement Disorder Center at the University of Kansas Medical Center. My only

disclosures are minor consultant Fasikl, Praxis and Sage regarding essential tremor, and a major association with the Parkinson's Foundation. Next slide.

So the International Essential Tremor Foundation was founded in 1988 as a nonprofit organization. The IETF is the largest essential tremor patient advocacy group currently. The mission of the IETF includes multiple components, including awareness, education, support and research related to essential tremor. We have engagement with more than 100,000 essential tremor patients and 500 physicians focused on the treatment of essential tremor. Our medical advisory board or scientific board is comprised of more than 20 movement disorder experts.

We have multiple activities. We provide education around therapy options, clinical care, assistive devices and other resources used by persons with essential tremor. We provide grants to support research in ongoing research involving the cause, the assessment and the management of essential tremor. And we've provided over $1.35 million

to date for the research cause. We've facilitated educational programs on timely diagnosis, current treatment, support groups, ongoing research. We also help to recruit patients for clinical trials ongoing for essential tremor, and provide up to ten scholarships annually for students with essential tremor. So we really appreciate the opportunity to be here today, and if we could move to the next slide please.

So in 2005, the American Academy of Neurology created guidelines for the treatment of essential tremor, and these guidelines were updated in 2011. The International Essential Tremor Foundation did endorse these guidelines when they were published as an appropriate evidence-based resource. In 2020 we realized that the guidelines had not been updated for quite some time and some new treatment options were available, so we conducted our own literature review and wanted to at least update the guidelines so people were aware of the new therapies such as ultrasound, surgical therapy and wearable devices such as TAPS, which had been approved for treatment. So in 2021 we did

a comprehensive literature review. This was performed by myself, by Dr. Holly Shill who is the director or our medical advisory board, and Dr. Kelli Reiling Ott, who is an occupational therapist, and we developed the Essential Tremor in Adult Patients guideline. If we could, next slide please.

So based on our review, we did add some additional information to the current treatment algorithm that had been presented by the Academy of Neurology. As I mentioned, this included adding focused ultrasound, surgical therapy to the surgical options available for people with essential tremor, and we also recommended wearable treatment options such as TAPS, be considered when patients have tried and failed first-line pharmaceutical therapies and did not want to proceed to surgery, were not interested in surgery or ready for surgery, and also for people when second or third-line pharmacotherapies were not indicated or desirable.

So as you know, essential tremor can cause significant disability, it can make everyday tasks that we often take for granted,

eating, drinking, writing, typing, dressing nearly impossible for many patients. For some people the tremor can be so disabling that they're isolated to their homes, they don't engage socially, it can really have a significant disabling effect on many people with tremor.

So we feel that the goal of therapy for essential tremor is to reduce the tremor. We want to increase independence, ultimately improve the ability to perform these activities of daily living, and ultimately improve the quality of life for people with essential tremor.

In addition, we see a lot of comorbid conditions associated with poor tremor control and social isolation, the inability to perform activities of daily living, and especially depression and anxiety, which are also something that are of keen importance in this population. We can go to the next slide please. Next slide please.

So in summary, again, I want to thank you for allowing us to be here today, and I'd just like to point out that the

patient-reported outcomes or activities of daily living to us are the most important reliable endpoints to evaluate the effectiveness of any tremor management strategy. Everyone can see the difference in the patient and their ability to perform their activities throughout the day. I want to remind you that ET is a debilitating condition for many American seniors, as well as people of other ages throughout their lifespan, but it's impact is often overlooked in comparison to other neurological conditions. We're very excited that essential tremor is part of this discussion and something that you're looking at more closely.

And it's critical to remember there's no such thing as a benign tremor. This is a term that was coined many many decades ago --

MS. HALL: Dr. Lyons, your time is up.

DR. LYONS: Okay. For someone who, this is not benign if you're not able to do your activities of daily living.

And finally, we need to access new and effective treatment options that have appropriately demonstrated the ability to

improve tremor-related ADL's in a safe and durable way. Thank you.

DR. ROSS: Thank you, Dr. Lyons. I was just told by Tara that you're not able to stay on, so I just wanted to open it up and to see if anyone on the committee has a question for you.

DR. LYONS: And I was going to try to sign back in at what would be 11 my time, so if there are questions, I can answer those at that time.

DR ROSS: The one question I would just ask you, when Terry went through the evidence review she talked about QUEST, FTM-TRS Part C as being good measures, or used measures of tremor-related ADLs. And I'm just curious whether you would agree with that or if there are other measure that you would propose.

DR. LYONS: I guess that's a bit of biased question. I was part of the development of the QUEST and the TETRAS which, I believe both are very effective measures. The QUEST has been essential tremor specific so it allows us to capture the ADLs and the impact on the quality of life with persons specific for the

problems with essential tremor, so I do think the QUEST is an important scale as it captures items that wouldn't be in the Parkinson's scales or general quality of life scales.

And then the TETRAS in the ADL section, as well as the motor section, again specific to essential tremor, so I do believe both scales are the appropriate scales for measuring change in essential tremor.

DR. ROSS: Great, thank you. Unless there's other questions, we can go to the next speaker.

DR. KHEMANI: Good morning, folks. Next slide please.

I appreciate the opportunity to speak today to you about the efficacy and safety as well in the treatment of essential tremor and tremor-predominant Parkinson's disease. I appreciate the agency's focus on these disorders and the impact that tremors have on patients' lives. I'm Pravin Khemani, I'm a movement disorders neurologist, practicing neurology for 21 years. I have experience with pharmacological treatment of tremor as well as interventions such as transcutaneous afferent

peripheral stimulation, which we will call TAPS going forward, focused ultrasound or FUS, and deep brain stimulation or DBS.

Over the next five minutes or so I will highlight first appropriate outcomes and endpoints for clinical evidence on devices for tremor. And second, I thought it would be helpful to add some comments on bridging the gap between treatment of essential tremor and tremor in Parkinson's disease. Next slide please.

Let's look at efficacy outcomes. On this slide I will focus on efficacy outcomes for clinical evidence and then on the next slide on safety outcomes for clinical evidence of treatment. The key outcomes for tremor efficacy for both essential tremor and Parkinson's disease as we've heard, are activities of daily living, which can be assessed through standardized instruments such as QUEST, TETRAS and FTM-TRS, the Fahn-Tolosa-Marin Tremor Rating Scale also called CRST. These scales assess the limitation of tremors on patients to perform tasks that those of us without tremor will take

for granted, writing, eating, holding a cup of water, using tools, et cetera. As a clinician I evaluate activities of daily living outcomes in tremor through standardized instruments routinely, and they really inform optimization of tremor treatment.

It must be noted that in developing guidelines for treating tremors, many items in the MEDCAC CER although characterized as health outcomes are safety outcomes of devices, rather than true efficacy outcomes related to tremor management. Because where some of those such as TAPS have demonstrated significant improvement in ADLs, it makes sense to implement them if pharmacological therapy fails or provides inadequate functional improvement before considering invasive surgical interventions such as shown in the table here, which is the IETF guidelines that Dr. Lyons showed earlier. Next slide please.

In terms of safety outcomes, it must be noted that therapies impact on symptoms like gait or speech are considerations for safety rather than efficacy. It is also important that safety data include long-term evidence,

especially for procedures such as FUS and DBS.

For a known category of wearables such as TAPS, because of its reversible and relatively benign side effects, it is prudent to implement TAPS before FUS and DBS, and instead of tremor drugs that are contraindicated due to drug-drug interactions and patients' existing comorbid conditions. And this is what the IETF guidelines also recommend, and this is what I do in my clinical practice with good results. Next slide please.

All right. So let's look at similarities between the neurophysiology of essential tremor and tremor-predominant Parkinson's disease, how is the treatment of essential tremor and action tremor in Parkinson's disease similar. This is best understood by briefly reviewing tremor circuitry in the brain without going into anatomical details, which is a topic in itself.

So let's focus on the area in the brain called the thalamus, which is a central contributor to tremor genesis. I don't have a mouse here, but if someone could point to the thalamus on that picture? All right, thank

you. So that is the area over there, and more specifically in the thalamus it's the ventral intermediate nucleus, it's a cluster of brain cells which is a common target for tremor treatment.

Lesioning therapy such as MRI guided focused ultrasound and circuit modulating treatment such as deep brain stimulation are targeted treatments for essential tremor and sometimes for the treatment of severe tremor-predominant Parkinson's disease. There are other areas of the brain that are also targeted for Parkinson's disease but not for essential tremor.

And just as surgical treatments disrupt electrical firing or abnormal electrical firing in the VIM to mitigate tremors, some wearables that use TAPS use the principle of noninvasive transcutaneous afferent peripheral stimulation in a similar fashion to modulate the firing of these cells in the VIM. And -- next slide?

This is likely going to be my last slide. And as insurers have recognized the applicability of tremor management devices for

essential tremor and tremor-prominent, tremor-dominant PD just as they have for surgical procedures, Medicare covers staged unilateral MRI guided focused ultrasound and deep brain stimulation, both of which target VIM for tremor-predominant PD and ET. The Veterans Health Administration maintains a national coverage policy for TAPS to manage tremor in ET and PD patients.

Based on the information I've provided today, I encourage the panel to recognize that the same points are applicable for both disorders, and efficacy data for either ET or tremor-predominant PD should be considered for coverage for either indication.

Thank you for your time and opportunity to present today. I am happy to take some questions if there is time available. And the next slide is I guess just a bonus slide, we don't have to go through that. Thank you.

DR. ROSS: Thank you, Dr. Khemani. You also have to leave in a minute, I was told by Tara?

DR. KHEMANI: Yes indeed.

DR. ROSS: Do any of the committee members have any questions? Dr. Dhruva?

DR. DHRUVA: Thanks. Sanket Dhruva, San Francisco UCSF.

Dr. Khemani, thanks so much for your presentation. You mentioned toward the end that you think that endpoints in your estimation for Parkinson's disease as well as tremor, that they kind of -- if one is validated and used in one condition, it can be used in the other condition. Are there any aspects where you don't think that that is the case? Because if I was understanding correctly, you were suggesting applicability if a study used in, one in essential tremor can be used for PD. Let me know if I misunderstand.

DR. KHEMANI: Yes, you understood correctly. Maybe I should have been, should have articulated better. The principle of a disruption of activities of daily living with essential tremor, which is an action tremor, is the same as in tremor-predominant Parkinson's disease where there's an action component, which disrupts the similar activities. So the scales are not similar, but the effect on

activities of daily living are similar because similar activities are affected. I hope that makes sense.

DR. DHRUVA: Thank you.

DR. ROSS: Dr. Mauri?

DR. MAURI: Yes, thanks. This is Laura Mauri from Medtronic.

Dr. Khemani, a similar question, maybe for more clarification of the question that Dr. Dhruva just asked, which is, are you suggesting that the PD and ET have the same endpoint profiles, or that there might be some overlap in the endpoints that are used? Because we have different symptoms that patients present with, although some may be common.

DR. KHEMANI: Yes, with respect to motor symptoms, yes, tremor interrupts activities of daily living similarly. But PD also has non-motor symptoms, a whole bunch, and these wearables are not designed to improve those, they look primarily at the motor aspect of tremor. I hope that answers your question.

DR. MAURI: So we have a series of endpoints that have been summarized by Terry

Rogstad earlier. Some are specific and some are in common between ET and PD. So I'm just trying to clarify the statement that you made, that there should be, the same endpoints should be used for ET and PD.

