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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

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Panelists

Chairperson

Joseph Ross, MD, MHS

Vice-Chair

Sanket Dhruva, MD, MHS, FACC

MEDCAC Members

Yi-Fen Irene Chen, MD

Robin Newman, OTD, MA, OTR/L, CLT, FAOTA

Sally Stearns, PhD

Patient Advocate

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MEDCAC Coordinator

Tara Hall

1	TABLE OF CONTENTS	
2		Page
3		
4	Opening Remarks	
5	Tara Hall, Tamara Syrek Jensen,	
6	Joe Ross, MD	5
7		
8	CMS Presentation of Clinical Endpoints Review	
9	Teresa Rogstad	11
10		
11	Summary of Subcommittee Deliberations; Review	
12	of Voting Questions and Discussion	
13	Joe Ross	21
14		
15	Scheduled Public Comments and Questions to	
16	Presenters	
17	Kelly Lyons, PhD	26
18	Pravin Khemani, MD	33
19	Helen Bronte-Stewart, MD	42
20	Stuart H. Isaacson, MD	55
21	Ashwini Sharan, MD	63
22	Joshua M. Rosenow, MD	70
23		
24	Open Public Comments	
25	(No Commenters)	

1	TABLE OF CONTENTS (Continued)	
2		
3	Open Panel Discussion of Domains	
4	Joe Ross, MD	80
5		
6	Voting Questions and Panel Member Comments	
7	Joe Ross, MD	96
8		
9	Final Open Panel Discussion	
10	Joe Ross, MD	130
11	Closing Remarks and Adjournment	141
12		
13		
14		
15		
16		
17		
18		
19		
20		
21		
22		
23		
24		
25		

1 PANEL PROCEEDINGS

2 (The meeting was called to order at
3 10:00 a.m. EDT, Wednesday, June 25, 2025.

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

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

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

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

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

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

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

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

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

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

25 The entire panel, including nonvoting

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

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

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

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

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

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

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

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

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

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

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

1 hopefully we will be announcing that in the
2 near future.

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

11 Tara?

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

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

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

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

25 So, the objective of this report was

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

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

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

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

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

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

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

25 So the CER report began with a

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

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

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

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

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

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

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

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

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

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

1 disease specific activities that are affected
2 by Parkinson's disease, often referred to in
3 the literature as experiences of daily living.

4 Next slide please.

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

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

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

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

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

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

1 clinical reserve. Next slide please.

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

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

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

3 We always request that there be a
4 section on applicability to Medicare
5 beneficiaries in our CER reports.
6 Applicability is another term for
7 generalizability. In the systematic reviews
8 that were collected, none of them focused on
9 older adults. However, the mean age across the
10 studies represented by those reviews was 54 to
11 77 years, so they represent a population that
12 includes a healthy percentage of older adults.
13 The studies were also representative of a mix
14 of disease severity. However, there was
15 insufficient information in the reviews on
16 other patient characteristics.

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

25 As I said before, additional detail

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

22 MS. NEWMAN: Can I just ask one?

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

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

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

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

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

17 MS. NEWMAN: Okay.

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

22 MS. ROGSTAD: Certainly.

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

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

1 first presenter, which is Dr. Kelly Lyons.

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

4 MS. HALL: I will keep the time.

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

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

12 MS. HALL: Yes.

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

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

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

5 So the International Essential Tremor
6 Foundation was founded in 1988 as a nonprofit
7 organization. The IETF is the largest
8 essential tremor patient advocacy group
9 currently. The mission of the IETF includes
10 multiple components, including awareness,
11 education, support and research related to
12 essential tremor. We have engagement with more
13 than 100,000 essential tremor patients and 500
14 physicians focused on the treatment of
15 essential tremor. Our medical advisory board
16 or scientific board is comprised of more than
17 20 movement disorder experts.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

1 especially for procedures such as FUS and DBS.

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

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

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

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

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

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

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

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

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

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

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

25 DR. KHEMANI: Yes indeed.

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

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

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

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

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

4 DR. DHRUVA: Thank you.

5 DR. ROSS: Dr. Mauri?

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

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

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

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

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

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

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

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

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

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

11 Tara, we can go to the next speaker.

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

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

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

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

1 over five years. Next slide please.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

8 DR. BRONTE-STEWART: Yes, those are
9 great questions, thank you. And yes, we've
10 been using this technology in my lab for over
11 25 years, so there is a lot of validation that
12 is represented in the bibliography. We have
13 recently now transformed this into a remote
14 monitoring pool and yes, we can --

15 (Unrelated audio interference.)

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

18 MS. JENSEN: Thanks. Sorry about
19 that.

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

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

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

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

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

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

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

25 DR. BRONTE-STEWART: Yeah, thanks for

1 those questions.

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

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

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

16 DR. BRONTE-STEWART: Yeah, thank you.
17 Actually one of the important features we
18 wanted to show in the remote monitoring trial,
19 our primary outcome was compliance to make sure
20 that people who might use this when approved,
21 that it would satisfy the remote monitoring
22 code. So our first outcome was compliance of
23 16 out of 30 days, which was a hundred percent.
24 We had 96 percent of people adhering one time a
25 day, and 86 percent to twice a day. And we

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

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

20 DR. ROSS: Dr. Stearns?

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

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

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

8 DR. BRONTE-STEWART: Absolutely, yes.
9 I think that's going to be something that is
10 very interesting. We've done a lot of this in
11 the lab, we published a large study back in
12 2009 looking at a wearable, and by wearable I
13 mean a sensor wearable, not just a stimulation
14 wearable and also QDG, and showed that in fact
15 over time you begin to see the more affected or
16 less affected hand nudge. And I think as we
17 shoed with fluctuations, you can see
18 fluctuations in motor performance over the day,
19 so the provider can get a very nice
20 quantitative metric of when they should start
21 thinking about deep brain stimulation or some
22 of the other interventions.

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

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

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

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

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

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

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

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

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

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

16 DR. ISAACSON: Promises, promises.

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

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

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

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

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

1 others. Next slide.

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

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

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

1 as well.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

19 DR. ISAACSON: Sure, thank you.

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

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

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

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

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

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

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

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

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

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

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

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

1 on average takes physicians 20 to 35 minutes to
2 administer in their office when they're well
3 trained in it, and the MDS-UPDRS, which was
4 adopted and suggested in 2008, can take 50 to
5 75 minutes but offers a lot more granularity on
6 the measurement of the nuances for patients
7 with Parkinson's disease, and safety as I
8 mentioned. So again, just reiterating that you
9 need multiple endpoints to test DBS technology
10 in the context of the clinical trial. Next
11 slide please.

12 The CER process was really aimed at
13 literature after 2016, but I just want to
14 highlight that there is also a rich and robust
15 literature on DBS starting from FDA approval in
16 1997 for essential tremor and in 2002 for deep
17 brain stimulation in high quality journals. As
18 an example, I'm going to give you two
19 particular cases that I want to highlight for
20 these patients. Next slide please.

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

1 dyskinesias are involuntary erratic writhing
2 movements that are often associated with
3 long-term dopamine therapy and often are
4 associated with peak dosing which occurs within
5 30 to 60 minutes.

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

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

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

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

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

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

1 potentially worsening.

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

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

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

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

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

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

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

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

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

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

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

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

1 slide please.

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

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

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

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

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

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

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

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

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

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

25 DR. ROSS: Thank you, Dr. Rosenow.

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

3 Dr. Dhruva?

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

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

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

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

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

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

22 DR. ROSS: Thanks. Dr. Stearns?

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

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

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

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

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

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

13 DR. ROSENOW: Correct.

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

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

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

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

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

1 on time and we're due for a break. We're a
2 little bit over, we were supposed to stop at
3 11:30 eastern standard time, so we will go for
4 ten minutes, allow people to refill their water
5 cups and stand up and move around for a second,
6 and we'll come back at 11:40, let's say 11:45
7 just for ease.

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

10 MS. HALL: No, we do not.

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

15 (Recess.)

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

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

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

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

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

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

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

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

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

24 DR. ROSS: Dr. Chen?

25 DR. CHEN: This is Irene Chen. I have

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

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

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

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

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

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

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

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

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

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

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

16 DR. ROSS: Please.

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

1 in terms of important clinical endpoints for a
2 particular treatment.

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

5 MS. ROGSTAD: Table --

6 DR. ROSS: -- in the summary?

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

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

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

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

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

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

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

7 (Laughter.)

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

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

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

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

10 MS. ROGSTAD: Right.

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

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

25 MS. ROGSTAD: Okay. So it did show

1 up, but not frequently enough to -- okay.

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

10 Other questions?

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

25 I guess the question is, like is this

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

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

1 instance, one speaker talked about how it took
2 80 minutes to administer one of the
3 questionnaires, and that provides a lot of
4 granularity that maybe you would expect that
5 for the device studies to guide coverage or
6 maybe you would not, right? So I think it's
7 worth sort of reflecting on that, provided that
8 it's a validated endpoint with a minimally
9 clinically important difference that can be
10 detected and used as part of a clinical study.

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

25 DR. ROSS: Sanket?

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

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

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

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

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

1 this group likes this endpoint, this group
2 likes that endpoint.

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

8 DR. ROSS: Yeah.

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

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

25 DR. ROSS: Yeah, I agree with that.

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

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

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

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

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

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

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

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

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

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

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

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

3 DR. STEARNS: Thank you.

4 DR. ROSS: Any other questions?

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

8 DR. MAURI: Thank you.

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

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

1 March 26th.

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

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

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

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

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

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

25 DR. STEARNS: So this goes to the

1 email that Tara sent, right?

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

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

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

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

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

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

25 DR. ROSS: Oh, I see.

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

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

11 DR. CHEN: Okay, thank you.

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

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

16 MS. HALL: Sally, are you logged on?

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

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

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

1 on the first question; is that right?

2 DR. ROSS: Yes.

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

5 DR. ROSS: It looks like you have
6 voted.

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

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

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

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

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

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

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

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

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

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

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

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

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

4 Sorry for the long comments.

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

8 Dr. Chen, how did you vote?

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

25 DR. ROSS: That's very helpful. And

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

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

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

25 So for the primary areas that I think

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

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

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

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

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

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

13 DR. ROSS: Yes, please.

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

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

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

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

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

10 DR STEARNS: Okay, thank you.

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

13 MS. HALL: The voting is done.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

1 related quality of life for essential tremor
2 very high.

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

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

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

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

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

9 DR. ROSS: Great, thank you.

10 Dr. Stearns, how did you vote?

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

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

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

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

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

3 DR. ROSS: Thank you. Ms. Goldsmith?

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

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

1 very important psychosocial aspect here that
2 probably should be considered when patients
3 are, you know, should be measured in another
4 piece as we go through this with the different
5 devices and the different measurements.