DR. KHEMANI: Not the same but similar, and particularly only for tremor, because Parkinson's disease has both motor and non-motor symptoms. There is a slight overlap between non-motor symptoms in ET and PD, but that has not really been looked at.

DR. ROSS: Dr. Khemani, if I can ask one last question, I appreciate the comment you made around safety and long-term followup for invasive therapies or devices. Could you speak to your clinical experience for noninvasive in terms of persistence of adverse effects upon discontinuing therapy? Is it generally if people experience any adverse effects from use of TAPS or other noninvasive devices, are they quickly reversible or do you ever see persistence of any adverse events over time, even after discontinuation?

DR. KHEMANI: No, no persistence. The adverse effects from the PROSPECT trial that we

saw were irritation of the skin, some burns, that I haven't seen in my clinic yet. Reducing the stimulation reverses a lot of those adverse effects, but not using the device completely reverses those. I have not seen any irreversible side effects yet.

DR. ROSS: Thank you. Any other questions from the committee? Okay, great. Thank you, Dr. Khemani, for making the time to speak with us today.

Tara, we can go to the next speaker.

DR. BRONTE-STEWART: My name is Helen Bronte-Stewart. Thank you very much for including us in this panel. I am a professor of neurology here at Stanford, and my -- next slide please -- my only disclosure is that I am the founder, very recent founder of QDG Health, with shares but no compensation. Next slide please.

So the QDG Health Management platform comprises a comprehensive remote monitoring and disease management system for Parkinson's disease, essential tremor and related conditions. The foundation is quantitative digitography or QDG technology, which provides

objective validated measures of all the motor signs in Parkinson's disease in real time, including tremor. The person performs the simple task guided by an app or a phone or tablet. The data is transmitted to the QDG HIPAA compliant server and is analyzed by our AI informed precise algorithm. The QDG metrics are transmitted in real time to the healthcare provider, who can also look at each measure over time on the dashboard. The healthcare provider can then make complex management decisions in real time with quantitative validated data.

QDG received FDA breakthrough device designation in late November of 2024. The publications are included in our bibliography at the end of the slide set. We've shown that it can differentiate Parkinson's disease from age matched controls, it's validated and all the metrics are validated with the old UPS III and UPDRS III overall score and all subscores. It can differentiate the off and the on medication states, the off and the on DBS states and follow adjustments to therapy, and documents progression of Parkinson's disease

over five years. Next slide please.

In the QDG mobility task, an individual presses and releases adjacent tensioned levers, alternating between their index and middle finger for 30 seconds. Two critical features of movement are extracted, which are shown over on the right in the upper panel, and that is the amplitude of the press and release phases and the corresponding timing of the press and release cycles. These precise temporal and spatial measures provide accurate quantitative measures of movement in tremor. The lower panel shows that the correct performance of the test requires alternating movement between one finger and the other, as shown by the red and the blue tracers. Next slide.

The trace in the upper panel here is from a healthy control who presses and releases the levers with full amplitude at high frequency and with a fast speed of movement, and you can't even differentiate between the blue and the red fingers, the different fingers. All aspects of the performance are consistent and regular.

In contrast, the trace in the lower panel is an example from a person with Parkinson's disease. There is a noticeable decrease in the amplitude of key presses over the trial and the time between each key press gets progressively longer, which are signatures of slowness of movement or bradykinesia. The rate of release of the lever is also slowed as you can see basically in the stripes around the ten-second time point there, and that has been robustly correlated with the clinical assessment of rigidity, which up to now has required an in-person examination. Next slide please.

This slide shows video of a person with tremor-dominant Parkinson's disease performing the QDG mobility task. On the video the voluntary movement is interspersed with and then overtaken by the involuntary movement of tremor, which has a different signature. The panels to the right show the raw data and the extracted metrics of amplitude, frequency and dwell time of each strike for the index and middle fingers respectively. The green vertical lines mark the start and the end of

the video. An AI-informed model demonstrates that tremor strikes have a unique signature in QDG and could be identified with over 98 percent accuracy and false positivity of only two percent, and these are represented by the red data points.

As you can see over time, the tremor takes over and you can see these are just consistent high frequency of very short duration strikes. So the algorithm recognizes tremor and then takes that out of the trace and separately analyzes the percent time with tremor, the average amplitude and frequency, and then only measures the metrics of bradykinesia through rigidity using voluntary strikes only. And this is an advance as tremor often contaminates the clinical assessment of bradykinesia in the clinical rating scales such as finger tapping in the UPDRS. Next slide please.

MS. HALL: You have a minute and a half left.

DR. BRONTE-STEWART: This table demonstrates the validation of all the QDG metrics, and I'll move to the next slide.

This slide shows that we can see representative QDG traces across the disease spectrum of people with Parkinson's disease, different disease durations, and shows that it, nicely shows the asymmetry that is unique to Parkinson's disease, especially early on, between the more and less affected side, and the progression of impairment over time. Next slide please.

This is an example of how QDG's precise metrics document the changes in motor function from a small adjustment to medication which had clinically meaningful functional outcomes. The person had presented with gait problems and falls and was on the standard dopamine replacement medication of Sinemet one tablet three times a day. Although overall he had improved on medication, he demonstrated fluctuations from day to day, but when a single table of Sinemet was added to his regimen, not only did his mobility score improve up into the normal range which is shown in green, but also he became more consistent.

And with this remote monitoring tool we have seen now that the fluctuation that we

used to be thinking was due to absorption of what they were eating from day to day is actually a measure of undertreatment. And I'll finish there, and sorry, just a final, to tell you that this small adjustment in therapy also had a functional improvement in that he stopped falling.

I thank you for listening. Next slide please. And the next slide just demonstrates the bibliography that should be in the packet. Thank you very much.

And I unfortunately have to leave after this to go to clinic.

DR. ROSS: Okay. Thank you, Dr. Bronte-Stewart. I'll open it up to questions from the panel if there are any.

I'm happy to start. This is very interesting as a digital endpoint. I wonder if you could just say a little bit more. Is the expectation that this measure allows patients to be monitored more frequently at home? Do you ask people to do it daily as opposed to coming into the clinic monthly or weekly to do something like the UPDRS or something of that nature?

And could you speak to whether -- you talked about how it's been validated, and of course I haven't read those papers, but do you have a sense of minimally clinically important difference that you would observe with the QDG versus, you know, as part of this assessment for efficacy?

DR. BRONTE-STEWART: Yes, those are great questions, thank you. And yes, we've been using this technology in my lab for over 25 years, so there is a lot of validation that is represented in the bibliography. We have recently now transformed this into a remote monitoring pool and yes, we can --

(Unrelated audio interference.)

DR. ROSS: Please go on mute in the background.

MS. JENSEN: Thanks. Sorry about that.

DR. BRONTE-STEWART: So yes, it's very much designed to be used as an adjunctive tool for the in-person visits, so that in between these patient visits the provider can then monitor the patient's performance over time. We have finished our first remote monitoring

trial and we expect that to come out in Major Parkinson's Disease soon and that is, that has shown really quite -- it's really changed my practice in the way that I use it. I feel I know the patient so much better, and it's designed so the provider can intervene over time outside of the clinic visits of course, so that the person can stay optimized, as opposed to deteriorating between those visits, which is sometimes only every six months. And so the person often is left to self medicate and that's when they get into trouble ending up in the emergency room. So this is a way that the patient and the provider can stay in communication without overflowing the provider's clinical schedule.

Yes, we've got a very strong correlation between the change in mobility score off and on medication, and the change in UPDRS III off and on medication, and from that we have extracted a minimal clinical improvement of 14 points in the mobility score that correlates to the improvement in MDS-UPDRS III, so we do have a metric. And the overall mobility score is a statistical compilation of

all of the metrics representing bradykinesia rigidity, which was designed to work with the UPS III score which as you know, is the addition of all integers. So it is designed to help the provider have an overall score that is statistically calculated with the metrics that they can use with the UPS III, and it has a nice correlation with UPS III. So I hope that answers some of the question.

DR. ROSS: Thank you for your responses. Dr. Dhruva?

DR. DHRUVA: Thanks. Sanket Dhruva, San Francisco, UCSF. A couple of questions totally unrelated.

One is, does this have regulatory clearance and approval or is it under regulatory review? And the other, again unrelated question, how is this tool used -- so this is addressing the tremor-related symptoms. How is this used with regards to, in clinical management, or how is it or would you recommend when it be used for sort of patient-reported outcomes and sort of combining these together in terms of adequacy?

DR. BRONTE-STEWART: Yeah, thanks for

those questions.

So we received the breakthrough in November, so we're lucky to be working with the top program to expedite our regulatory process. So no, we're not FDA cleared yet, we're hoping to be able to put that application in the beginning part of 2026. We are currently working under IRB guidelines to explore the research tool.

Sorry, just remind me of your second question again, was about how we do --

DR. DHRUVA: So how would this be used with other outcomes? This is capturing potentially a slice of outcomes. How would we handle them in making a decision?

DR. BRONTE-STEWART: Yeah, thank you. Actually one of the important features we wanted to show in the remote monitoring trial, our primary outcome was compliance to make sure that people who might use this when approved, that it would satisfy the remote monitoring code. So our first outcome was compliance of 16 out of 30 days, which was a hundred percent. We had 96 percent of people adhering one time a day, and 86 percent to twice a day. And we

then correlated with the quality of life Unified Parkinson's Disease Rating Scale quality of life scores. So we did this every week, we assessed this over the four weeks of the trial, and then we averaged those, and as shown in the paper, we had a high statistical correlation between the QDG mobility score and the patient-reported outcomes on how their motor impairment was affecting their activities of daily living. And so yes, it does reflect the patient's perception.

We're currently doing a head to head home diary study with QDG and the Hauser home diary, also including the patient perception of how off and on they are, and we've been doing that in all of our remote studies to make sure that what we're seeing in this very high precision tool does reflect the patient's perception of how off or on they are.

DR. ROSS: Dr. Stearns?

DR. STEARNS: This may follow the -- oh, I'm Sally Stearns, University of North Carolina at Chapel Hill, a professor there.

I was interested in the progression over time and I'm also thinking perhaps of

certain devices that might be considered by CMS, it might not so much be used to assess improvement from those devices depending on, for some of the wearable devices how it would change function, but also an appropriate point for intervening with a device. Is that a reasonable statement?

DR. BRONTE-STEWART: Absolutely, yes. I think that's going to be something that is very interesting. We've done a lot of this in the lab, we published a large study back in 2009 looking at a wearable, and by wearable I mean a sensor wearable, not just a stimulation wearable and also QDG, and showed that in fact over time you begin to see the more affected or less affected hand nudge. And I think as we shoed with fluctuations, you can see fluctuations in motor performance over the day, so the provider can get a very nice quantitative metric of when they should start thinking about deep brain stimulation or some of the other interventions.

Especially, you know, with tremor I mean, I agree with Dr. Khemani about TAPS being used early. I think things that are

noninvasive are very helpful and this can monitor how well the person's doing, and of course when it's beginning to maybe not work so well, and maybe they need to think about another therapy. But this is very much in the end hopefully targeted towards non-movement disorders, neurologists and other doctors who don't necessarily know how to use the UPS III, and so it will be there in their pocket basically to help them have something quantitative and validated that they can use then in their assessment of their patient, and know when to move them on to that next level of care.

DR. ROSS: Okay. Dr. Bronte-Stewart, thank you for making time to present to us today.

DR. BRONTE-STEWART: Thank you very much for having me.

DR. ROSS: Tara, if we could go to our next speaker?

DR. ISAACSON: Hi. I'm Stuart Isaacson and I appreciate the opportunity to join my colleagues to address this advisory committee.

Medicare patients are particularly important, as you've heard, but for too many reasons I think. For one, they have increased functional need because they've had an increase and longer duration of essential tremor. And two --

DR. ROSS: Dr. Isaacson, sorry to interrupt. The slide stuck, or at least it stuck on my screen. Is it stuck for other people?

MS. HALL: Yes, it did. We're getting them back.

DR. ROSS: Okay, great, just wanted to make sure. Don't worry, we will not take that off your time.

DR. ISAACSON: Promises, promises.

MS. HALL: You can start now, Doctor. I started your six minutes over.

DR. ISAACSON: Okay, thank you. I still appreciate the opportunity to address the advisory committee.

I think Medicare patients are particularly important to discuss for two main reasons. One, they've had essential tremor for a longer duration and thus have increased

functional need with this progressive condition, as Dr. Lyons has highlighted. And two, they're at higher risk of medical pharmacotherapy systemic effects with increased risk of falls and cognitive impairment as side effects of current pharmacotherapies, and they're also at higher surgical risk, leaving them with few options to treat their progressive problems that they experience, Parkinson's disease patients of course as well.

I'm a movement disorder specialist neurologist and for the past 25 years director of the Parkinson's Disease and Movement Disorders Center in south Florida. Our center cares for over 1,500 patients with Parkinson's disease and essential tremor, and over 70 percent of our patients are above the age of 65. We've also been a site for many of the Parkinson's and essential tremor clinical trials, and I have been personally involved in protocol development and steering many of these trials, including TAPS, a peripheral therapy that you've already heard a bit about. I've also been a consultant with many of these companies including Cala, Fasikl and many

others. Next slide.

I think that I just want to highlight to the advisory committee as you have heard, that assessment of daily function is critical, peoples ability to maintain their daily tasks, to live alone, to maintain their socialization, their activities of daily living are essential, and this is what truly is affected in the aging population with tremor and Parkinson's, but especially in tremor and essential tremor. Parkinson's disease, which I won't focus on, UPS part two, motor experiences are validated in the scale we use routinely.

In essential tremor, though, I think there are three assessments that can assess daily activities. Dr. Lyons mentioned the QUEST. The TETRAS ADL I think will be covered quite a bit by Dr. LeWitt in the next speaker. And I'd like to highlight the Bain & Findlay Activities of Daily Living assessment.

It's important to recognize that the degree of improvement, the minimally clinically significant improvement and the long-term durability of functional improvement has to reflect the risk of the therapy being evaluated

as well.

The Bain & Findlay ADL scale -- you can go to the next slide please -- is one of the scales that has been used in trials along with other trials that used QUEST or the TETRAS ADL scale, but the Bain & Findlay ADL scale has also been noted in the American Academy of Neurology guidelines for annual assessment of essential tremor. It's been recommended as a recommended scale for ADLs in the Movement Disorder Society evidence-based review. I also use the Bain & Findlay ADL scale in my clinical practice to assess patients and evaluate their responses to therapy.

We use this scale in published research using the wearable neuromodulation therapy called TAPS therapy, this is the Cala device. This is the transcutaneous afferent pattern stimulation that stimulates peripheral nerves noninvasively using a wrist worn device, and this actually changes brain activity and results in a reduction in upper limb tremor.

The Bain & Findlay ADL scale measures, the modified version that we used, using a soup spoon, pouring the milk, using, holding a cup

of tea, dialing a telephone, picking up change, inserting a plug, unlocking a door, and writing a letter. Patients are asked to rate these, can they do these tasks without difficulty, with little effort, a lot of effort, or cannot do it at all.

And I'd also not that Medicare finalized the positive coverage determination for TAPS therapy in 2024, noting many of these studies as supporting coverage for a select Medicare beneficiary population with essential tremor symptoms that significantly impair their ability to perform the dominant hand related activities of daily living, and I would concur with this assessment.

For example, in the PROSPECT trial, using TAPS and using the Bain & Findlay ADL scale, we found in this trial by the way an average median age of 69 years, an onset of essential tremor at the age of 44, a duration average of 25 years of essential tremor. 66 percent were on oral pharmacotherapies. And yet when we added and used the Bain & Findlay scale to evaluate, we found that 68 percent of patients using TAPS therapy who were rated as

severe or moderate improved to mild or slight. And 60 to 72 percent of patients improved on each of these measured daily tasks that I reviewed. This was mirrored as well on the Patient Global Impression scale of change. Next slide.

So just in summary, I'd recommend that the MEDCAC panel consider the Bain & Findlay ADL scale as a valid outcome measure based on the trials that have been performed, based on the usefulness in TAPS, and for other tremor management devices that are being evaluated. The Bain & Findlay ADL scale is validated, it's been successfully used in clinical studies and in clinical practice, including at our center, and has been suggested as a recommended scale by the Movements Disorder Society evidence-based review and the American Academy of Neurology annual assessment of essential tremor.

I can stop there on the next slide and just point -- I'm sorry, one other thing. I point out that this scale can be reevaluated before to evaluate need for therapy, assess the response to therapy, and this can be done as I

think I agree with the committee, at intervals of one, three and six months for this type of therapy.

So I want to thank you again for the opportunity to present and am happy to answer any questions the committee might have.

DR. ROSS: Thank you, Dr. Isaacson. We'll stick with asking people questions just right after as we've done with prior presenters.

If I could just ask quickly, the Bain Findlay scale didn't come up, or at least wasn't as frequently recommended as the QUEST or the TETRAS subscore for tremor-related ADLs. Is there a particular reason why you think the scale is more valuable or more advantageous to use than the ones that have been recommended in the guidelines?

DR. ISAACSON: I think all three scales are useful. I think reviews in other TAPS therapy, the TETRAS ADL scale, I think the Bain & Findlay ADL scale is very user friendly and patients can understand the tests that are being done, the tests that are selected in the modified version that we used are very simple

tasks that are used regularly by patients, and often are tasks that lead people to seek therapy and need to have better therapies, things like writing a letter or using a soup spoon, a cup of tea, pouring. And I think we need to maintain clinical assessments that are not only validated and internally consistent and used over time, but also clinically relevant to our patient population and the daily lives, and the Bain & Findlay I think achieves all those things. I think the TETRAS ADL is also a scale that's validated and we can use and have used. I think the QUEST can be helpful but may not be as useful as the other two scales.

DR. ROSS: Any other questions for Dr. Isaacson? Okay. Thank you for making the time to meet with us.

DR. ISAACSON: Sure, thank you.

DR. ROSS: Tara, we can go to our next presenter.

MS. HALL: We're just waiting for his slides to come up.

DR. SHARAN: Thank you, Tara, and thank you to the committee for this

opportunity. We actually start off by congratulating the MEDCAC and the CER process. We truly enjoy the spirit. Next slide.

I am Ash Sharan, I am representing Medtronic as chief medical officer for Medtronic neuromodulation and our company represents over 180,000 people with stimulation implants worldwide. I'm also professor of neurosurgery and neurology at Sydney Kimmel Medical College in Philadelphia, and I have implanted 500 patients or more with deep brain stimulation. So on behalf of Medtronic, we appreciate this opportunity to give a perspective on the CER and it tools in the management of patients with Parkinson's disease and ET. Next slide please. And I'll go to the next one.

So Medtronic recognizes like all my colleagues before me the importance of identifying the most appropriate endpoints for evaluating tremor motor outcomes in patients with PD and ET, and supports the categorization and endpoints identified in the CER. And we want to highlight that there is a complex symptom profile of patients with movement

disorders, particularly those with Parkinson's disease, which may result in the need for variable endpoints, so focusing a little bit on the Parkinson's population in this statement.

And we've seen in the CER and also highlighted by my colleagues that the clinician-assessed impact on tremor and movement is important to insure that the DBS system is managing the movement system, and in this statement on this slide I've highlighted three different ways that somebody can assess tremor, the UPDRS, the CRST and FTM, and each one of them has different degrees of granularity and incorporation of other measures and outcomes, and also particularly highlighting the need for patient-reported outcomes, which are very important for the full picture of DBS symptom impact, you know, having often been chosen as primary endpoints in DBS studies.

And we wholly also agree, like our colleagues have identified, that there are, there is the need for assessing the potential adverse effects of the DBS system, which can include what's known in the UPDRS III, I and

IV, including the cognitive functions, speech, depression and anxiety type effects that can happen.

And DBS symptoms are intended to create motor and tremor symptoms and are unlikely to address all symptoms apparent in these disease states. But nevertheless, a broad array of clinical endpoints are necessary. And also to state that CMS should prioritize minimally burdensome and flexible study design, understanding many different data sources and measurement tools have been highlighted, and methods of collecting data. Next slide please.

So this one I won't go, but I think my colleagues have spoken about, you know, different ways to think about the assessment, and including patient-reported measures, and I'm going to highlight on time without troubled dyskinesia and quality of life as noted in the PDQ-39. Just also highlighting that there are physician-rated scales and to highlight the difference between the UPDRS and the MDS-UPDRS for example, and these tools are very appropriate for clinical trials, but the UPDRS

on average takes physicians 20 to 35 minutes to administer in their office when they're well trained in it, and the MDS-UPDRS, which was adopted and suggested in 2008, can take 50 to 75 minutes but offers a lot more granularity on the measurement of the nuances for patients with Parkinson's disease, and safety as I mentioned. So again, just reiterating that you need multiple endpoints to test DBS technology in the context of the clinical trial. Next slide please.

The CER process was really aimed at literature after 2016, but I just want to highlight that there is also a rich and robust literature on DBS starting from FDA approval in 1997 for essential tremor and in 2002 for deep brain stimulation in high quality journals. As an example, I'm going to give you two particular cases that I want to highlight for these patients. Next slide please.

So this is an article, so I'm giving you two studies that are RCTs that were designed to understand the role of dyskinesias in the care of patients with Parkinson's disease, and particularly they define that

dyskinesias are involuntary erratic writhing movements that are often associated with long-term dopamine therapy and often are associated with peak dosing which occurs within 30 to 60 minutes.

This study by Weaver was showing progression with patients with late Parkinson's disease and the results, and the next slide please, and this study by Scheupbach looked at quality of life instead. So using patients with later stage Parkinson's disease and earlier stage Parkinson's disease, choosing different endpoints to highlight the impact of DBS surgery.

So in conclusion, I want to say that Medtronic really does support elevating care with data. We should identify the most appropriate endpoints for evaluating tremor and motor outcomes. These patients have a complex symptom profile and that may result in the need for variable endpoints like my colleagues have suggested. And lastly, clinical trials are very different from the practice of medicine, and we hope that CMS prioritizes the measures that are minimally burdensome and include

flexible study designs. And we do acknowledge that the MEDCAC process and CRE review have been very comprehensive. Thank you.

DR. ROSS: Thank you, Dr. Sharan. Any questions from the committee?

If I may, I always have questions. This is Joe Ross. Could you -- you mentioned on slide five around safety that therapies impact on psychological and cognitive outcomes. Could you speak to that, because that's not an adverse, or safety-related sort of outcome that I've seen before. Just curious what you mean by that.