6 Anyway, that's, you know, a glaring five.

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

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

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

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

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

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

25 (The panel voted and votes were

1 recorded by staff.)

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

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

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

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

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

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

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

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

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

13 DR. ROSS: Thank you. Dr. Newman?

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

24 DR. ROSS: Great. Dr. Stearns?

25 DR. STEARNS: I voted a five and I

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

12 DR. ROSS: Okay. Ms. Goldsmith?

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

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

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

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

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

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

12 DR. ROSS: Great, thank you.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

1 lot of small but important issues.

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

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

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

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

7 DR. ROSS: Yeah.

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

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

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

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

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

25 DR. STEARNS: Yes. There goes my

1 mantra of overall quality of life.

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

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

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

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

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

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

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

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

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

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

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

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

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8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25

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

WORD INDEX

< \$ >	25 1:20 5:3 49:11 57:12 60:21	96 4:7 52:24	107:5 108:12	12, 23 60:17
\$1.35 27:25	26 3:17	98 46:3	112:3 113:15	61:9, 13 62:21,
< 1 >	26th 100:1	< A >	114:3 119:12	22 63:12 74:17
1,500 57:15	< 3 >	a.m 5:3 7:17	120:6 124:14,	88:19 108:3, 18
1:10 142:25	30 14:19 26:19	ability 30:11	15 132:14	132:15
10:00 5:3	44:5 52:23	31:6, 25 58:5	activity 59:21	ADL-related
100,000 27:13	68:5 90:9	60:13 143:5	77:12 131:17,	133:8
11 3:9 7:17	33 3:18	able 19:17	25 132:2	ADLs 32:16, 24
32:9	35 67:1	31:21 32:4	133:13	35:14 59:10
11:30 80:3	< 4 >	52:6 86:8, 11	actual 76:21	62:14 104:13
11:40 80:6	40 141:10	93:6 101:10	acute 76:16	107:24 108:14
11:45 80:6, 12	42 3:19	103:3 104:13	adaptive 131:21	110:11 114:9
12 112:23	44 60:20	106:19 116:3	add 29:8 34:8	116:11, 23
121:2	45 89:23	124:5 142:2	86:14 109:8	132:10, 14
127 89:22	< 5 >	abnormal 37:16	124:9 129:24	134:13
12-item 74:17	5 3:6	absolute 91:11	141:2	ADL's 32:1
12-month 72:2	50 67:4	Absolutely 54:8	added 16:19	119:10
13 80:13	500 27:13	111:7 140:18	47:20 60:23	administer
130 4:10	64:11	absorption 48:1	85:11	67:2 92:2
14 50:22	54 20:10	abstracted	adding 29:12	administered
141 4:11	55 3:20	14:20	addition 8:15	16:14 23:10
15 80:18	< 6 >	academia 15:11	30:15 51:4	Administration
16 52:23	60 61:2 68:5	Academy 28:11	99:24 119:10	38:7
180,000 64:7	63 3:21	29:11 59:7	additional	adopted 67:4
1988 27:6	65 57:18	61:18 95:16	15:11 20:25	adopting 136:8
1997 67:16	66 60:21	access 31:23	29:9 84:18	Adult 29:6
< 2 >	68 60:24	accompanied	95:5, 7 102:24	adults 20:9, 12,
20 27:17 67:1	69 60:19	17:19	address 7:14,	19 95:24 99:18
2002 67:16	< 7 >	accuracy 46:4	17 55:24 56:20	104:7 126:3, 10
2005 28:11	70 3:22 57:16	accurate 23:8	66:6	141:5
2008 14:2 18:2	70s 95:19	44:11	addressed 130:5	advance 46:16
26:21 67:4	72 61:2	achieve 8:8	addresses 6:5	120:14 131:2
2009 54:12	75 67:5	72:5	addressing	advantageous
2010 86:1	7500 1:23	achieves 63:11	51:19	62:16
2011 28:14	77 20:11	acknowledge	adequacy 51:24	adverse 17:16
2016 67:13	< 8 >	69:1 129:12, 17	adequate	20:23 41:17, 19,
2020 28:17	80 4:4 92:2	Act 8:25 9:1	115:25 116:4	22, 25 42:3
2021 28:25	86 52:25	acting 128:5	adhere 7:4	65:24 69:11
2023 14:3	8th 143:10	action 36:16	adhering 52:24	advice 10:2
2024 43:15	< 9 >	39:21, 23 130:3	adjacent 44:3	21:16
60:9	21 3:13 33:23	active 72:1	Adjournment	advise 5:23
2025 1:20 5:3	22 70:14	activities 16:22,	4:11	advisor 11:17
143:10		24 17:1 25:8	adjunctive	Advisory 1:13
2026 52:7		27:18 30:11, 18	49:21	5:8 8:24 9:1,
21 3:13 33:23		31:1, 7, 22	adjustment	25 27:15 29:3
22 70:14		34:19 35:3	47:12 48:5	55:24 56:21
		39:20, 24 40:1,	adjustments	58:3
		2, 19 53:9 58:7,	43:24	advocacy 27:8
		16, 20 60:14	ADL 33:5	Advocate 2:14
			58:17 59:2, 6,	

affect 6:10 91:10 92:20 121:17	amplitude 23:21 44:8, 20 45:4, 22 46:13	appendices 82:11	Ashwini 3:21	assistive 27:20 131:15
afferent 33:25 37:20 59:18	Amy 2:15 7:21 92:12 129:12	Appendix 81:14 86:18 87:8, 20	aside 113:18	associated 6:6 14:6 30:16 68:2, 4 133:16 140:6, 13
age 20:9 43:19 57:17 60:19, 20 95:23	130:24 133:14, 18 135:23	Apple 101:5, 6, 8	asked 6:12 22:7 40:10 60:3 80:24 124:21 142:4	association 27:3 70:16 131:13
Agency 130:8	Amy's 129:17	applicability 20:4, 6 37:25 39:14	asking 25:7 26:8 62:8 98:10 126:24 132:5 133:7	assuming 137:4
agency's 33:19	Analysis 2:20 6:4 9:18 11:18	applicable 38:12	aspect 40:22 83:8 93:2 110:9 123:1	assure 142:7
agenda 7:5	analyzed 43:6	application 52:6	aspects 39:12 44:24 98:1, 3	asymmetry 47:5
ages 31:10	analyzes 46:12	appreciate 10:22 11:4 25:6 28:8 33:15, 19 41:13 55:23 56:20 64:13 79:24 81:19 84:13 88:22 91:2 119:4 127:16	assess 12:8 16:25 34:23 54:2 58:15 59:13 61:24 65:11 69:25 86:8 107:15, 20 118:1, 14 126:25 127:10	attendance 8:16 21:8
aging 58:8	anatomic 86:2	appropriate 6:1 20:1 28:16 33:8 34:5 54:5 64:20 66:25 68:18 79:16 121:1 137:8 140:17	assessed 16:11, 13 23:7, 9 34:20 53:4 88:11 91:9 104:1 106:21 110:2 117:3 126:18 134:14 139:16	attendees 7:14 9:5
ago 31:18 90:9 117:1	anatomical 36:20	approved 28:25 52:20 71:4 84:25	assessment 20:20 23:17 27:24 45:12 46:17 49:6 55:12 58:4, 20 59:8 60:15 61:19 66:17 91:8 109:19 111:10, 11, 22 113:18 117:17 120:23 137:24	attention 21:2 85:10 137:23, 24
agree 32:17 54:24 62:1 65:21 95:25 108:10 111:7 112:20 127:8 133:22 135:14	and/or 13:20	area 8:11 36:21 37:1 96:7 139:14	assessing 20:19 24:8 65:23 89:2 105:18 115:16, 24	audio 8:8 49:15 86:1 143:4, 8
ahead 96:4 130:19 132:1 141:9, 12	announce 10:13, 25	areas 37:12 92:23 111:25	assessments 58:15 63:6 98:16 111:13	August 14:3
AI 43:7	announcement 6:5	array 66:8 129:19	assist 131:3	authors 14:4, 14
AI-informed 46:1	announcing 11:1	article 67:21		available 8:3 16:1 28:20 29:13 38:18 104:18, 22 130:2 136:20 141:23
aimed 67:12	annual 59:8 61:19	articulated 39:19		average 46:13 60:19, 21 67:1
algorithm 29:10 43:7 46:10	annually 28:7	Ash 64:4		averaged 53:5
allotted 7:10	ans 97:1			avoid 77:25 109:11
allow 7:6 80:4	answer 32:10 62:5 132:3			avoided 73:3
allowing 26:14 30:24	answered 23:15			avoiding 74:18
allows 32:23 48:20 98:25	answering 25:9 79:21			aware 9:5 28:22
alluding 86:4	answers 40:23 51:9			awareness 27:10 139:4
alongside 135:17	anterior 71:13			
alternating 44:4, 14	anticipated 99:11			
American 28:11 31:9 59:7 61:18 70:16 131:12	anticipating 94:13			
amount 19:15	anxiety 30:19 66:2 69:19			
	anxious 9:6			
	anymore 77:17			
	Anyway 123:6 134:12			
	apologize 108:5			
	app 43:4			
	apparent 66:6			
	appear 15:24			
	appeared 131:14			