DR. SHARAN: There is literature that speaks about the lead placement and you know, the targets that are typically used are subthalamic and they have motor manifestations and limbic manifestations, which could include anxiety, depression, and the studies are suggesting that there is a natural history of long-term cognition. So one to one, the standard of care is patients who get Parkinson's disease DBS, they get neuropsychological outcomes and you want to assess what is the probability of that

potentially worsening.

DR. ROSS: Got it. Any other questions from the committee? Okay. Thank you for making the time.

I think we have one last public speaker left, Dr. Rosenow seems to be in the OR, but thank you for joining us.

DR. ROSENOW: Good morning. We are actually doing DBS for Parkinson's disease today, so this just fits with the topic of this presentation.

So, I am Joshua Rosenow. I am faculty and the director of functional neurosurgery for the last 22 years at Northwestern University. I'm also the chair of the joint drugs and devices committee for the American Association of Neurological Surgeons and the Congress of Neurological Surgeons. Thank you for giving us the opportunity to discuss this today. I think there's been a range of topics presented today and I'm going to try not to reiterate a lot of what has previously been said. Next slide please.

These are my disclosures. I have done some consulting for some of the companies and

received research funding from some of the companies that have an interest in neuromodulation. Next slide please.

So as you've heard, the FDA approved indications for deep brain stimulation are primarily essential tremor and Parkinson's, but also a humanitarian device exemption for dystonia. Next slide please. A humanitarian device exemption for obsessive compulsive disorder, next slide. And epilepsy, next slide please, in two different modalities, responsive neurostimulation, next slide, and stimulation of the anterior nucleus of the thalamus. Next slide please.

When we think on the movement disorder surgery side, there are four measures for evaluating outcomes from implanted devices. We think of such things as dopamine responsiveness, so you've heard about the motor subsection of the UPDRS III that we used during the evaluation, we look at the on-off studies as you've heard, and this is also reasonable to look at the off score postoperatively as well.

Cognitive testing is a routine part of the preoperative evaluation for these patients.

Most active DBS centers are doing both presurgical and 12-month postsurgical testing. Sometimes insurance coverage is somewhat difficult for the postsurgical testing, but many centers will do this when they can achieve coverage from insurance for that. And the things we look at presurgically as the main cognitive risk factors are things such as poor performance in verbal recognition, language, visual spatial function and executive function. And we use these sorts of things to help counsel patients better about their list for postoperative cognitive dysfunction. And remember, the cognitive dysfunction that we sometimes see after surgery is not a stimulation related cognitive function decline but it is an insertional effect.

And the quality of life, the main patient-reported outcome is the PDQ-39. Next slide please.

We also sometimes look at modified Hoen and Yahr grades, measures of sleep, motor complications using UPDRS IV, and non-motor skills such as the Movement Disorder Society non-motor scale and part I of the UPDRS. Next

slide please.

So there are also certain outcome measures that we think should be avoided as necessarily poor measures, for instance balance. We know that balance function declines over time in many patients with Parkinson's disease. We know that balance as a function is not something that we typically look at as being something responsive to surgery, and not something that we counsel patients on as something that we intend to necessarily improve with surgery. And it's sometimes difficult to distinguish from insertional effects as a balance problem and disease progression effect. So for this reason, and similar with speech and swallowing, these are certain outcomes that we do not think are, should be part of the core outcome measures for deep brain stimulation for Parkinson's disease.

There's been some discussion about risk of suicidality in patients with DBS systems but if you look overall across the board, patients with PD often have higher rates of suicidal thoughts compared to the general

population. We see this when we do our pre-procedural cognitive screening and one of the things we look for are measures of this so that we can handle it, treat these before having someone proceed to surgery. And there's very little data looking at any risk of suicide in PD.

The same thing with device discomfort. There was some discussion in some of the pre-meeting materials about this device discomfort but again, this is very subjective and difficult to truly measure in a repeatable and validated way. Next slide please.

If we look at essential tremor, you've heard about things like FTM and TETRAS. TETRAS is the more modern scale. Again, I'm not going to belabor the 12-item ADL subscale within TETRAS, but similar to avoiding looking at balance as a core measure in Parkinson's, similarly, you know, we would not look at balance as a core measure from essential tremor.

Cognitive testing in ET is typically less intensive, it's more simply dimension screening rather than the more intensive

screening that we do for PD, and routine repeat testing over time is not performed unlike what we typically look at for PD when we like to do one-year outcomes. Next slide.

We would love if there were physiologic markers for outcomes. Unfortunately, while these are subjected right now to significant research, we don't really have validated physiologic markers to look at outcomes measures from surgery for movement disorders. Next slide.

In terms of safety outcome, these are things that are frequently discussed, things such as infection requiring device removal, symptomatic intracranial hemorrhage, device performance measures such as hardware malfunction, extension breakage, electrical breakage and mechanical generator issues, and possible significant declines in mood and cognition over time. Next slide.

I think I just squeezed it in under six minutes, so thank you for giving us this opportunity to present. This has really been a very interesting meeting.

DR. ROSS: Thank you, Dr. Rosenow.

Let me first ask if there are any questions from other members of the committee.

Dr. Dhruva?

DR. DHRUVA: Thanks. Sanket Dhruva, UCSF. Thanks so much, Dr. Rosenow. A couple of unrelated questions.

One is, is there any information as to what might drive the differences in suicidality, and am I right that the data you shared suggests that there is actually no difference in data by suicide, that is suicidality? And then I have an unrelated question, this is about the device discomfort and you said that this improves over time, or is that something that is more in a periprocedural acute phase?

DR. ROSENOW: So regarding the first point, in discussing this with our neuropsychology colleagues, they feel that there was no firm evidence that there is increase in either suicidal thinking or actual death by suicide after surgery for movement disorders.

And the second part, which is does the device discomfort get better, I don't think we

would look at short-term periprocedural device discomfort as an outcome measure. People sometimes have soreness, either from tunneling wires between the head and the chest or making a pocket for the battery, especially in very slender people, but when we think about device discomfort, it's something that we see chronically and that is actually very very very rare. We don't typically see people come back and tell us that they find the presence of the device either uncomfortable or limiting in any way in terms of activity or sleep.

We've now developed surgical techniques and devices that are smaller, the batteries are smaller, they're slender, they fit in better. We don't have to use very large chunky batteries anymore, and we've slimmed down the extension wire connectors, so people don't have issues sleeping on that side of their head where they have hardware under the scalp.

DR. ROSS: Thanks. Dr. Stearns?

DR. STEARNS: Sally Stearns, University of North Carolina Chapel Hill. I think that the outcome measures to avoid, I

understood your points about balance and suicidality, but could you just repeat why the issues about speech and swallowing as not being good outcomes?

DR. ROSS: And actually I was going to ask a related question if I could tag on to Dr. Stearns, which was about, you know, in the evidence review the measures that MDS-UPDRS and MDS-MMS were proposed as measuring speech function and swallowing. And I'm curious what problems -- I was surprised also that you said that that was difficult or at least maybe less reliable in surgical patients, so if you could speak to that?

DR. ROSENOW: So when we look at outcomes from surgery, we want to look at outcomes we feel that surgery can actually have a beneficial effect for, meaning things that we are counseling patients on, what we expect to get better from surgery, and we would not do surgery typically to improve speech and swallowing function. We may counsel patients who have significant dysphasia or hypophonia going into surgery that they might be at increased risk for issues, but we wouldn't look

at that as a poor outcome measure, because it's not something that we would typically think would improve with surgery. So there's no, that's a measure in surgery that has very little upside to it, and yet is very difficult to distinguish from the progression of PD or things that people come in already with a deficit.

DR. ROSS: I understand. So these specific interventions, you don't speak these outcomes to actually, to improve, so that makes sense.

DR. ROSENOW: Correct.

DR. ROSS: It's not that the scales are bad, it's that the scales are not appropriate for this intervention.

DR. ROSENOW: Correct, that's a better way to put it, thank you.

DR. ROSS: Okay, thank you. Any last questions for Dr. Rosenow? Well, thank you for making the time and for answering our questions.

DR. ROSENOW: Thank you, everybody, appreciate it.

DR. ROSS: Okay. So we're pretty much

on time and we're due for a break. We're a little bit over, we were supposed to stop at 11:30 eastern standard time, so we will go for ten minutes, allow people to refill their water cups and stand up and move around for a second, and we'll come back at 11:40, let's say 11:45 just for ease.

And Tara, do we have individuals scheduled to make public comments?

MS. HALL: No, we do not.

DR. ROSS: Okay. So we will come back at 11:45 and start with an open panel discussion, so see everybody in 13 or so minutes.

(Recess.)

DR. ROSS: Okay. Welcome back, everyone. We're now scheduled to have up to, or at least 15 minutes of just open panel discussion. It's just an opportunity for panel members to reflect on both what we've heard from Terry in the presentation of the clinical endpoints review, as well as from the public speakers who joined us this morning.

Specifically, I think we're just asked to think a little bit more about the domains

that have been identified. It does seem like the general consensus around, for both PD and ET, that there's a good group of clinician-assessed health outcomes measures in that domain, there's a good group of patient-reported outcomes that are important depending on the purpose of the intervention, as well as safety related endpoints.

I'm curious whether people have any reflections on what they've heard or any questions that have come up, especially for Terry, who's still with us. Sally?

DR. STEARNS: There's a table, I think it's in Appendix C that I would personally find helpful if we could touch on it, because it does give evidence about MCIDs from the current literature. And since I'm not familiar with some of these instruments in terms of use in my own research, I would kind of appreciate knowing the panel's perspective on that evidence.

DR. ROSS: Terry, anything you would like to reflect on on that Table C? I'll just say what I took away from it is that the vast majority of the measures that were identified

in the evidence review had established MCIDs, which is not always true of a measure, although I'm curious, you know, what more you learned, particularly from the specialist feedback, the two neurologists and the neurosurgeon around their perspective on whether the MCID matched the clinical experience.

MS. ROGSTAD: I'm glad MCID was brought up because there is quite a bit of detail there. So we're referring to the full CER report, the appendices were in a separate document from the main report, and there is detail there not only on MCIDs but also validation studies. I don't know what else to comment on.

I did notice that some of the instruments for ET for which no validation studies were found by the commissioned CER report, those instruments were referred to as validated in some of the public presentations, so we will try to track down those validation studies since we seem to be missing some information.

DR. ROSS: Dr. Chen?

DR. CHEN: This is Irene Chen. I have

a different question. To me, medical devices, the wide range of like the DBS and the wearable are just very different on the spectrum in terms of medical devices. So my question is as we have further discussion about deciding, you know, whether they're important endpoints to consider in the duration, especially when it comes to the safety aspect, I think they're very different, but would it be one size fits all, that they would have to be for all medical devices? It's my first time on the committee so I just wasn't sure, you know, how we take topics like that when it's a wide range of devices.

DR. ROSS: Dr. Chen, that's a great question, and we're happy to have you, thank you for taking the time to join the committee. You know, this type of clinical endpoint review is relatively new, it's been done a few times now, but the general idea is I not one size fits all, the general idea is which domains are important to capture, that then there have to be tailored to the relevant intervention. So the idea is as we talk about safety, we're going to say whether safety domains are

important, kind of yes or no or why, but then the expectation would be that the safety information that's collected as part of that study would be tailored to the device, which obviously, it would be different for an implantable versus non.

Terry, if I could ask a question -- oh, please, Dr. Mauri?

DR. MAURI: I was following up on your question. To clarify before going on, my role here is representing industry, I wanted to clarify that, but I am presenting more broadly as a physician myself, and I appreciate the variety of information that was presented by Terry, but also by the public.

I guess my first question really relates to Terry. When you said there were additional endpoints that you heard about that you think require more consideration, I recognize when we talk about validation, we need something quite different when we're talking about a clinical endpoint from a study as opposed to something that would be used in clinical practice. The endpoints that were presented might not yet be approved for use,

but focusing maybe on those endpoints that have a history of publication in the past, were there specifics that you heard that should be considered by the panel?

MS. ROGSTAD: I didn't pick up on any endpoints that haven't been covered in the CER or mentioned by our external reviewers. I did notice that the instrument discussed by Dr. Isaacson, the Bain-Findlay scale, that had not come to our attention before, so it sounds like that's something that should be added to the list of instruments, and I haven't looked up the validation information or anything like that.

DR. MAURI: Okay, thank you. And maybe just one comment if I may. Thinking about my impression of the variety that we're presented with and that we'll have to think about when we move on to the voting questions, and Irene, this may relate to your comment. As we look at the range of devices as well as the indication in treatments to treat PD and essential tremor, you know, you have really established endpoints over a period of time that dates even before the CER and you know,

(audio breakup) back to 2010, at the same time for anatomic placement. There's a range of different endpoints, as I think Joe was alluding to earlier, so I just wanted to concur that I don't think it's a one size fits all, and that as we think about these endpoints we're thinking about them as instruments to be able to best assess what the benefit is that we want to measure, and being a useful tool for communicating to patients what benefit they might be able to receive, but also holding these endpoints to a standard where they're reproducible and implementable in trials.

MS. ROGSTAD: May I add a comment to that?

DR. ROSS: Please.

MS. ROGSTAD: There's another table in the appendix document for the full CER, Table C.2, and it lists the devices that were studied according to each prioritized clinical endpoint. So you can see that for the prioritized endpoints, they were studied for a variety of treatments, but the frequency varies by type of treatment, and that speaks to the concern that there's not one size that fits all

in terms of important clinical endpoints for a particular treatment.

DR. ROSS: Terry, which table is that? Is it --

MS. ROGSTAD: Table --

DR. ROSS: -- in the summary?

MS. ROGSTAD: It's not in the summary, it's in the full, in the appendix document for the full CER and it's Table C.2.

So for instance, let's see, what was I looking at? Speech function, one of the presenters said that DBS is not expected to improve that disability or that symptom, and Table C.2 shows us that actually it wasn't studied in very many studies at all and only in a handful of studies of DBS.

DR. STEARNS: So by the way, I started sharing my screen. Is this the Table C.2 or, just have Table C.

DR. ROSS: Sally, it's in the appendix document of the report. This is the summary document.

DR. STEARNS: All right, I'll stop sharing my screen, but I'm wondering if maybe it would be helpful if we can --

MS. ROGSTAD: Yeah, I can share my screen if you'd like.

DR. STEARNS: Yeah, I did everything on my laptop and I just don't have documents printed from looking at the tables. I actually did it on my daughter's laptop.

(Laughter.)

MS. ROGSTAD: Okay. Does everyone see this table? I will scroll up to the heading. So you can see that, you know, motor symptoms were changed, were assessed by the majority of studies that looked at the more invasive treatments, they're not going to have the studies of the wearable sensors for example. So what I was referring to before, the sleep function, hardly any studies look at that, a small minority of DBS studies did.

DR. STEARNS: And I'm interested also in discussing the ADL measures that are used, because from my perspective I don't, I'm not familiar with the specifics of the Bain-Findlay, but I do appreciate the fact that it sounded like something based on Dr. Isaacson's presentation that really does get at daily function for patients.

MS. ROGSTAD: Yeah, and there are different instruments for assessing that. The part two of the United Parkinson's Disease Rating Scale gives us that, and there are several others listed here in this column.

MS. NEWMAN: All of those came up, is that why -- all of those were mentioned in this review and that's why they are in that column, correct?

MS. ROGSTAD: Right.

MS. NEWMAN: So other ones are, you know, are frequently used, like the Barthel for example, outside of the domain of Parkinson's per se, but yeah.

DR. ROSS: I will say, Terry, as I'm looking at the table what I found interesting, just because the Bain-Findlay was one we hadn't seen in the review, but if you look at Table B.2, it was identified but used much less frequently, and so that may be why it didn't sort of rise to the top. For essential it was only used in one of 127 studies for tremor, and in and four of 45 studies for motor symptoms, so that was interesting to me.

MS. ROGSTAD: Okay. So it did show

up, but not frequently enough to -- okay.

DR. ROSS: Okay. But again, we're more focused on the domains than the specific measures per se, but it's important for us to raise those measures that have been used. So this is out there, it just hasn't been used as frequently, or perhaps it was just used more in the past, because I did note that it was first published as a scale more than 30 years ago. Other questions?

MS. NEWMAN: I just had one about the cognition domain. In the presentations I feel like we were hearing about the larger neuropsych batteries being primarily used and here I'm seeing like the MoCA and the Stroop test, which are very very quick and short screening tools, so I don't know, I guess I'm just wondering about that, like how do I interpret hearing about more elaborate testing, particularly with the DBS, right, the pre-post was what sounded like a significant neuropsych battery and here, you know, a screening tool. Can someone help me clarify or understand that maybe better?

I guess the question is, like is this

tool that we're considering more, like are we essentially trying to appreciate the simplicity of the tool, like this is a quick screen, right, and then that's it, right, versus what we were hearing in some of these presentations where we -- I mean, I guess I would say we're mostly supposed to be identifying the key domains. I will say that I make an assessment that if a domain can be assessed very quickly, that that would affect my ranking of -- I don't know about the absolute ranking of the domain, but cognition is very important and if it's very difficult to measure, maybe it's not the most important one for these types of interventions that would be considered. But if it's very easily measured, then there would be some value to understanding impact.

DR. ROSS: Yeah, this is Joe. I do think that it's important for us as we discuss the measures within the domains or even the sort of subdomains of the domains, right, because it's not just patient-reported outcomes but also the quality of life, sleep quality, all the various things, we want to offer some perspective on the burden of testing. For

instance, one speaker talked about how it took 80 minutes to administer one of the questionnaires, and that provides a lot of granularity that maybe you would expect that for the device studies to guide coverage or maybe you would not, right? So I think it's worth sort of reflecting on that, provided that it's a validated endpoint with a minimally clinically important difference that can be detected and used as part of a clinical study.

DR. GOLDSTEIN: I thought it was interesting how much -- this is Amy -- the time piece, I thought like that was touched on but not really a big focal point, as well as the comfortability, you know, a slight, someone that might have pain involved, but I don't feel like that was really, that was sort of a side note, where maybe that would be something that's important to have as a factor, if that really does affect comfortability, especially since quality of life and patient, you know, buy in would be really important. So I think those two areas, I don't know, that stuck out to me.

DR. ROSS: Sanket?

DR. DHRUVA: Thanks. Just on the timing aspect, I was also impressed certainly with some of the discussion about timing and intensity of the data obtained. I was also thinking from a clinical, you know, translating these tools to clinical practice and being able to titrate treatment to sort of step up treatment that a patient wants or the intensity of treatment. Obviously the focus here is on devices used to treat ET and Parkinson's disease.

I think that also becomes a relevant factor, I know we heard about the digital endpoint or a device-based endpoint that is currently not yet, doesn't have yet regulatory approval, but it seems like there may be more opportunities like that in terms of remote monitoring as well. And again, how is this actually going to be translated to practice, is there an opportunity to really be looking at those data and making titrations. We know that's challenging.

DR. ROSS: Yeah, Sanket, that's also something that was real interesting and sort of challenged me to think about what the purpose

of our committee, right, which is we're not, it's not the endpoints that we expect to be used in clinical practice as part of routine use to monitor or manage the devices, but more like what's the evidence that would be expected to have been generated to form a coverage decision. So obviously, you know, with time, perhaps that endpoint that's undergoing validation and undergoing FDA clearance may be useful as part of clinical studies until that happens, right? So it's sort of like a TBD to be monitored, whereas like what we're anticipating, at least now, is to guide CMS.

I will say, Laura, and Sanket too, because you've been on a few of these now, I thought the evidence review and the public speakers were unique in that there's more consensus than I've seen previously on the domains that are important and the measures everyone's using. I don't know if that's because it's generally a smaller field and everyone's already kind of stacked hands and said that these are the measures that we just always use. In the past we've had to sort of navigate much more sort of choppy waters, like

this group likes this endpoint, this group likes that endpoint.

DR. MAURI: I think there's some credit to Terry and the work that was done that was really thorough with the additional review with the external neurosurgeons providing additional information and updating that.

DR. ROSS: Yeah.

DR. MAURI: I'd just say that, you know, thanks for the thoroughness of all that. That probably had something to do with it.

DR. DHRUVA: Yeah, I was thinking the same and I was thinking, I think we are really fortunate for, number one, Terry and team, but also the fact that we have the guidelines, we have the European Academy of Neurology, the Movement Disorder Society, we have guidelines and we also have, as Terry said, the sum of the population was I think in the mid 70s, and I think it's pertinent to the Medicare beneficiary population in a larger way than I think we've seen sometimes in the past, at least certainly based on age being the older adults.

DR. ROSS: Yeah, I agree with that.

Are there any other broad reflections or questions for Terry and the evidence review team before we move on to the voting questions specifically? Okay. Sally, please go ahead.

DR. STEARNS: Yeah. You know, once again, the specific disease end measures are not my area of expertise, so when I think about the different domains, and maybe this is getting into the voting, I am still kind of juggling the importance of the, the relative importance of the domains, especially in terms of what I understand to be current treatments or potential interventions under development. So when we get into the voting, I'm still feeling a little uncertain about the level of importance that I will be giving.

Is there any other discussion that's helpful to help get the group on the same page on that issue or is it just going to evolve in the voting?

DR. ROSS: I expect it to evolve. This is actually a great setup for the voting and how we'll proceed, which is to say what I'll ask you to do, we have three sets of domains on which to vote, clinician-assessed

health outcomes, patient-reported outcomes, ans device-related safety. And for each, while I'll ask you to cast a vote in terms of how important that domain is as an endpoint for medical device study in PD and ET, and to inform CMS's coverage decision, I'll also ask you to reflect after you cast your vote on which, sort of your first principles, like we're not all neurologists here, so what are sort of your first principles and sort of what you're thinking about and why a particular type of measure is important, maybe you have a particular feeling about a specific measure and its value, but as well as thinking about the importance of there being an established MCID, when, what period of followup you would want to see, and how that might vary by device type, right?

So we heard one of the speakers talk about the differentiation between an implantable versus a non-implantable device, and how that might change their point of view on what safety outcomes to follow.

I guess what I would ask is maybe we can hold open Terry's slides and you can touch

on in your comments sort of the aspects that are being, of the health function, symptom burden, quality of life aspects that are being measured, whether it's motor symptom severity versus cognitive function versus speech function, and if you have a particular point of view on which are most important or least important, because it would have been too unwieldy for us to go by subdomain by subdomain by subdomain asking you to vote.

But we do want to hear from each committee member, you know, what you would prioritize.

DR. STEARNS: And just to clarify, we're making these recommendations or assessments based on medical devices broadly defined, and not distinguishing between wearables versus implantables, or implantables versus non-implantables.