114:15 117:22 126:1 142:11	benefit 86:8, 10 124:6 136:19 137:4, 7, 8, 14 138:6 139:9	brain 12:23 34:3 36:19, 22 37:3, 8, 12 38:5 54:21 59:21 64:11 67:17 71:5 73:19	call 11:12 34:1 130:23	central 36:22 122:6
background 8:13 11:21 49:17 124:8	benefits 105:20 112:21 123:18	brainstem 12:14	called 5:2 12:24 34:23 36:22 59:17 113:24 138:13	CER 11:19 13:25 14:14 15:9, 23 16:1, 8, 18 17:10 18:19 19:7, 11, 17 20:5 21:1 35:9 64:2, 14, 23 65:5 67:12 82:11, 18 85:6, 25 86:18 87:9
bad 79:15	benign 31:17, 21 36:4	break 9:12 80:1	calling 111:12	17:10 18:19 19:7, 11, 17 20:5 21:1 35:9 64:2, 14, 23 65:5 67:12 82:11, 18 85:6, 25 86:18 87:9
Bain 58:19 59:2, 6, 12, 23 60:17, 23 61:8, 13 62:11, 22 63:10	best 8:8 36:17 86:8 143:5	breakage 75:17, 18	capacity 142:5	65:5 67:12 82:11, 18 85:6, 25 86:18 87:9
Bain-Findlay 85:9 88:22 89:17	better 10:18 39:19 50:5 63:3 72:12 76:25 77:16 78:20 79:17 90:24 107:8	breakthrough 43:14 52:2 139:19	capture 32:24 83:22	65:5 67:12 82:11, 18 85:6, 25 86:18 87:9
balance 73:5, 7, 14 74:19, 21 78:1 108:16	biomarkers 138:11	breakup 86:1	captures 33:2	certain 14:24 54:1 73:2, 17 121:11 136:9
Baltimore 1:24	biased 32:20	bridging 34:8	capturing 52:13	Certainly 25:22 93:2 95:23 104:11 105:6 109:16 120:16 128:8 140:8
Barthel 89:12	big 92:14	briefly 36:18	care 27:20 55:14 67:24 68:16 69:22 117:15, 16 135:2 140:8	93:2 95:23 104:11 105:6 109:16 120:16 128:8 140:8
based 14:24 22:1 23:17 29:8 38:10 61:9, 10 88:23 95:23 98:16 107:1 109:2 125:21	bibliography 43:16 48:10 49:12	bring 121:6	caregiver 25:13 109:14	CERTIFICATE 143:1
Baltimore 1:24	bit 10:12 16:21 23:19 32:19 48:19 57:23 58:18 65:3 80:2, 25 82:9 117:9 118:17 127:7 129:24 141:9	broad 66:8 96:1 123:13	cares 57:15 139:2	143:1
Barthel 89:12	black 16:16 135:12	broader 123:19, 21	Carolina 53:23 77:24	certify 143:3, 6 126:11
based 14:24 22:1 23:17 29:8 38:10 61:9, 10 88:23 95:23 98:16 107:1 109:2 125:21	blinding 115:25 116:3 117:24	broadly 84:12 98:16	cascade 126:10	cetera 35:2 126:11
basically 45:9 55:10 142:20	blue 44:16, 23	Bronte-Stewart 3:19 42:12, 13 46:23 48:15 49:8, 20 51:25 52:16 54:8 55:15, 18	case 39:13 114:25	chair 21:4 70:15
basis 7:15 10:7 99:1	board 27:15, 16 29:3 73:24	burden 23:1 91:25 98:3	cases 67:19	Chairperson 2:3 5:5 10:16, 20
batteries 77:15, 17 90:14	bonus 38:19	brought 82:9	cast 97:3, 7 100:10	2:3 5:5 10:16, 20
battery 77:5 90:22	booked 141:10	building 140:20	catastrophic 104:12	challenge 122:22 127:23
begin 13:25	bothersome 128:4	bunch 40:20	categories 112:11	challenged 93:25
beginning 12:21 14:2, 16 52:7 55:3	bottom 16:23	burden 23:1 91:25 98:3	categorization 64:22	challenges 22:22
behalf 64:12	Boulevard 1:23	burdensome 66:10 68:25	category 36:2 117:19, 20 127:12	challenging 93:22
belabor 74:17	bradykinesia 45:7 46:15, 18 51:1	burns 42:1	cause 27:23 28:1 29:24 127:22	chance 109:3
believe 32:21 33:7 109:12, 14 114:9		buy 92:22	causing 128:5	change 33:9 50:18, 19 54:5 60:1 61:5 97:22 105:8, 22 107:3, 12 108:2, 14 109:4 112:2 132:18, 20 140:24
beneficial 78:18		< C >	CCC-SLP 2:15	50:18, 19 54:5 60:1 61:5 97:22 105:8, 22 107:3, 12 108:2, 14 109:4 112:2 132:18, 20 140:24
beneficiaries 20:5 104:8		C.2 86:19 87:9, 14, 18	cells 37:4, 21	107:3, 12 108:2, 14 109:4 112:2 132:18, 20 140:24
beneficiary 60:11 95:21 141:4		CAG 9:14 98:20	Center 26:24, 25 57:14 61:15 104:19	107:3, 12 108:2, 14 109:4 112:2 132:18, 20 140:24
		Cala 57:25 59:17	centered 110:7	changed 50:3 88:11
		calculated 51:6	CENTERS 1:11, 22 72:1, 5	
		calibrate 109:5		
		calibrated 23:4		

changes 20:22 47:11 59:21 115:18 140:21	94:9 cleared 52:5 clearly 104:4 127:15 128:23	close 16:23 110:24 130:18 closely 31:15 Closing 4:11 141:7, 20 142:10	50:1 62:12 63:23 77:9 79:7 80:6, 11 81:11 85:10 132:7	common 12:1 17:23 37:4 40:16 41:2
Chapel 53:23 77:24	clinic 42:2 48:13, 23 50:7	CLT 2:11 cluster 37:3	comes 83:8	commonly 12:7 114:7
characteristic 12:18	Clinical 3:8 5:14, 18, 23 10:3, 6 12:1, 2, 15 14:9, 20, 22 15:2, 11 16:17, 19 17:23 18:24, 25 19:1, 6, 23 21:9 27:20 28:5 34:6, 14, 15 36:10 41:16 45:11 46:17, 18 50:16, 21 51:20 57:19 59:12 61:14, 15 63:6 66:8, 25 67:10 68:22 80:21 82:7 83:18 84:22, 24 86:20 87:1 92:10 93:5, 6 94:3, 10 99:16 100:6, 12 101:18 103:15 113:23 120:13, 22 132:7 138:9 140:7	Closing 4:11 141:7, 20 142:10	comfortability 92:15, 20	communicating 86:10
characteristics 20:16	clinician 16:11, 12, 14 23:7, 11, 23 35:2 103:25 110:2 111:10, 12 117:2 120:23	CMS 3:8 5:16, 23 9:7, 20, 22 10:2 11:8, 20 21:14 54:2 66:9 68:24 94:13 136:21 137:5 138:20	coming 11:6 48:23	communication 50:15
characterized 35:9	clinician- assessed 16:10 22:17, 23 65:7 81:4 96:25 101:16 104:2 109:13 116:25 121:9 124:17	CMS's 97:6 101:20	comment 16:21 17:21 41:13 82:15 85:16, 20 86:14 107:18 115:12 129:25 136:4 139:12 141:11	community 119:11
characterizes 13:13	close 16:23 110:24 130:18	cochair 10:15, 25	commentary 5:20	comorbidity 122:20 126:11
chat 102:19	code 52:22	code 52:22	commented 117:10	comorbid 30:15 36:8
checkmarks 19:5	cognition 69:21 75:20 90:12 91:12	cognition 69:21 75:20 90:12 91:12	Commenters 3:25 103:24	comorbidities 118:5 126:6 135:9
Chen 2:10 7:20 82:24, 25 83:15 101:9, 22 102:1, 11 106:8, 9 107:21 108:1 117:6, 7 119:3 126:21, 22	cognitive 20:22 57:5 66:1 69:9 71:24 72:8, 13, 14, 16 74:2, 23 98:5 104:9 108:17 110:16	cochair 10:15, 25	Comments 3:15, 24 4:6 7:13 16:3 23:18 24:3 25:24 34:8 80:9 98:1, 22 103:21 104:21 106:4, 6 111:7, 15 123:21 129:12, 18 130:25 141:7, 20 142:8, 15	comorbidity 122:20 126:11
Chen's 121:8	coined 31:18	code 52:22	commented 117:10	companies 57:25 70:25 71:2
chest 77:4	colleagues 55:24 64:19 65:6, 22 66:16 68:21 76:19	cognition 69:21 75:20 90:12 91:12	Commenters 3:25 103:24	company 6:19 64:6
chew 133:13	collected 14:4, 7 20:8 25:10 84:3	cognitive 20:22 57:5 66:1 69:9 71:24 72:8, 13, 14, 16 74:2, 23 98:5 104:9 108:17 110:16	Comments 3:15, 24 4:6 7:13 16:3 23:18 24:3 25:24 34:8 80:9 98:1, 22 103:21 104:21 106:4, 6 111:7, 15 123:21 129:12, 18 130:25 141:7, 20 142:8, 15	compare 117:16
chief 64:5	cohort 118:11	cognitive 20:22 57:5 66:1 69:9 71:24 72:8, 13, 14, 16 74:2, 23 98:5 104:9 108:17 110:16	commented 117:10	compared 73:25 131:22
choice 129:2, 6	coined 31:18	cognitive 20:22 57:5 66:1 69:9 71:24 72:8, 13, 14, 16 74:2, 23 98:5 104:9 108:17 110:16	Commenters 3:25 103:24	comparison 31:11
choosing 68:12	colleagues 55:24 64:19 65:6, 22 66:16 68:21 76:19	cognitive 20:22 57:5 66:1 69:9 71:24 72:8, 13, 14, 16 74:2, 23 98:5 104:9 108:17 110:16	Comments 3:15, 24 4:6 7:13 16:3 23:18 24:3 25:24 34:8 80:9 98:1, 22 103:21 104:21 106:4, 6 111:7, 15 123:21 129:12, 18 130:25 141:7, 20 142:8, 15	compensation 42:18
choppy 94:25	collected 14:4, 7 20:8 25:10 84:3	cognitive 20:22 57:5 66:1 69:9 71:24 72:8, 13, 14, 16 74:2, 23 98:5 104:9 108:17 110:16	commented 117:10	compilation 50:25
chosen 65:19	coined 31:18	cognitive 20:22 57:5 66:1 69:9 71:24 72:8, 13, 14, 16 74:2, 23 98:5 104:9 108:17 110:16	Commenters 3:25 103:24	complete 102:23 104:13
chronically 77:8	colleagues 55:24 64:19 65:6, 22 66:16 68:21 76:19	cognitive 20:22 57:5 66:1 69:9 71:24 72:8, 13, 14, 16 74:2, 23 98:5 104:9 108:17 110:16	Comments 3:15, 24 4:6 7:13 16:3 23:18 24:3 25:24 34:8 80:9 98:1, 22 103:21 104:21 106:4, 6 111:7, 15 123:21 129:12, 18 130:25 141:7, 20 142:8, 15	completed 15:9
chunky 77:17	collected 14:4, 7 20:8 25:10 84:3	cognitive 20:22 57:5 66:1 69:9 71:24 72:8, 13, 14, 16 74:2, 23 98:5 104:9 108:17 110:16	commented 117:10	completely 42:4
circuit 37:7	coined 31:18	cognitive 20:22 57:5 66:1 69:9 71:24 72:8, 13, 14, 16 74:2, 23 98:5 104:9 108:17 110:16	Commenters 3:25 103:24	completion 6:25
circuitry 36:19	colleagues 55:24 64:19 65:6, 22 66:16 68:21 76:19	cognitive 20:22 57:5 66:1 69:9 71:24 72:8, 13, 14, 16 74:2, 23 98:5 104:9 108:17 110:16	Comments 3:15, 24 4:6 7:13 16:3 23:18 24:3 25:24 34:8 80:9 98:1, 22 103:21 104:21 106:4, 6 111:7, 15 123:21 129:12, 18 130:25 141:7, 20 142:8, 15	complex 43:11 64:24 68:19
citation 14:25	collected 14:4, 7 20:8 25:10 84:3	cognitive 20:22 57:5 66:1 69:9 71:24 72:8, 13, 14, 16 74:2, 23 98:5 104:9 108:17 110:16	commented 117:10	compliance 52:19, 22
cited 17:11	coined 31:18	cognitive 20:22 57:5 66:1 69:9 71:24 72:8, 13, 14, 16 74:2, 23 98:5 104:9 108:17 110:16	Commenters 3:25 103:24	compliant 43:6
clarification 40:9 116:9	colleagues 55:24 64:19 65:6, 22 66:16 68:21 76:19	cognitive 20:22 57:5 66:1 69:9 71:24 72:8, 13, 14, 16 74:2, 23 98:5 104:9 108:17 110:16	Comments 3:15, 24 4:6 7:13 16:3 23:18 24:3 25:24 34:8 80:9 98:1, 22 103:21 104:21 106:4, 6 111:7, 15 123:21 129:12, 18 130:25 141:7, 20 142:8, 15	complicated 100:10
clarified 114:24	collected 14:4, 7 20:8 25:10 84:3	cognitive 20:22 57:5 66:1 69:9 71:24 72:8, 13, 14, 16 74:2, 23 98:5 104:9 108:17 110:16	commented 117:10	complication 13:3 110:12 126:7, 9
clarify 41:3 84:10, 12 90:23 98:14 107:22	coined 31:18	cognitive 20:22 57:5 66:1 69:9 71:24 72:8, 13, 14, 16 74:2, 23 98:5 104:9 108:17 110:16	Commenters 3:25 103:24	complications 12:25 13:7, 9,
clarifying 22:1 25:18 26:8	colleagues 55:24 64:19 65:6, 22 66:16 68:21 76:19	cognitive 20:22 57:5 66:1 69:9 71:24 72:8, 13, 14, 16 74:2, 23 98:5 104:9 108:17 110:16	Comments 3:15, 24 4:6 7:13 16:3 23:18 24:3 25:24 34:8 80:9 98:1, 22 103:21 104:21 106:4, 6 111:7, 15 123:21 129:12, 18 130:25 141:7, 20 142:8, 15	
clarity 6:3	collected 14:4, 7 20:8 25:10 84:3	cognitive 20:22 57:5 66:1 69:9 71:24 72:8, 13, 14, 16 74:2, 23 98:5 104:9 108:17 110:16	commented 117:10	
clear 19:15 103:22 114:18	coined 31:18	cognitive 20:22 57:5 66:1 69:9 71:24 72:8, 13, 14, 16 74:2, 23 98:5 104:9 108:17 110:16	Commenters 3:25 103:24	
clearance 51:16	colleagues 55:24 64:19 65:6, 22 66:16 68:21 76:19	cognitive 20:22 57:5 66:1 69:9 71:24 72:8, 13, 14, 16 74:2, 23 98:5 104:9 108:17 110:16	Comments 3:15, 24 4:6 7:13 16:3 23:18 24:3 25:24 34:8 80:9 98:1, 22 103:21 104:21 106:4, 6 111:7, 15 123:21 129:12, 18 130:25 141:7, 20 142:8, 15	

21 24:17 72:23 104:6 112:4 component 39:23 114:5 119:11 124:18 components 25:4 27:10 112:10 comprehensive 19:2 29:1 42:21 69:3 comprised 27:16 comprises 42:21 compulsive 71:9 computer 8:7 102:21 concern 86:25 concerned 111:18 121:23 concerns 125:12 concise 8:6 concluded 142:25 concludes 130:13 conclusion 9:10 68:15 concur 60:14 86:4 condition 31:8 39:10, 11 57:2 118:4 conditions 30:16 31:12 36:8 42:24 139:9 conduct 116:1 conducted 28:20 conflict 6:8 conflicts 6:6, 13 7:24 congratulated 141:16 congratulating 64:2 Congress 70:17 connectors 77:18	consensus 14:9 81:2 94:18 99:12 consent 8:16, 19 consider 5:17 61:8 83:7 130:9 138:21 consideration 84:19 116:7 considerations 35:23 considered 19:9, 14 29:16 38:14 54:1 85:4 91:15 123:2 129:18 considering 35:17 91:1 121:22 consistent 44:25 46:9 47:23 63:7 120:12 consists 18:3 consultant 27:1 57:24 consulted 14:14 consulting 70:25 contaminates 46:17 CONTENTS 3:1 4:1 context 16:13 67:10 139:3 continue 111:23 112:16, 24 130:9 Continued 4:1 contraindicated 36:7 contrast 13:15 45:1 contribute 118:7 contributor 36:23 control 30:16 44:19 125:10	controlled 116:5 controls 43:19 conversation 130:17 conversations 9:3 convinced 138:4 cool 142:19 Coordinator 2:23 5:9 copy 102:18 core 73:18 74:19, 21 correct 44:13 79:13, 17 89:9 108:1 143:7 correctly 39:14, 18 correlate 140:3 correlated 45:11 53:1 correlates 50:23 correlation 50:18 51:8 53:7 corresponding 44:9 cost 120:21 counsel 72:12 73:10 78:22 counseling 78:19 couple 51:13 76:5 104:16, 21 117:1 125:8 140:1 course 24:23 49:3 50:7 55:3 57:10 110:15 134:2 courts 141:22 cover 17:13 21:13 Coverage 1:12 2:20 5:8 6:4 9:17, 25 11:18 38:8, 15 60:8, 10 72:3, 6 92:5 94:6 97:6	98:21 101:20 106:16 covered 18:19 58:17 85:6 123:15 covers 38:3 CRE 69:2 create 66:5 created 28:12 credit 95:4 critical 19:10 31:16 44:6 58:4 110:2, 5, 17 128:24 CRST 34:23 65:12 cup 35:1 59:25 63:5 cups 80:5 curious 32:16 69:12 78:10 81:9 82:3 current 18:1 26:20 28:3 29:9 57:6 81:16 96:12 112:22 118:3 currently 27:9 52:7 53:12 93:15 cycle 104:12 cycles 44:10 < D > daily 16:22, 24 17:3 25:8 30:12, 18 31:2, 22 34:19 35:3 39:20 40:1, 19 48:22 53:10 58:4, 5, 7, 16, 20 60:14 61:3 63:10 88:25 108:13 112:3 113:16 114:3 119:22 120:7, 19 122:2 124:14, 15 131:17 132:9, 13	dashboard 43:10 data 18:23 35:25 38:13 43:5, 13 45:21 46:6 66:11, 13 68:17 74:6 76:9, 11 93:4, 21 107:20 110:4 115:15 139:24 140:22 date 28:1 dates 85:25 daughter's 88:6 day 31:7 47:17, 19 48:2 52:25 54:18 142:24 143:10 days 52:23 DBS 34:3 36:1, 5 43:23 65:8, 18, 19, 24 66:4 67:9, 15 68:14 69:23 70:9 72:1 73:22 83:2 87:12, 16 88:17 90:20 deal 136:22 death 76:22 115:2 debilitated 128:19 debilitating 31:8 decades 31:18 deciding 83:5 decision 21:12 52:15 94:7 97:6 99:2 137:15 decisions 11:9 21:16 43:12 101:21 136:22 decline 20:22 72:16 118:3 declines 73:6 75:19 decrease 45:4 deep 34:3 37:8 38:5 54:21
---	--	--	--	---

64:11 67:16 71:5 73:19 deficit 79:8 deficits 132:18, 20 define 67:25 defined 98:17 defining 100:14 definitely 126:25 133:7 definition 18:5 definitions 12:9 18:13 degree 58:22 degrees 65:13 deliberates 137:5 Deliberations 3:11 22:8 99:25 demonstrated 31:25 35:13 47:18 demonstrates 46:1, 24 48:9 department 25:1 dependent 118:22 134:16, 19 depending 19:23 54:3 81:7 134:18 depends 107:15 127:8 depression 30:19 66:2 69:19 describing 111:5, 24 description 23:8 design 66:11 designation 43:15 139:19 designed 40:21 49:21 50:6 51:2, 4 67:23 105:15 designs 69:1 desirable 29:22	detail 15:25 20:25 82:10, 13 details 9:9 36:20 detected 92:10 deteriorating 50:9 determination 60:8 determine 106:19 determined 16:8 17:7 139:23 determining 106:16 detriment 105:22 developed 13:11 29:5 77:13 138:20 139:13 developing 35:7 Development 1:12 5:8 9:25 15:14 23:5 32:20 57:21 96:13 device 14:5 21:11 42:4 43:14 54:6 59:18, 20 71:7, 9 74:8, 10 75:14, 15 76:13, 25 77:1, 6, 11 84:4 92:5 97:5, 17, 21 98:24 101:19 105:24 106:1 111:17 115:19 122:9 123:15 125:6, 7, 10, 21, 25 126:1, 20 127:9, 11, 12 132:20 133:17 134:16, 19 135:18, 22 136:9, 17, 20 137:12, 25 139:18, 22 140:4	device-based 93:14 116:2 device-related 18:15 97:2 124:22 126:7, 8 Devices 1:15 5:11, 14 8:9 10:4 11:6, 9 12:2 13:10, 24 17:18 18:24 20:2 21:19, 21 27:20 28:24 34:6 35:10 37:25 41:15, 20 54:1, 3, 4 61:12 70:16 71:17 77:14 83:1, 4, 11, 14 85:21 86:19 93:10 94:4 98:16 99:17 105:1, 2, 9 108:23 112:8, 9, 20 113:9 115:6, 11 123:5 125:10, 15 127:3, 4 129:20 130:1, 2, 5 131:2, 8, 15 132:17 135:16 136:25 137:21 Dhruva 2:7 7:19 10:21 39:2, 3 40:4, 10 51:11, 12 52:12 76:3, 4 93:1 95:12 103:17, 19 106:5, 11 111:23 114:15, 17 116:8, 14 117:22 125:3, 5 139:8 140:18 diagnosis 28:3 dialing 60:1 diaries 24:4 diary 24:15, 16, 19 53:13, 14 differ 141:6 difference 18:6 31:5 49:5 66:23 76:11	92:9 115:2 135:5 differences 12:10 76:8 103:14 different 15:13 20:2 21:9 40:14 44:23 45:20 47:4 65:11, 13 66:11, 17 68:13, 23 71:11 83:1, 3, 9 84:5, 21 86:3 89:2 96:8 102:20 105:12 106:23 112:21 118:15 122:15, 19 123:4, 5, 25 125:21 126:14 127:11 129:20, 21 130:2, 3, 4 131:18 132:7 133:10, 11 differentiate 43:18, 22 44:22 98:23 117:12 differentiated 19:24 differentiation 97:20 difficult 25:16 72:4 73:13 74:12 78:12 79:5 91:13 116:1 117:11 difficulty 60:4 digestible 141:19 digital 48:18 93:13 digitography 42:25 digits 140:12 dimension 74:24 directly 8:7 16:12 23:22 139:10 Director 2:20 9:15, 17 26:22	29:3 57:12 70:13 disability 29:24 87:13 disabling 30:3, 6 disclose 6:12, 17 8:21, 22 disclosure 6:23 42:16 disclosures 27:1 70:24 discomfort 74:8, 11 76:13, 25 77:2, 7 discontinuation 41:23 discontinuing 41:18 discuss 5:10 56:23 70:19 91:19 133:20 discussed 75:13 85:8 99:22 103:16 133:4 discussing 9:8, 11 10:9 76:18 88:19 Discussion 3:12 4:3, 9 8:2 15:5 16:5 22:6 31:14 73:21 74:9 80:13, 19 83:5 93:3 96:17 100:8 109:3 130:15 136:6 141:13 discussions 5:22 Disease 1:16 5:12, 15, 25 10:4 11:7 12:4, 12, 19 13:15 17:1, 2, 8 18:17 20:14 21:21 23:14 24:12, 14 25:14 26:24 33:18 34:10, 18 36:15, 17 37:11, 13 39:8, 23 41:8 42:22, 23
---	--	---	---	--