DR. ROSS: That's right, but the CAG, the coverage group, you know, the number that you vote is useful. The comments that you make and how you might differentiate between those two device types is more important. What you say out loud in the transcript allows them to

have a basis for when they then have to go and make a decision.

DR. STEARNS: Thank you.

DR. ROSS: Any other questions?

And Laura, while you won't vote, I will ask you to reflect on what you would like to see as most important, if that's okay.

DR. MAURI: Thank you.

DR. ROSS: Okay. Well, I guess we're a smaller group so we're moving a little more quickly than anticipated. That's okay. There also seems to be more consensus, but maybe we can go to our first voting question.

So let me just read the preamble. The following endpoint domains and suggested clinical endpoints pertain to studies evaluating medical devices to manage tremor in older adults who have Parkinson's disease or essential tremor. These domains and endpoints have been identified through a systematic literature review, that was already presented and discussed. The review included input from two external neurologists and a neurosurgeon in addition to -- that was sort of external expert feedback, and deliberations of our panel on

March 26th.

At this meeting we are going to use a rating scale as shown from one to five, not at all important to extremely important, to indicate for each panel member what they feel like is the importances of each clinical endpoint within each domain.

We'll separate our discussion by disease just so things don't get too complicated, but I'll ask you when you do cast your vote, after, to reflect on the subdomains for which clinical endpoints have been identified, as well as the duration of followup and the threshold for defining an MCID.

Tara, should people pull up their voting sign-on now for the voting?

MS. HALL: Yes, if you're ready to vote, everyone should sign in.

DR. ROSS: Okay. So you have all received voting instructions to sign onto the ttpoll.com, you have the session ID. Is anyone having trouble with that?

MS. HALL: And please don't say the session ID.

DR. STEARNS: So this goes to the

email that Tara sent, right?

MS. HALL: I will send you the information, Sally.

DR. STEARNS: Okay, thank you, just because I'm not unusually an Apple user and I'm on an Apple laptop here.

DR. ROSS: I can relate to that. I'm a ThinkPad and my kids use Apple and I'm lost.

DR. CHEN: This is Irene Chen. I was able to get but I have a question about what we're voting on, so when the question is the right time, let me know.

DR. ROSS: So first I will ask you to vote on whether, how important are endpoints that relate to Parkinson's disease specifically in the clinician-assessed health outcome domain, and if you could vote from one to five, having these types of endpoints in a clinical study evaluating a medical device, how important should that be to CMS's coverage decisions.

DR. CHEN: Excuse me, Dr. Ross. We don't have separate questions for Parkinson's and essential tremor.

DR. ROSS: Oh, I see.

DR. CHEN: And we also don't have separate questions for each line that's shown on the screen, going from line three, four, five, six, seven, eight and nine. Are we voting all of them together or each one of them individually?

DR. ROSS: No, no, all of them together, but we are going to say, we are going to combine for Parkinson's disease and essential tremor.

DR. CHEN: Okay, thank you.

(The panel voted and votes were recorded by staff.)

DR. ROSS: It looks like one person has voted so far.

MS. HALL: Sally, are you logged on?

DR. STEARNS: No. I've got a screen where I've got to copy my thing. I saw in the chat what you sent me but I'm trying to get back to it. I'm sorry, it's the different computer that's messing me up here.

MS. HALL: Once your number is selected, it's complete, there is nothing additional.

DR. STEARNS: No, no, no. And we're

on the first question; is that right?

DR. ROSS: Yes.

DR. STEARNS: Now, should I be able to see --

DR. ROSS: It looks like you have voted.

MS. HALL: Everyone has voted, Dr. Ross.

DR. ROSS: We now have five votes. So now what I'm going to do is we're going to go person by person and I'll go in the order of the roster, and I'll ask you to just rationalize, or justification for your vote, and reflect on the differences in specific clinical endpoints between the two diseases and the other questions we've discussed.

So Dr. Dhruva, if you could start, how did you vote?

DR. DHRUVA: Thanks. Sanket Dhruva. I voted five, extremely important, and I'll make a few comments.

I think it seemed clear to me from Terry's presentation, from reading the material and from our public commenters that there are, that the health outcomes domain as clinician

assessed, which also includes both objective clinician-assessed as well as including patient outcomes is extremely important.

I think clearly in PD, the motor symptoms are very important. Thinking about complications is also important but really focusing on older adults as Medicare beneficiaries, it was very helpful to hear the importance of cognitive function, gait function, postural instability. We know certainly the risk of falls and the catastrophic cycle that those can sometimes start, as well as being able to complete ADLs.

For essential tremor, I know we have just reduction in tremor as one.

To a couple of the points that you made, Dr. Ross, I think, you know, when we have an MCID available, I think that's very helpful, it just helps to center and helps to have a helpful target.

And just a couple of other comments. So I think MCID available is very helpful. I think in terms of followup, I think that while long-term followup with these symptoms is more important -- excuse me, with this domain is

more important for more implanted devices, devices that are permanently implanted. As we heard, I think for those that are wearable or that can be easily removed, I think that having a shorter followup such as six months certainly, I think longer than a month or two or three because symptoms can fluctuate or change over time so I think at least six months. And I think for implanted devices, at least a year at minimum would be very helpful.

And the last point I'll make, I know there are lots of different symptoms. I know we heard from one of the speakers as well that, you know, some treatments may only target and may only be designed to improve this endpoint and this endpoint, and not that endpoint and that other endpoint. But I think it's still very important to be assessing all of these endpoints. I think that helps to provide information as to where the benefits may be, and in particular there may end up being some detriment, some lack of change, and I think that's very important to know to have a holistic understanding of a device because a patient doesn't -- a patient who may receive a

device, gets a device and will have all of the relevant endpoints both positive, negative and neutral, and not just the positive impacts.

Sorry for the long comments.

DR. ROSS: No, thanks, Dr. Dhruva, long comments are good comments, so that's very helpful.

Dr. Chen, how did you vote?

DR. CHEN: Thank you. I voted five, which is extremely important. And very similar to what Dr. Dhruva shared, I think it's very important to have evidence-based studies to really inform in terms of interventions because it's effective, but also, you know, making sure that this information will be helpful for determining coverage, that you are investing money in something that is going to be helpful and with that, you know, I think that being able to determine the outcomes when specifically using tools that have been assessed and proven to be helpful is actually important.

And out of the different subdomains within the number one domain, like let's just take Parkinson's disease, I think it's most

important based on the information that's been teed up, and thank you for the very kind of well organized package, that the global change in sort of motor symptoms, the gait function and the motor-related activities are most important, because that is the reason why we want to treat Parkinson's disease, is to insure that those symptoms get better.

And then the other ones, I would rank them a little lower in terms of needing to insure that there is strong kind of endpoint change.

But with all that said, in terms of looking at duration of how long you should assess, I think it really depends on the type of treatment it is. And so perhaps not knowing which specific treatment we're talking about, it's harder to comment, but I think all of these together will be very helpful to have and assess objective data.

DR. ROSS: Thanks, Dr. Chen. Can I just clarify? When you were talking about the motor related, you were talking about among the subdomains, did you include motor-related ADLs, was that one of the things you mentioned?

DR. CHEN: That's correct, yes. So the first one is global change in motor symptoms, the second one would relate to ADL, and then the fourth one, motor related -- I apologize, it's the -- yes, I'm sorry, those two are the most important ones. Thank you.

DR. ROSS: That's helpful, thank you. Dr. Newman?

MS. NEWMAN: I also voted five and agree very much with what has been said. The domains that I felt were of higher importance to me were the motor-related activities, the experience of daily living, particularly this focus on ADLs, the global change in motor symptom severity and the gait function, postural stability, balance, falls.

I would put cognitive function sort of just right under the motor and ADL subsets. The others, I didn't rank in my opinion as highly. Again, I feel these are very important in giving us an understanding of progress and what, you know, patients look like and how they are progressing with the use of these devices.

DR. ROSS: Okay, thank you. Dr. Stearns?

DR. STEARNS: So I voted four and I honestly based on what I've heard in the discussion, I probably if I had a chance to change my vote I would move it to a five. So maybe there is a need to calibrate within the group. I would reiterate all the points that have been made. I don't know that I have anything specific to add.

The other reason why I might have voted four rather than five is just trying to avoid voting everything as very important, and that I do believe that this is clinician-assessed health outcomes, and I do believe that patient and caregiver reported outcomes are extremely important. But certainly these domains, all the points listed are extremely important, and my inclination would be to move to a five in terms of final assessment.

DR. ROSS: Great, thank you. Ms. Goldsmith?

MS. GOLDSMITH: Thank you. I voted a four, and like Dr. Stearns said, the reason I voted a four is partially because I didn't want everything to be a five, you're right, same.

But I feel very strongly that, you know, that the clinician assessed is critical, so yes, very important. But I think having objective data, measurable in this space is critical, so that sticks out to me. But I feel very strongly that everything should be patient driven and patient centered and from their reporting, because I don't think anything moves without that patient driven aspect, so that's why I said a four.

I would say that the ADLs were primary for me and the motor complication I think are really really tightly in there. I think that's a huge driver.

Of course I'm going to say swallowing and cognitive function right together. You know, I think speech is critical, but you know, working with someone with Parkinson's and even significant essential tremor, I think that's such a large part of the quality of life on the swallowing piece, the nutritional piece, engagement with family, everything else that drives joy in life, so I would put those as a close third, kind of in a tie.

DR. ROSS: That's very helpful. And

Dr. Mauri, how would you have voted and why?

DR. MAURI: I would have voted, maybe this is -- I'll start with the way that I thought about it and maybe that's helpful for describing how I would have voted and why. As we think about the, we're looking at endpoints, and I absolutely agree with the comments about reflecting and whatnot on what matters most to patients. Some of the endpoints incorporate both the clinician assessment and the patient assessment into the overall scale. So even though we're calling these clinician assessments I just want us to note that.

And then as we think about, I thought that some of the comments presented by the physicians were helpful in that they noted where a specific device was likely to have an impact, as well as where we're concerned with monitoring for disease progression or potential unintended effects. And so I distinguish between those two when I think about what's the primary assessment versus what do we want to continue to track, similar to what Dr. Dhruva was describing.

So for the primary areas that I think

are important and would grade a five would be the global change in motor symptom severity, the motor related activities of daily living and the motor complications, and specifically with focus on the on and off time that patients experience with Parkinson's disease, and that's because those aren't the target for most of the medical devices, but we can also envision that there might be other devices that would target other components, so I think it's worth being open to the other categories, but most of the focus is on treating those symptoms that are related to being on medications for a long term to treat Parkinson's disease.

The other ones for sure I think are helpful to continue to measure so we continue to understand whether those impact or what are the new therapies going forward.

In terms of the duration of therapy, I agree that implanted devices would have different potential benefits and different durations of followup, and that the current follow-up rates of at least 12 months are reasonable to continue, as we've seen in the literature that was presented.

DR. ROSS: Great, that's terrific, very helpful. Okay.

So now we can move to our second domain, the patient-reported outcomes domain, and again, we're going to ask everybody to vote on a scale from one to five, not at all important to extremely important in terms of these endpoints being used as part of trials and evaluations of medical devices for both Parkinson's disease and essential tremor.

DR. STEARNS: Can I ask one question about this?

DR. ROSS: Yes, please.