43:2, 18, 25	distinguishing	dopamine	7, 11, 14, 17, 25	100:13 107:14
45:3, 16 47:2, 3,	98:17	12:23 47:16	103:2, 3, 5, 8, 9,	112:19 137:25
4, 6 50:2 53:2	distractions	68:3 71:18	17, 19 104:17	durations 6:2
57:10, 13, 16	8:13	dopaminergic	106:5, 8, 9, 11	47:4 112:22
58:11 64:15	distribution	12:13, 22	107:21 108:1, 7,	dwelt 45:23
65:2 66:7 67:7,	8:17, 19	dosing 68:4	8, 24, 25 109:1,	dysfunction
25 68:8, 11, 12	Doctor 56:17	dot 7:1	20, 23 110:25	72:13, 14
69:23 70:9	117:15	Dr 7:19, 20, 22	111:1, 2, 23	dyskinesia 13:4
73:7, 15, 20	doctors 55:7	10:13, 20 21:3	113:1, 11, 13, 14,	24:19 66:20
89:3 93:11	document	23:24 24:20, 23	21, 25 114:6, 10,	dyskinesias
96:6 99:18	15:25 21:1	25:18, 23 26:1,	14, 15, 17, 24	67:23 68:1
100:9 101:15	47:11 82:12	2, 5, 10, 13, 18	116:8, 14 117:2,	dysphasia 78:23
102:9 106:25	86:18 87:8, 21,	29:2, 4 31:19,	5, 6, 7, 22 119:3,	dystonia 71:8
107:7 111:19	22	20 32:3, 8, 12,	5 120:9, 10, 11	
112:6, 14	documented	19 33:10, 13	122:3 123:7, 9,	< E >
113:10, 20	136:23	35:19 38:22, 25	21 124:19	earlier 11:19
114:1, 21 115:7,	documents	39:1, 2, 3, 5, 17	125:2, 3, 5	35:20 41:1
8 118:20	13:6 14:8 15:2,	40:4, 5, 6, 8, 10,	126:21, 22	68:12 86:4
121:10, 19	4, 8 18:19 19:3	17, 24 41:6, 12,	127:13, 24, 25	124:11 139:1
126:5 134:20	43:25 88:4	24 42:7, 9, 12	128:12, 13	early 47:6
136:12, 13	doing 53:12, 15	46:23 48:14, 15	129:8, 10	54:25
137:20, 21	55:2 70:9 72:1	49:8, 16, 20	130:12 132:4	ease 80:7 121:3
138:15	119:15 131:16	51:10, 11, 12, 25	133:3, 18, 24	easily 91:16
disease-related	132:5 133:12	52:12, 16 53:20,	134:16, 18	105:4 120:25
124:12	134:8	21 54:8, 24	136:3, 5 138:7,	139:1
diseases 103:15	domain 16:9	55:15, 18, 20, 22	24 139:7, 8	east 142:20
121:16 131:4	17:6 22:12, 19	56:7, 13, 16, 19	140:15, 18, 25	eastern 80:3
142:1	23:9 81:5	57:2 58:16, 18	141:2, 24 142:7,	easy 116:6
disorder 13:13,	89:13 90:12	62:7, 19 63:16,	19, 21, 23	141:18
14 26:24 27:17	91:9, 11 97:4	17, 19, 20, 24	draft 14:17	eating 30:1
57:11 59:11	100:7 101:17	69:4, 14 70:2, 6,	dressed 119:13	35:1 48:2
61:17 71:10, 15	103:25 104:25	8 75:25 76:3, 4,	dressing 30:1	119:13
72:24 95:17	106:24 113:4	5, 17 77:22, 23	drinking 30:1	echo 119:7
disorders 14:11,	117:20 120:7	78:5, 7, 15 79:9,	drive 76:8	124:10
13, 16 18:2	121:11 124:20	13, 14, 17, 19, 20,	driven 110:7, 9	economist
33:20, 22 38:13	126:17 128:24	23, 25 80:11, 16	122:16	121:12
55:7 57:14	130:15	81:13, 22 82:24,	driver 110:14	EDT 5:3
65:1 75:11	Domains 4:3	25 83:15 84:8,	drives 110:23	education
76:23	22:9 80:25	9 85:9, 15	drug-drug 36:7	26:23 27:11, 19
disrupt 37:16	83:21, 25 90:3	86:16 87:3, 6,	drug-induced	educational
disruption	91:8, 20, 21	17, 20, 23 88:3,	13:4	28:2
39:20	94:19 96:8, 11,	18, 24 89:15	drugs 12:22	effect 30:6
disrupts 39:24	25 99:15, 19	90:2 91:18	36:6 70:15	39:25 72:17
distinction	108:11 109:16	92:11, 25 93:1,	due 36:7 48:1	73:15 78:18
127:17	116:25 118:15	23 95:3, 8, 9, 12,	80:1	effective 31:24
distinctions	123:24 132:15	25 96:5, 21	durability 58:24	32:22 106:14
137:19	141:14	98:14, 20 99:3,	durable 32:2	133:12
distinguish	dominant 60:13	4, 8, 9 100:19,	duration 19:18,	effectiveness
73:13 79:6	door 60:2	25 101:4, 7, 9,	25 46:10 56:5,	13:2 24:18
111:20		13, 22, 25 102:1,	25 60:20 83:7	31:4

effects 36:4 41:17, 19, 25 42:4, 6 57:4, 6 65:24 66:2 73:14 111:20 128:4, 9	15:3, 6 16:7, 11, 17, 19 18:9, 24 19:6 20:18 21:17 22:9 31:3 34:6 39:7 40:13, 25 41:4 64:20, 23 65:3, 19 66:8 67:9 68:13, 18, 21 80:22 81:8 83:6 84:18, 24 85:1, 6, 24 86:3, 6, 12, 22 87:1 94:2 99:16, 19 100:12 101:14, 18 103:15 105:19 106:2 111:6, 9 113:8 120:22 124:3 126:18 131:7 132:7, 22 140:7	13:12, 16 14:7 18:8 21:22 26:15 27:2, 5, 8, 12, 13, 15, 21, 24 28:6, 8, 13, 14 29:5, 14, 23 30:9, 13 31:13 32:23 33:1, 7, 9, 17 34:9, 17 36:14, 16 37:9, 14 38:1 39:15, 21 42:23 56:5, 24 57:16, 19 58:7, 10, 14 59:9 60:11, 20, 21 61:19 67:16 71:6 74:14, 21 85:23 89:21 99:19 101:24 102:10 104:14 110:19 113:10, 15 114:21 115:8 118:10 119:1 126:5 137:10 138:14	evaluation 21:19 71:21, 25 131:8 evaluations 113:9 events 17:17 20:23 41:22 125:23 128:9 everybody 79:23 80:13 113:5 118:9 125:3 142:23 everyday 29:25 119:15 133:13 everyone's 94:20, 22 Evidence 1:12 5:7, 24 9:25 10:6 21:14 22:1 23:3 24:6 32:14 34:6, 14, 15 35:25 76:20 78:8 81:16, 21 82:1 94:5, 16 96:2 141:17 evidence-based 28:17 59:11 61:18 106:12 evolve 96:19, 21 exact 126:8 examination 45:13 examine 5:13 example 25:6 45:2 47:10 60:16 66:24 67:18 88:14 89:13 117:25 125:24 130:7 139:23 Examples 13:21 excited 31:13 exclusive 135:17 Excuse 101:22 104:25 126:16 executive 72:10 exemption 71:7, 9 existing 36:8	exists 122:20 expand 130:1 expect 50:1 78:19 92:4 94:2 96:21 123:16 132:6, 8 138:19 expectation 48:20 84:2 129:14 expected 87:12 94:5 130:4 expedite 52:4 experience 22:25 23:5 33:23 41:16, 19 57:9 82:7 108:13 112:6 122:14, 15 132:9 137:2, 3 experiences 17:3 23:1 58:12 113:16 114:2 120:18 122:1 expert 5:19 10:2 17:14 18:16, 21 19:8, 12 24:7 99:24 125:17 expertise 9:20 11:5 14:15 96:7 experts 15:10, 16 27:17 explain 117:8 123:12 explaining 10:7 explicit 15:5 explicitly 113:16 138:12 exploratory 134:8 explore 52:8 expressed 19:21 extension 75:17 77:18 external 13:24 16:9, 20 17:18, 25 19:20 20:17
efficacy 13:2 33:16 34:12, 13, 17 35:11, 24 38:13 49:7 effort 60:5 eight 10:14 102:4 either 15:4 16:12 19:7 25:12 38:13, 15 76:21 77:3, 11 elaborate 90:19 electrical 37:16, 17 75:17 elevating 68:16 email 6:23, 25 7:16 101:1 emergency 50:13 emphasis 19:15 124:13 emphasized 15:3 employees 6:9 employer's 6:11 encourage 38:11 130:8 ended 117:7 endorse 28:15 endpoint 19:24 21:9 40:12 48:18 83:18 84:22 86:21 92:8 93:14 94:8 95:1, 2 97:4 99:15 100:7 105:15, 16, 17 107:11 113:23 119:15 126:16 127:10 138:9 Endpoints 3:8 5:14, 23 12:1, 8 14:10, 21, 23	engage 30:5 131:25 engagement 27:12 110:22 119:11 enjoy 64:3 142:23 entire 7:25 entirely 23:8, 15 envision 112:8 epilepsy 71:10 equal 116:23 Equally 120:5 132:16 equipment 131:21 132:24 135:16 erratic 13:5 68:1 especially 20:18 22:19 30:18 36:1 47:6 54:23 58:10 77:5 81:11 83:7 92:20 96:11 Essential 1:16 5:12, 16, 25 10:5 11:8 12:4	essentially 91:2 established 10:1, 19 82:1 85:24 97:15 estimation 39:8 ET 31:8 35:2 38:6, 9, 13 40:11 41:2, 5, 10 64:16, 22 74:23 81:3 82:17 93:10 97:5 126:11 European 19:4, 10 95:16 evaluate 31:3 35:3 59:13 60:24 61:24 132:6 evaluated 58:25 61:12 evaluating 64:21 68:18 71:17 99:17 101:19		