DR. STEARNS: So I was just struck that for essential tremor and activities of, or experiences of daily living are explicitly mentioned, and they are not listed at a separate item aside from the overall assessment of the quality of life for the Parkinson's disease. Is there a reason for that?

DR. ROSS: These were the measures that were most frequently observed in the clinical endpoint review and that's why they were called out.

DR. STEARNS: Okay. But as I vote, I

can interpret the Parkinson's disease related quality of life to include experiences of activities of daily living versus sleep quality, which is a separate specific component?

DR. ROSS: Yes. The PDQ-39 was the one that was most commonly used for that quality of life measure which also included, I believe has a subdomain of the ADLs.

DR STEARNS: Okay, thank you.

(The panel voted and votes were recorded by staff.)

MS. HALL: The voting is done.

DR. ROSS: Everyone has voted so let's start back with Dr. Dhruva. How did you vote and why?

DR. DHRUVA: Thanks. I voted a five, extremely important. I think it's very clear that understanding the patient's perspective from PROs is extremely important for both Parkinson's disease as well as for essential tremor.

I was in particular struck that there might be, although Dr. Rosenow clarified that it seems this is not the case, but some

potential even increased suicidality risk, although no difference in death by suicide. I think obviously that is the worst possible outcome, but I mean that in a way that that influenced me that it's so important to know how these devices are impacting patients' quality of life. Obviously the disease, Parkinson's disease or essential tremor is substantially impacting the patient's life and we want to know what the impact of these medical devices are.

As with my prior comment in terms of if there is an MCID, I think that's extremely important and very helpful. And again in terms of followup, while we are getting PRO data, I think that assessing these out at least six months, ideally one year is important. We know there are going to be some new changes in particular with an implanted device with periprocedural outcomes.

And I would also just mention that I think that it's important that when these investigations are performed, that as we are assessing patient outcomes, that there is adequate blinding as possible. It is

oftentimes very difficult to conduct in these types of device-based studies, but we know the importance of blinding when we are able to do so, and we know the importance of adequate well controlled studies, again as feasible. I realize it's not always easy, but I think it's an important consideration.

DR. ROSS: Thanks, Dr. Dhruva. Just, can I ask for clarification? I appreciated the points about suicidality. Just in terms of quality of life and ADLs, sleep quality, is there a sense of how you would rank them as important measures.

DR. DHRUVA: Oh, sorry. So I would say in terms of Parkinson's, I think we have the quality of life, I think the quality of life was larger, loomed larger for me because the quality is obviously very important and can obviously have an impact on the overall quality of life.

And then I think in terms of tremor, again, the quality of life is very important. The ADLs, I think again, on equal footing and again similarly, as part of the clinician-assessed domains that we just talked

about a couple of minutes ago, and which Dr. Mauri pointed out, not just clinician assessed but also getting the patient's perspective.

DR. ROSS: Great, thank you. Dr. Chen, how did you vote?

DR. CHEN: Thank you. I ended up voting a four and let me maybe just explain a little bit about why I voted a four.

Just like many of you commented on the question before, it's difficult to differentiate between -- by the way, patient-reported outcomes, the patient's point of view is so important and to me as a family care doctor, and that is really why I am in health care. But if I had to compare what are the tools and assessment we could do in gathering information on the patient versus the prior category, which was the health outcome domain, I would rank the prior category higher because the tools are more objective.

And going back to what Dr. Dhruva had mentioned about how do you insure there is blinding of the survey when you study this. So for example, if you have a study that goes on

six months, one year, it may be hard to assess whether the patient's sort of outcome is because of the natural decline in their current condition related to Parkinson's, or are there other comorbidities because older patients, they have so many other things going on that may contribute to a lower quality of life or sleep quality, so it will be very hard to tease that out. Not everybody with Parkinson's or essential tremor is going to progress the same way so even if you pick a cohort it may be hard to tease that out.

And just because of, you know, it's just harder to assess for me if I have to pick between, to rank the two different domains, the first one versus this one, I would rank this one just a little bit lower, but I still think it's very important. And then with the subdomain that's listed here, I would rank Parkinson's disease related quality of life way above the sleep quality, because to me again, the sleep quality may be dependent on so many other things, it may not be because of the intervention or because of the Parkinson's itself. And I would also rank the tremor

related quality of life for essential tremor very high.

DR. ROSS: Thank you, Dr. Chen, that was very helpful, I appreciate your thoughts on that. Dr. Newman?

MS. NEWMAN: I voted a five as well. Again, to echo the importance of patient-reported outcomes, I was thrilled to see that included. I was really happy to see in the PDQ-39 that in addition to ADL's, that there's this component of community engagement, so out of the home activities, that got people not just dressed and eating, which is extraordinarily important and an important endpoint, but also doing their everyday lives, so you can see that sort of reflected here and I think that was really important, so five five five for that.

The sleep quality I also felt was extremely important for a few reasons, particularly, you know, having poor sleep quality impacts all of these other daily functions. So I feel like they're, I don't know if I can really, it's hard to sort of separate them, because the quality of life

rises to the very top, to me it's the outcome of all of this, but the sleep quality is also extremely important, I wouldn't rank it too much lower.

Equally as important, and I'm glad to see here is that the tremor-related activities of daily living were there own domain and very important.

DR. ROSS: Great, thank you. Dr. Stearns, how did you vote?

DR. STEARNS: So I voted five and somewhat consistent, I think, in the sense between the patient-reported and the clinical. I have been thinking in advance that I might give the most importance to the patient-reported. I'm going to make, certainly in terms of these measures, I already made the point about the importance of the experiences of daily living.

I think that I have two other points. I do think that, you know, there is a cost in measuring some of these clinical endpoints and getting a clinician assessment of gait or some of the other functions. It may not be as easily done at the key points over an

appropriate follow-up period, be that six months or 12 months. And so I think there's some value in potentially the ease of collecting some of these measures regularly for a patient population.

The other point that I want to bring up and this relates to, I appreciated Irene Chen's point about, that some of the clinician-assessed measures may very much focus on the Parkinson's disease improvement in a certain domain, and yet my training as an economist gives me, leads me to put some weight on the value of overall quality of life. And to me, the value of some of these measures is they will pick up the overall quality of life which, you know, people do have other diseases, it does affect their quality of life. And while there could be value from improving a specific measure that's very Parkinson disease specific and is improved by something, if it's not affecting the overall qualify of life, I think there is some value to considering, you know, why aren't we concerned with overall quality of life, and that we really want to be focusing on interventions that improve both

overall quality of life and experiences of daily living, and those are my main points.

DR. ROSS: Thank you. Ms. Goldsmith?

MS. GOLDSMITH: I voted a five, I know that's a shocker. So I feel like this is, you know, a central piece on making anything work for these patients and what they would, it would influence I think their value of a device, or their perspective on, you know, how it's going. I think the quality of life, I think overarchingly affects, you know, I think that's the largest piece. I think that's what I might say is important and I want to focus on, and it might be that my experience is very different from what you might experience. And so I think that, you know, being driven from that patient perspective, what they value and what they want to see improved and if they think it's working is very different in every population with every comorbidity that exists, you know, everything, so I think that's the challenge.

I mean, I would put see quality in the quality of life, so that's hard for me to tease out, those two items, and I think there's a

very important psychosocial aspect here that probably should be considered when patients are, you know, should be measured in another piece as we go through this with the different devices and the different measurements. Anyway, that's, you know, a glaring five.

DR. ROSS: Great. And Dr. Mauri, how would you have voted.

DR. MAURI: Yeah. The numbers are high, and it's not so much that I would, I guess I would say perhaps a four, but I just want to explain why. In that, I think as we think about specific or broad, and we think about the hierarchy of what needs to be measured for a device to be covered, I think it should begin with does it do what we expect it to do for patients. And then on top of that, we should also have benefits that are measurable that are broader than that.

So I'm just reflecting on, Dr. Stearns, your comments about the broader measure of quality of life versus the more specific. Yes, ideally we would have single therapies that would improve all domains but in practicality, the different therapies have

specific impacts, and so I think it is important that when we think about what endpoints we're using, that we think specifically about what's, what is required to be able to say this actually does have a benefit for patients, and then also to measure and show impacts.

So that's my background on why I would say that, and then I would add, you know, just to echo some of the things that I heard earlier, I would put Parkinson's disease-related quality of life over sleep quality in terms of where to put the emphasis. And then just note that activities of daily living, motor-related activities of daily living are part of, are included under the clinician-assessed symptoms and they have a component that's been reported.

DR. ROSS: Thank you. Okay. So now I think we can turn to the third domain which we have been asked to vote on, which is device-related safety, again on a scale of one to five from not at all important to extremely important.

(The panel voted and votes were

recorded by staff.)

DR. ROSS: Okay, it looks like everybody has voted Dr. Dhruva, how did you vote?

DR. DHRUVA: Thanks. I voted a five, extremely important for device safety as well, and as I was thinking about the device safety, I think in a couple of ways. One is, again, for I think noninvasive wearable personal control devices, I think the device safety is going to be identified if there are safety-related concerns more quickly, so I think three months at minimum ideally again, or following longer would be reasonable, whereas I think for implantable devices, I think at least one yeah would be ideal.

I realize that in the expert report that Terry identified there was not a lot written about safety and again, there's obviously going to be a lot of heterogeneity based on the different type of device, but I think that we know, and obviously we know that there's going to be periprocedural events if a patient is undergoing for example a permanently implanted device. But I think just stepping

back overall, device safety is just extremely important. We have, we are talking about older adults who oftentimes are frail or extremely frail, and we are talking not just about their Parkinson's disease or essential tremor but other comorbidities that they may have, and so a device-related complication is oftentimes not just about that exact device-related complication but again, it can sometimes set off a cascade in older adults who have multi comorbidity, who have frailty, et cetera. It's something that may seem like a small thing but it leads to a fall, it can lead to lots of different issues.

So I think that overall this is an extremely important endpoint, excuse me, extremely important domain with heterogeneity in the endpoints that are going to be assessed that are more tailored to this type of medical device.

DR. ROSS: Okay, thank you. Dr. Chen?

DR. CHEN: Hi. So I also voted a number five, extremely important. I think from just asking the question, is it important to assess patient safety, it's definitely

extremely important, but the question is the what and the how, and if we separate out implantable or invasive devices, procedure-related devices versus wearable, I might say that for invasive or implantable, extremely important whereas the wearable may be a little bit lower rank of very important.

And again, I agree that it depends on what the device is, what the procedure is, how we assess the endpoint, and how we monitor the safety will be very different from device to device or from category to category.

DR. ROSS: Thank you. Dr. Newman?

MS. NEWMAN: I would say the same. I rated that a five as well. Clearly safety is of utmost importance and I can appreciate the distinction between the implantables and the wearables. I think it's just, when you think about, you know, we just talked about fall and the fall prevention, and just be mindful what these safety, what these features could do that might cause, you know, a safety-related challenge.

DR. ROSS: Great. Dr. Stearns?

DR. STEARNS: I voted a five and I

think my main reasons have already been stated, that there's, you know, with the non-implantable, I think studies will show that if there are any bothersome effects such as spoons acting weirdly or wearables causing skin irritation, that people will stop using them, that should be known in the study. But certainly safety for implantables is, and side effects or whether other events following implantation, would be very important to focus on safety.

DR. ROSS: Okay. Ms. Goldsmith?

DR. GOLDSTEIN: I voted -- I'm the loan soldier, I voted four. I think safety is extremely important, let me just start by saying I think it's extremely important, but I voted very important because I don't think it should be a limiting factor if someone is extremely debilitated and they're willing, they know the risk factors and they're willing to risk that safety because they want something that has those risk factors, I think that needs to be very clearly outlined obviously in this domain. Obviously it is critical, but I don't think it should be a limiting factor in giving

them the possibility of having something if they are willing to risk their choice. So that's why I voted that, because if people are up against the wall and want to try something, I think that that should be like I said, a patient choice, an option, but safety is very important, extremely important.

DR. ROSS: Great. And Dr. Mauri, how would you have voted?

DR. MAURI: I would have voted a five. I think safety's very important but just to acknowledge, Amy, your comments, and maybe this relates to it. When somebody undergoes an invasive procedure, I think the expectation is that not necessarily will it have the same recovery that a noninvasive procedure would. So I think I just want to acknowledge Amy's comments as being something to be considered when we look at that options for an array of different types of devices that might actually have impacts on different types of symptoms for people.

And I guess the other thing that I would add, which is a little bit of a side comment but related to safety, is that as not

only the devices expand in terms of what different types of devices are available that have different modes of action that might have different expected safety questions that would be addressed, even for the same devices over time, the methods of using them can become less invasive over time, as one example. And so I just encourage the opportunity for the Agency to continue to consider, you know, reflecting on the safety, but as the field progresses, the practice of how these procedures are done.

DR. ROSS: Great, thank you.

So that concludes our voting portion, and we sort of combined the last section of the discussion of each domain regarding specific measures, followup, MCIDs into that conversation.

But I wonder if before we close, particularly since we're ahead of schedule, if I could just pose two separate questions I wanted to pose to the group just to get your feedback on.

The first, and not to call anyone out, because I think Robin and Amy might have a word to say here, is there were comments from the

occupational therapy group that were submitted in advance that were related to devices that I would say assist or help manage the symptoms of these diseases, as opposed to sort of treating them. I just want to know if you anything you want to reflect on in terms of which types of endpoints would you want to see in an evaluation of sort of those types of devices, and if other people have something to say about that.

MS. NEWMAN: I think what you're -- I did see that letter from the American Occupational Therapy Association that was in the file, and to me it appeared to me that those were assistive devices, so things that people might use to support themselves in doing a daily activity that's not implantable or wearable. So it could be a range of different things sort of tailored to the individual's needs. So it's sort of like a piece of adaptive equipment if you imagine it what way, compared to, you know, the TAPS or something like that, which I would more in the world of occupational therapy, would think of that more as a preparatory activity, you would engage

with that technology and then go ahead and perform an activity thereafter. Does that help to answer?

DR. ROSS: It does, but I guess what I'm asking, if someone was doing a study to evaluate them, would you expect them to use different clinical endpoints than have come up today, or would you expect them to similarly measure experience of daily living through ADLs?

MS. NEWMAN: Yeah, I think they would be affected. I mean, we are looking at the ultimate end goal of performing your daily activities or you know, ADLs. So in that way I think those motor-related ADL scores or domains would be equally as important. The thing here is sometimes these devices, they're not going to change some of the underlying deficits so maybe here we're thinking oh, some of the motor-related deficits may change with device use but that's not perhaps the intended outcome. So I think the endpoints in large part would stay the same, except I think there will be a piece of external equipment that someone's going to pick up in order to help

them write, or in order to help them get a spoon to their mouths or have, you know --

DR. ROSS: So the measures that have been discussed, the UPDRS and stuff, they incorporate those types of --

MS. NEWMAN: So that's what you're asking, okay. So there are definitely more specific ADL-related measures that we use. So if we're getting at it that way, you know, you can look at different function-related scales, different patient-reported, you know, outcomes for how effective are you in doing this everyday activity. So I mean, let me chew for a minute while you ask Amy, but I do think you can have some more specific related function oriented measures that would be associated with device use.

DR. ROSS: Okay. Amy, or anyone else if you want to reflect on that? I just though it would be useful for us to discuss since we had the time.

MS. GOLDSMITH: I mean, I agree with everything that Robin was saying. I think that that's a lot of what, was it Dr. Isaacson was talking about with the B-F, was talking about a

little more function-focused measurements. It would take a little more time, but of course I think that's extremely valuable, to have things very function related. I thinks that's what really impacts someone's quality of life.

I mean, obviously we didn't really talk about swallowing hardly at all, you know, and doing any exploratory muscle strengthening, nothing like that was touched on. I do think swallowing is a huge part of someone's quality of life, so that might be something else.

But anyway, I think that there's a lot more granular functional ADLs that could be assessed and looked at for sure, there's a myriad of them honestly.

DR. ROSS: Dependent on the device, the purpose --

DR. GOLDSTEIN: Depending on the device, dependent on the severity of the tremor or the Parkinson's disease, I think there's a lot of nuances within each of those, I would say.

And really the patient's motivation, where they're at. If that's not what they want to look at or work on, they're not -- even

though I know, it doesn't matter, because if they don't know and they don't care and they don't want that, that that's going to impact their life, I don't think that's going to even make a difference. So I think that patient, you know, interest, motivation, level of wherever they're at is a huge factor, and I think a lot of us touched on it with the comorbidities and the other things that are going on with them, and meds, I mean there's just so many factors, but yeah, I think there's a lot and it's so hard to just make it so black and white when it so isn't.

MS. NEWMAN: That I agree with wholeheartedly. This is to say that those pieces of equipment, those devices aren't mutually exclusive of being used alongside a device, right, an implantable or a wearable, right? So it's not so say oh, you would go this way or this way, and you only do something that you would pick up and use to help you do something, or you would use a device. So there are, I mean Amy is speaking to this nuance in the functional side of this, that it's so hard to separate out. You know, it's like

everything is so interrelated, that's the trick. That's the trick.

DR. ROSS: Sally, do you want to make a comment?

DR. STEARNS: Yes. And actually it relates to in part of the discussion we were just having in terms of the patients themselves will actually be interested in adopting a certain device, or proceeding with a certain procedure.

You know, if you think about the timing of the disease, there could be a place in the progression of the disease where a wearable might have incredible improvement for the patient and yet the patient's inclination might be not to get it at that point because of stigma of needing the device, versus they later in the progression say okay, I'll use it, but in fact the phase where the most benefit from the device would be available has actually passed. I think that's a hard thing for CMS to deal with in terms of their decisions, but I think it's important to have it documented, because you can start using some of these devices way too late.

You know, I've said I don't have a lot of experience with these instruments, but I have a lot of experience with the Medicare hospice benefit, which by the way, I'm assuming when CMS deliberates in terms of payment for these things, that it's for people who have not moved to the hospice benefit, and yet moving to the hospice benefit is appropriate for people with Parkinson's, at least with Parkinson's. I know a lot less about essential tremor. But at that point it would be up to the hospice whether or not to reimburse for the device. It's my understanding that the way the hospice benefit would work with respect to these, they would need to make the decision that it was going to improve the quality of life for the patient.

We're not here to make those distinctions but once again, I think timing of disease is, or sorry, of the progression of disease, that time path and when the devices or implantables or wearables are most relevant is something to pay attention to, it should be paid attention to in terms of assessment of the duration for the device and you know, it's a

lot of small but important issues.

That's why I was very interested like in the finger one, you know, and maybe a patient could be convinced by knowing now is where I should start using that wearable if I want to get the most benefit from in it.

DR. ROSS: Actually, that relates to the second sort of question I was going to ask, which is in the clinical endpoint reviews in the past, we spent much more time talking about surrogate measures, biomarkers, pathophysiology measures, and at least one speaker explicitly called out that there just aren't reliable measures of that type for essential tremor or Parkinson's disease, and I just didn't know if any of you wanted to jump in and offer reflection on those types of measures. There's a lot of research in the space, and just what you would expect to see in terms of validation should one be developed, and CMS might want to consider putting it on the record if you guys have a point of view on that, or maybe no one has anything to say.

DR. MAURI: When we think of surrogate measures, we're thinking of something that

could be measured more easily or earlier than that that the patient cares about, so I just offer that in the context of validating, but I don't have an awareness of surrogates that we should be using but when I do see new measures, I think about that maybe in the same light.

DR. ROSS: Yeah.

DR. DHRUVA: I wonder if it's because we have the benefit in these conditions of having so much opportunity to hear directly from the patient about how they feel functions survive. I'd just make a larger comment that if surrogate measures are developed in this area around the validations, we know that a lot of surrogate measures are oftentimes used and can be assessed.

And we heard even about one, I think the second or third presenter, the device that has the FDA breakthrough designation that sounds like it's going to be undergoing or is in the process of regulatory review right now. Not specifically about that device, but if that is determined to, I think that's an example of potentially data that could be like a surrogate that is tracking. We saw the speaker provide a

couple of graphs that were snapshots of individual patients and that seemed to then correlate with the patient symptoms. I would then ask, again, not about that specific device but the general principle, you know, how well is this associated with how patients feel function provides those clinical endpoints, because certainly we know that patients care about their quality of life, about their tremor, about their sleep quality, about if they're having falls, and not necessarily, you know, about how their digits are moving, unless that the reliably associated with one or more of the other outcomes.

DR. STEARNS: Or it could be used to help clinicians understand a point for an appropriate intervention.

DR. DHRUVA: Absolutely, for sure, and I think that's a great point. And I would just, building on that, Sally, and then do those intervention changes that are made as a result of that data improve patient outcomes, that is, does it test and translate to improved outcomes, not just a change.

DR. STEARNS: Yes. There goes my

mantra of overall quality of life.

DR. ROSS: I guess I would only add, we would want to see that kind of validation in the Medicare beneficiary population specifically, because in older adults symptoms may differ.

Okay. Any other closing comments that people want to make on reflection? We moved, we're a little bit ahead of schedule but that's in part because we booked 40 minutes for open public comment that we didn't need, so we're not actually that far ahead. We've had a pretty thorough discussion of all three sets of domains and more, and I think we had really useful public speaker presentations after everyone sort of already congratulated Terry on a great evidence review that she put forth for us in and a very easy to understand and digestible way.

All right. Any other closing comments that members of the panel want to make? Of courts, thank you for making yourselves available for this time. Oh, Sally?

DR. STEARNS: Just when I agreed to this, I thought there was so little about these

diseases and measures, I thought am I going to be able to be useful, but I actually really found this to be very interesting and I've been asked to judge on things that I think I have the capacity to, versus specific instruments where I don't know.

DR. ROSS: I can assure you we found your comments very helpful.

Tamara, is there anything you wanted to say in closing? I know you haven't been feeling great, but if you want to jump back on?

MS. SYREK JENSEN: No. Just thank you again to everyone, and to everyone who participated not only on the panel but also the public comments and all the speakers. I found it also very interesting hearing all of you. So again, thank you, and I hope everyone has a wonderful week.

DR. ROSS: And stay cool if you're east of the Rocky Mountains basically.

DR. STEARNS: I'm in Montana by the way, the weather is very nice.

DR. ROSS: Thanks everybody, and enjoy the rest of your day.

(The meeting concluded at 1:10 p.m.)

TRANSCRIBER'S CERTIFICATE

I, Paul Gasparotti, hereby certify that I transcribed from audio file the proceedings to the best of my ability in the foregoing-entitled matter; and I further certify that the foregoing is a full, true and correct transcript of the audio files produced.

IN WITNESS THEREOF, I have subscribed my name on the 8th day of July 2025.

Transcriptionist

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