85:7 95:6 99:23, 24 132:24 extra 7:6 extracted 15:2 44:6 45:22 50:21 extraordinarily 119:14 extremely 100:4 103:20 104:3 106:10 109:15, 17 113:7 114:18, 20 115:13 119:20 120:3 124:23 125:6 126:1, 3, 16, 17, 23 127:1, 6 128:15, 16, 19 129:7 134:3 < F > FACC 2:7 facilitated 28:2 fact 54:14 88:22 95:15 136:19 factor 92:19 93:13 128:18, 25 135:7 factors 72:8 128:20, 22 135:11 faculty 25:1 70:12 Fahn-Tolosa- Marin 34:22 failed 29:17 fails 35:15 fairness 6:15 fall 126:13 127:19, 20 falling 48:7 falls 47:15 57:5 104:11 108:16 140:11 false 46:4 familiar 81:17 88:21	family 6:18 110:22 117:14 FAOTA 2:11 far 17:22 18:14 102:15 141:12 fashion 37:21 Fasikl 27:1 57:25 fast 44:21 FDA 43:14 52:5 67:15 71:4 94:9 139:19 feasible 116:5 features 44:6 52:17 127:21 Federal 8:24 feedback 82:4 99:25 130:22 feel 30:8 50:4 76:19 78:17 90:12 92:16 100:5 108:20 110:1, 5 119:23 122:5 139:11 140:6 feeling 96:15 97:13 142:11 fees 6:21 fell 16:9 felt 108:11 119:19 field 94:21 130:10 file 15:25 131:14 143:4 files 143:8 Final 4:9 48:4 109:18 finalized 60:8 finally 31:23 financial 6:11, 12, 19, 22 find 17:10 77:10 81:14 findings 15:23 Findlay 58:19 59:2, 6, 12, 23 60:17, 23 61:8,	13 62:12, 22 63:10 finger 44:5, 15 46:19 138:3 fingers 44:23, 24 45:24 finish 48:4 finished 21:23 49:25 firing 37:16, 17, 21 firm 76:20 first 7:15 9:18 12:20 14:17 20:19 21:8 26:1 34:5 49:25 52:22 76:1, 17 83:11 84:16 90:8 97:8, 10 99:13 101:13 103:1 108:2 118:16 130:23 first-line 29:17 fit 77:16 fits 70:10 83:9, 21 86:5, 25 five 15:1, 8 34:4 44:1 69:8 100:3 101:17 102:4 103:9, 20 106:9 108:9 109:4, 10, 18, 25 112:1 113:6 114:17 119:6, 17, 18 120:11 122:4 123:6 124:23 125:5 126:23 127:15, 25 129:10 flexible 66:10 69:1 Florida 57:14 fluctuate 105:7 fluctuation 47:25 fluctuations 13:1 24:18 47:19 54:17, 18 focal 92:14	focus 11:22 12:5 15:6 33:19 34:13 36:21 58:11 93:9 108:14 112:5, 12 121:9 122:13 128:10 focused 17:12 20:8 27:14 29:12 34:2 37:7 38:4 90:3 focusing 65:3 85:1 104:7 121:25 folder 16:3 folks 33:13 follow 43:24 53:21 97:23 following 6:5 8:3 15:22 84:9 99:15 125:14 128:9 follows 16:5 followup 19:22, 25 20:1 41:14 97:16 100:13 104:23, 24 105:5 112:22 115:15 130:16 follow-up 6:2 19:18 112:23 121:1 font 16:16, 18 footing 116:23 foregoing 143:6 foregoing- entitled 143:5 form 6:24 94:6 formal 6:19 forms 12:25 forth 141:17 fortunate 95:14 forum 9:4 forward 22:2 34:2 112:18 found 18:13 21:1 60:18, 24 82:18 89:16 142:3, 7, 15	Foundation 26:15 27:4, 6 28:15 42:24 founded 27:6 founder 42:17 four 18:3 53:4 71:16 89:23 102:3 109:1, 10, 23, 24 110:10 117:8, 9 123:11 128:14 fourth 108:4 frail 126:3, 4 frailty 126:11 Francisco 39:4 51:13 frequency 44:21 45:22 46:9, 13 86:23 frequently 17:11, 24 48:21 62:13 75:13 89:12, 20 90:1, 7 113:22 friendly 62:22 front 22:15 FTM 65:12 74:15 FTM-TRS 32:14 34:21 full 44:20 65:17 82:10 86:18 87:8, 9 143:7 function 12:15 16:25 20:21 23:20 25:4 47:12 54:5 58:4 72:10, 16 73:5, 8 78:10, 22 87:11 88:16, 25 98:2, 5, 6 104:9, 10 107:4 108:15, 17 110:16 133:15 134:4 140:7 functional 23:1 35:16 47:13 48:6 56:4 57:1
---	--	---	--	---

58:24 70:13	giving 8:16, 18	Goldsmith 2:15	90:17, 25 91:6	122:24 135:12,
134:13 135:24	67:21 70:18	7:21 109:21, 22	97:24 99:9	24 136:21
function-focused	75:22 96:16	122:3, 4 128:12	123:11 129:23	harder 107:18
134:1	108:21 128:25	133:22	132:4 141:2	118:14
function-related	glad 82:8	GOLDSTEIN	guests 5:6	hardware
133:10	120:5	92:11 128:13	guidance 5:19	75:16 77:20
functions 66:1	glaring 123:6	134:18	10:2, 17 13:6	Hauser 53:13
119:23 120:24	Global 61:5	Good 5:4 9:16	14:8 15:2	head 53:12
139:11	107:3 108:2, 14	11:16 23:6	18:18 19:3	77:4, 20
funding 71:1	112:2	26:13 32:15	guide 92:5	heading 88:9
further 83:5	go 10:11 11:23	33:13 36:11	94:13	health 8:23
143:6	22:2, 5 25:25	70:8 78:4 81:3,	guided 37:6	16:10 21:6
FUS 34:2 36:1,	26:17 30:21	5 106:6	38:4 43:4	22:17 35:9
5	33:11 38:20	government	guideline 29:6	38:7 42:17, 20
future 10:23	42:11 48:13	6:9 8:25	guidelines	81:4 97:1 98:2
11:2	49:16 55:20	grade 112:1	14:12 18:20	101:16 103:25
< G >	59:3 63:20	grades 72:22	19:4, 10, 13	109:13 117:16,
gait 20:20	64:16 66:15	granted 29:25	28:12, 13, 15, 18,	19
23:20 25:6	80:3 96:4 98:9	35:1	22 35:8, 19	healthcare 43:8,
35:23 47:14	99:1, 13 103:10,	grants 6:21	36:9 52:8 59:8	10
104:9 107:4	11 123:4 132:1	27:22	62:18 95:15, 17	healthy 20:12
108:15 120:23	135:19	granular 134:13	guys 138:21	44:19
gap 34:9	goal 13:18	granularity	< H >	hear 10:24
Gasparotti	30:8 132:13	65:14 67:5	half 46:22	26:6 98:11
143:3	goes 100:25	92:4	Hall 2:24 3:5	104:8 139:10
gathering	117:25 140:25	graphs 140:1	5:4, 7 11:12	heard 34:18
117:18	going 10:6	gray 14:3	25:25 26:4, 12	56:2 57:23
general 16:25	11:5, 19 14:2	great 22:4	31:19 46:21	58:3 71:4, 19,
33:4 73:25	15:22 22:10	26:2 33:10	56:11, 17 63:22	22 74:15 80:20
81:2 83:20, 21	25:25 32:8	42:8 49:9	80:10 100:17,	81:10 84:18
140:5	34:2 36:19	56:13 83:15	23 101:2	85:3 93:13
generalizability	37:23 54:9	96:22 109:20	102:16, 22	97:19 105:3, 13
20:7	66:19 67:18	113:1 117:5	103:7 114:13	109:2 124:10
generally 41:18	70:21 74:16	120:9 123:7	hand 9:3	139:17
94:21	78:5, 24 83:25	127:24 129:8	54:16 60:13	hearing 90:13,
generated 94:6	84:10 88:13	130:12 140:19	handful 18:9	19 91:5 142:16
generator 75:18	93:19 96:19	141:17 142:11	87:16	heed 9:2
genesis 36:23	100:2 102:3, 8	greatest 21:17	handle 52:15	held 8:14
getting 56:11	103:10 106:17	22:10	74:4	26:21
96:9 115:15	110:15 112:18	green 45:24	hands 94:22	Helen 3:19
117:3 120:23	113:5 115:18	47:22	handy 16:4	42:12
133:9	117:22 118:6,	Group 2:20	happen 66:3	help 6:2 7:9
give 11:5	10 120:16	9:18 27:8 81:3,	happening 25:5	8:8 11:8 28:4
21:24 64:13	122:10 125:11,	5 95:1 96:18	happens 94:11	51:5 55:10
67:18 81:16	20, 23 126:18	98:21 99:10	happy 38:17	72:11 90:23
120:15	132:17, 25	109:6 130:21	48:17 62:5	96:18 131:3
gives 89:4	135:3, 4, 10	131:1	83:16 119:9	132:2, 25 133:1
121:12	137:16 138:8	groups 28:3	hard 118:1, 8,	135:21 140:16
	139:20 142:1	guess 32:19	11 119:24	helpful 17:15
		38:19 84:16		19:18 34:8

55:1 63:14 81:15 87:25 96:18 104:8, 18, 20, 22 105:10 106:7, 15, 17, 21 107:19 108:7 110:25 111:4, 16 112:16 113:2 115:14 119:4 142:8 helps 104:19 105:19 hemorrhage 75:15 heterogeneity 125:20 126:17 Hi 55:22 126:22 hierarchy 123:14 high 44:20 46:9 53:6, 17 67:17 119:2 123:10 higher 57:3, 7 73:24 108:11 117:20 highlight 34:5 58:2, 19 64:24 66:19, 22 67:14, 19 68:13 highlighted 57:2 65:6, 10 66:13 highlighting 65:16 66:21 highly 108:20 Hill 53:23 77:24 HIPAA 43:6 history 69:20 85:2 hits 16:20 Hoehn 72:22 hold 97:25 holding 35:1 59:25 86:11 holistic 105:24 Holly 29:2	home 48:21 53:13 119:12 homes 30:4 honestly 109:2 134:15 hope 40:2, 23 51:8 68:24 142:17 hopefully 11:1 55:6 hoping 52:5 hospice 137:4, 7, 8, 11, 13 huge 110:14 134:10 135:7 humanitarian 71:7, 8 hundred 52:23 hypophonia 78:23 < I > ID 100:21, 24 idea 83:20, 21, 24 ideal 5:23 125:16 ideally 115:17 123:23 125:13 identifiable 8:20 identified 17:16 18:9 19:6 46:3 64:23 65:22 81:1, 25 89:19 99:20 100:13 125:11, 18 identify 12:1, 7, 8 68:17 identifying 64:20 91:7 IETF 26:15, 19 27:7, 9 35:19 36:9 III 43:20, 21 50:20, 24 51:3, 7, 8 55:8 65:25 71:20 imagine 131:21 immediate 6:18	impact 31:11 32:24 33:20 35:22 65:7, 18 68:13 69:9 91:17 111:18 112:17 115:10 116:19 135:3 impacting 115:6, 9 impacts 106:3 119:22 124:1, 7 129:21 134:5 impair 60:12 impaired 12:15 impairment 23:2 47:8 53:9 57:5 implantable 84:6 97:21 125:15 127:3, 5 131:17 135:18 implantables 98:18 127:17 128:8 137:22 implantation 128:10 implanted 64:11 71:17 105:1, 2, 9 112:20 115:19 125:25 implants 64:8 implement 35:15 36:5 implementable 86:13 implication 15:4 implied 15:7 importance 21:18 22:10 30:20 64:19 96:10, 11, 16 97:15 104:9 108:11 116:3, 4 119:7 120:15, 18 127:16 importances 100:6 important 16:8 17:7 18:6 19:7,	11, 13, 14 20:18 26:16 31:2 33:2 35:24 49:4 52:17 56:2, 23 58:21 65:8, 17 81:6 83:6, 22 84:1 87:1 90:4 91:12, 14, 19 92:9, 19, 22 94:19 97:4, 12 98:7, 8, 24 99:7 100:4 101:14, 20 103:20 104:3, 5, 6, 25 105:1, 18, 23 106:10, 12, 22 107:1, 6 108:6, 20 109:11, 15, 17 110:3 112:1 113:7 114:18, 20 115:5, 14, 17, 22 116:7, 13, 18, 22 117:14 118:18 119:14, 17, 20 120:3, 5, 8 122:13 123:1 124:2, 23, 24 125:6 126:2, 16, 17, 23, 24 127:1, 6, 7 128:10, 15, 16, 17 129:7, 11 132:16 136:23 138:1 impossible 30:2 impressed 93:2 Impression 61:5 85:17 improve 13:19 30:11, 12 32:1 40:21 47:21 73:12 78:21 79:3, 11 87:13 105:15 121:25 123:24 137:16 140:22 improved 47:18 61:1, 2 121:20 122:18 140:23	improvement 35:14, 16 48:6 50:22, 23 54:3 58:22, 23, 24 121:10 136:14 improves 76:14 improving 121:18 inability 30:17 inadequate 35:16 inclination 109:17 136:15 include 12:16 13:22 35:25 65:25 68:25 69:18 107:24 114:2 included 14:21 15:12 29:12 43:16 99:22 114:8 119:9 124:16 includes 6:21 20:12 27:9 104:1 including 7:25 9:5, 22 13:20 27:10 42:14 43:3 53:14 57:22, 25 61:15 66:1, 18 104:2 incorporate 111:9 133:5 incorporated 15:19 incorporation 65:14 increase 30:10 56:4 76:21 increased 56:3, 25 57:4 78:25 115:1 incredible 136:14 independence 30:10 independent 10:2
--	---	--	--	--

index 44:5 45:23	instrument 12:10 16:13 17:23 85:8	interpret 90:19 114:1	Isaacson 3:20 55:22, 23 56:7, 16, 19 62:7, 19 63:17, 19 85:9 133:24	< K >
indicate 100:5	instruments 6:2 12:7 18:11, 13 23:10 34:20 35:4 81:18 82:17, 19 85:12 86:7 89:2 137:2 142:5	interrelated 136:1	Isaacson's 88:24	Kansas 26:25
indicated 29:21	insufficient 20:15	interrupt 56:8	isolated 30:4	keen 30:20
indication 38:15 85:22	insurance 72:3, 6	interrupts 40:18	isolation 30:17	keep 16:4 26:2, 3, 4
indications 71:5	insure 7:12	interspersed 45:18	issue 19:21 96:19	Kelli 29:4
individual 44:3 140:2	insurers 37:24	intervals 62:1	issues 75:18 77:19 78:3, 25 126:14 138:1	Kelly 3:17 26:1, 18
individually 102:6	integers 51:4	intervene 50:6	item 113:18	key 15:23 34:16 45:4, 5 91:7 120:25
individuals 80:8	intend 73:11	intervening 54:6	items 33:3 35:8 122:25	Khemani 3:18 33:13, 21 38:22, 25 39:5, 17 40:8, 17 41:6, 12, 24 42:9 54:24
individual's 131:19	intended 66:4 132:21	intervention 79:16 81:7 83:23 118:24 140:17, 21	its 9:10 36:3 97:14	kind 13:3 39:9 81:19 84:1 94:22 96:9 107:2, 11 110:24 141:3
Industry 2:17 84:11	intensity 93:4, 8	interventions 33:25 35:18 54:22 79:10 91:15 96:13 106:13 121:25	IV 66:1 72:23	kids 101:8
infection 75:14	intensive 74:24, 25	invasive 35:17 41:15 88:12 127:3, 5 129:14 130:7	< J >	Kimmel 64:9
influence 122:8	interactions 36:7	intracranial 75:15	January 14:2	kind 13:3 39:9 81:19 84:1 94:22 96:9 107:2, 11 110:24 141:3
influenced 115:5	interest 5:16 6:6, 8, 13, 15, 19 7:24 71:2 135:6	introduction 6:14	JD 2:21	kinds 12:14 23:22
inform 35:5 97:6 106:13	interested 29:19 53:24 88:18 136:8 138:2	introductions 6:14	Jensen 2:21 3:5 9:14, 16, 17 49:18 142:12	know 9:24 24:9 25:11 29:23 39:16 49:6 50:5 51:3 54:23 55:8, 13 65:18 66:16 69:15 73:5, 7 74:20 78:7 82:3, 14 83:6, 12, 18 85:23, 25 88:10 89:12 90:17, 22 91:11 92:15, 21, 23 93:5, 13, 21 94:7, 20 95:10 96:5 98:12, 21 101:12 104:10, 14, 17 105:11, 12, 14, 23 106:14, 18 108:22 109:7 110:2, 17 115:5, 10, 17 116:2, 4 118:13 119:21,
information 8:20, 23 11:21 16:15 19:18 20:15 25:10 26:16 29:9 38:10 76:7 82:23 84:3, 14 85:13 95:7 101:3 105:20 106:15 107:1 117:18	interesting 48:18 54:10 75:24 89:16, 24 92:12 93:24 142:3, 16	investigations 115:23	Joe 3:6, 13 4:4, 7, 10 21:4 69:7 86:3 91:18	
inform 35:5 97:6 106:13	interests 6:11	investing 106:16	join 55:24 83:17	
information 8:20, 23 11:21 16:15 19:18 20:15 25:10 26:16 29:9 38:10 76:7 82:23 84:3, 14 85:13 95:7 101:3 105:20 106:15 107:1 117:18	interference 49:15	involuntary 13:5 45:19 68:1	joined 80:23	
informed 43:7	intermediate 37:3	involved 15:14 26:19 57:20 92:16	joining 70:7	
informing 7:8	internally 63:7	involves 12:12 13:4	joint 70:15	
in-person 45:13 49:22	International 26:14 27:5 28:14	involving 27:23	Joseph 2:4 7:22 10:13	
input 15:18 23:12 99:22		IRB 52:8	Joshua 3:22 70:12	
inserting 60:2		Irene 2:10 7:20 82:25 85:20 101:9 121:7	journals 67:17	
insertional 72:17 73:14		irreversible 42:6	joy 110:23	
instability 104:10		irritation 42:1 128:6	judge 142:4	
instance 23:13 73:4 87:10 92:1			juggling 96:10	
instructions 100:20			July 143:10	
			jump 138:16 142:11	
			June 1:20 5:3	
			justification 103:13	

24 120:21 121:16, 23 122:4, 6, 9, 11, 16, 21 123:3, 6 124:9 125:22 127:19, 22 128:2, 20 130:9 131:5, 22 132:14 133:2, 9, 11 134:7 135:1, 2, 6, 25 136:11 137:1, 10, 25 138:3, 15 139:14 140:5, 8, 12 142:6, 10 knowing 81:20 107:16 138:4 known 36:2 65:25 128:7	121:12 126:13 learned 82:3 leave 38:23 48:12 leaving 57:7 left 46:22 50:11 70:6 left-hand 17:17 Lesioning 37:6 letter 60:3 63:4 131:12 level 55:13 96:15 135:6 lever 45:8 levers 44:4, 20 levodopa 12:21 LeWitt 58:18 life 17:6 24:11 30:13 32:25 33:4 53:1, 3 66:20 68:10 72:18 91:23 92:21 98:3 110:20, 23 113:19 114:2, 8 115:7, 9 116:11, 16, 17, 20, 22 118:7, 20 119:1, 25 121:13, 15, 17, 21, 24 122:1, 10, 24 123:22 124:12 134:5, 11 135:4 137:16 140:9 141:1 lifespan 31:10 light 139:6 likeness 8:17 likes 95:1, 2 limb 59:22 limbic 69:18 limit 8:13 limitation 34:24 limiting 77:11 128:18, 25 limits 7:4 line 12:20 102:2, 3 lines 45:25	list 14:22 16:20 25:15 72:12 85:12 listed 19:13 89:5 109:16 113:17 118:19 listening 48:8 lists 86:19 literature 5:19 14:1, 3 17:3, 24 22:21 28:21 29:1 67:13, 15 69:14 81:17 99:21 112:25 little 10:12 48:19 60:5 65:3 74:6 79:5 80:2, 25 96:15 99:10 107:10 117:9 118:17 127:7 129:24 134:1, 2 141:9, 25 live 58:6 lives 33:21 63:10 119:15 living 16:22, 24 17:3 25:8 30:12, 18 31:2, 22 34:19 35:3 39:20 40:1, 19 53:10 58:7, 20 60:14 108:13 112:3 113:16 114:3 120:7, 19 122:2 124:15, 16 132:9 loan 128:14 logged 102:16 long 106:4, 6 107:14 112:13 longer 45:6 56:5, 25 105:6 125:14 long-term 12:23 35:25 41:14 58:23 68:3 69:21 104:24	look 34:12 36:12 40:22 43:9 71:21, 23 72:7, 21 73:9, 23 74:3, 14, 20 75:3, 9 77:1 78:15, 16, 25 85:21 88:16 89:18 108:22 129:19 133:10 134:25 looked 41:11 68:9 85:12 88:12 134:14 looking 21:15 31:14 54:12 74:6, 18 87:11 88:5 89:16 93:20 107:14 111:6 132:12 looks 102:14 103:5 125:2 loomed 116:17 loss 12:13 lost 101:8 lot 30:15 42:3 49:11 54:10 60:5 67:5 70:21 92:3 125:18, 20 133:24 134:12, 21 135:8, 12 137:1, 3, 10 138:1, 18 139:14 lots 105:12 126:13 loud 98:25 love 75:5 lower 44:13 45:1 107:10 118:7, 17 120:4 127:7 lucky 52:3 Lyons 3:17 26:1, 10, 13, 18 31:19, 20 32:3, 8, 19 35:19 57:2 58:16	< M > MA 2:11, 15 main 56:23 72:7, 18 82:12 122:2 128:1 maintain 58:5, 6 63:6 maintains 38:7 major 27:3 50:1 majority 10:15 22:16 81:25 88:11 making 6:16 21:12, 15 42:9 52:15 55:16 63:17 70:4 77:4 79:21 93:21 98:15 106:14 122:6 141:22 malfunction 75:17 Manage 1:15 5:15, 24 38:8 94:4 99:17 131:3 management 5:11 12:3 14:12 27:24 31:4 35:12 37:25 42:20, 22 43:11 51:21 61:12 64:15 managing 10:4 11:7 65:9 manifestations 69:17, 18 mantra 141:1 March 100:1 mark 45:25 markers 75:6, 9 market 11:7 Maryland 1:24 matched 43:19 82:6 material 103:23
--	---	--	--	---

materials 16:3 22:14 24:1 74:10	77:2 79:1, 4 82:2 86:9 91:13 97:12, 13 112:16 114:8 121:19 123:22 124:6 132:9	medical 12:2 26:25 27:15 29:3 57:3 64:5, 10 83:1, 4, 10 97:5 98:16 99:17 101:19 112:8 113:9 115:11 126:19	58:16 67:8 69:7 85:7 89:7 107:25 113:17 117:23	mobility 44:2 45:17 47:21 50:18, 22, 25 53:7
matter 15:10, 15 135:1 143:6	measured 16:12 17:8 23:22 61:3 91:16 98:4 123:3, 15 139:1	MEDICARE 1:11, 12, 22 5:7 9:24 20:4 21:13, 14 38:3 56:1, 22 60:7, 11 95:20 104:7 137:3 141:4	messaging 102:21	MoCA 90:15
matters 6:10 111:8	measurement 6:1 66:12 67:6	medicate 50:11	met 16:17	modalities 71:11
Mauri 2:18 7:23 40:5, 6, 7, 24 84:8, 9 85:15 95:3, 9 99:8 111:1, 2 117:2 123:7, 9 129:8, 10 138:24	measurements 123:5 134:1	medication 12:3 43:23 47:12, 16, 18 50:19, 20	methods 66:13 130:6	model 10:20 46:1
MCID 18:14 82:6, 8 97:15 100:14 104:18, 22 115:13	measures 18:22 20:20 22:11 23:4, 8 24:2 32:15, 22 43:1 44:11, 12 46:14 59:23 65:14 66:18 68:24 71:16 72:22 73:3, 4, 19 74:3 75:10, 16 77:25 78:8 81:4, 25 88:19 90:4, 5 91:20 94:19, 23 96:6 113:21 116:13 120:17 121:4, 9, 14 130:16 133:3, 8, 16 138:11, 12, 14, 17, 25 139:5, 13, 15 142:1	medicine 21:5 68:23	metric 50:24 54:20	moderate 61:1
MCIDs 81:16 82:1, 13 130:16	measuring 33:9 78:9 120:22	meds 135:10	metrics 43:7, 20 45:22 46:14, 25 47:11 51:1, 6	modern 74:16
McKesson 6:24 7:16	mechanical 75:18	Medtronic 40:7 64:5, 6, 12, 18 68:16	MHS 2:4, 7	modified 59:24 62:25 72:21
m-c-k-e-s-s-o-n 7:2	medication 112:13	meet 63:18	mic 8:7	modulate 37:21
MD 2:4, 7, 10, 18 3:6, 18, 19, 20, 21, 22 4:4, 7, 10	measuring 33:9 78:9 120:22	meeting 5:2, 7 6:7 7:19 8:3, 14, 18, 22 9:4, 5, 9, 12, 14 11:22 15:18 16:2 21:5 22:3 24:2 75:24 100:2 142:25	mid 95:19	modulating 37:7
MDS-MMS 78:9	mechanical 75:18	Member 4:6 6:11, 17 25:1 98:12 100:5	middle 44:5 45:24	money 106:17
MDS-UPDRS 50:23 66:23 67:3 78:8	MEDCAC 2:9, 23 5:6, 13, 17, 22 9:19, 22 10:1, 8, 14, 15, 18 35:9 61:8 64:2 69:2	Members 2:9 5:6, 22 7:18, 22 8:1 9:2 21:25 22:6 24:21 25:19 39:2 76:2 80:20 141:21	mild 61:1	monitor 49:24 55:2 94:4 127:10
mean 16:11 20:9 54:13, 24 69:12 91:6 115:4 122:23 132:12 133:13, 22 134:6 135:10, 23	measuring 33:9 78:9 120:22	mention 115:21	milk 59:25	monitored 48:21 94:12
meaning 78:18	mechanical 75:18	mentioned 29:11 39:6	million 27:25	monitoring 42:21 47:24 49:14, 25 52:18, 21 93:18 111:19
meaningful 12:9 47:13	MEDCAC 2:9, 23 5:6, 13, 17, 22 9:19, 22 10:1, 8, 14, 15, 18 35:9 61:8 64:2 69:2		mindful 127:20	Montana 142:21
measurable 110:4 123:19	measuring 33:9 78:9 120:22		minimal 18:5 50:21	month 105:6
measure 18:11 32:18 43:9 48:3, 20 61:9 74:12, 19, 21	measuring 33:9 78:9 120:22		minimally 49:4 58:22 66:10 68:25 92:8	monthly 48:23

47:11 53:9 54:18 58:12 64:21 66:5 68:19 69:17 71:19 72:22 88:10 89:23 98:4 104:4 107:4, 23 108:2, 4, 14, 18 110:12 112:2, 3, 4 motor-related 107:5, 24 108:12 124:15 132:15, 20 Mountains 142:20 mouse 36:24 mouths 133:2 move 28:10 46:25 55:13 80:5 85:19 96:3 109:4, 18 113:3 moved 137:7 141:8 movement 12:16 13:14 14:15 18:2 26:24 27:17 33:22 44:6, 12, 15, 21 45:7, 18, 19 57:11, 13 59:10 64:25 65:8, 9 71:15 72:24 75:10 76:22 95:17 movements 13:5 61:17 68:2 moves 110:8 moving 99:10 137:7 140:12 MRI 37:6 38:4 MSc 2:18 multi 126:10 multiple 27:10, 18 67:9 muscle 12:16 134:8	mute 8:9 49:16 mutually 135:17 myriad 134:15 < N > name 8:5, 17 11:16 15:25 21:4 24:24 42:12 143:10 national 6:3 38:8 natural 69:20 118:3 nature 48:25 navigate 94:25 near 11:2 nearly 30:2 necessarily 23:11 55:8 73:4, 12 129:15 140:11 necessary 21:13 66:9 need 31:23 55:4 56:4 57:1 61:24 63:3, 6 65:2, 16, 23 67:9 68:20 84:21 109:5 137:15 141:11 needing 107:10 136:17 needs 123:14 128:22 131:20 negative 106:2 nerves 59:20 neurological 31:12 70:17, 18 neurologist 14:15, 17 15:14 33:22 57:12 neurologists 15:13 55:7 82:5 97:9 99:23 neurology 26:22 28:12 29:11 33:23 42:15 59:8	61:19 64:9 95:16 neuromodulation 59:16 64:6 71:3 neurons 12:14 neurophysiology 36:13 neuropsych 90:14, 21 neuropsychological 69:24 neuropsychology 76:19 neurostimulation 71:12 neurosurgeon 15:12 82:5 99:23 neurosurgeons 95:6 neurosurgery 64:9 70:13 neutral 106:3 nevertheless 66:7 new 28:19, 22 31:23 83:19 112:18 115:18 139:5 Newman 2:11 7:20 24:22, 25 25:17 89:6, 11 90:11 108:8, 9 119:5, 6 127:13, 14 131:11 132:11 133:6 135:14 nice 51:8 54:19 142:22 nicely 47:5 nine 102:4 noises 8:13 non 84:6 non-implantable 97:21 128:3	non-implantables 98:19 noninvasive 37:19 41:16, 20 55:1 125:9 129:16 noninvasively 59:20 non-motor 12:18 13:16 40:20 41:9, 10 72:23, 25 non-movement 55:6 nonpharmacologic 13:10, 18 nonpharmacological 13:22 nonprofit 27:6 Nonvoting 7:21, 25 normal 47:22 normally 17:13 North 53:22 77:24 Northwestern 70:14 note 90:8 92:18 111:13 124:14 noted 35:7, 22 59:7 66:20 111:16 notice 82:16 85:8 noticeable 45:3 noticed 24:15 noting 60:9 November 43:15 52:3 nuance 135:23 nuances 67:6 134:21 nucleus 37:3 71:13 nudge 54:16 number 11:23 18:20 95:14	98:21 102:22 106:24 126:23 numbers 123:9 numerous 7:4 nutritional 110:21 < O > objective 11:25 12:6 43:1 104:1 107:20 110:4 117:21 observable 25:6 observations 23:19 observe 49:5 observed 113:22 obsessive 71:9 obtained 93:4 obviously 21:20 23:20 84:5 93:9 94:7 115:3, 7 116:18, 19 125:20, 22 128:23, 24 134:6 occupational 25:2 29:4 131:1, 13, 24 occur 13:16 20:22 occurs 13:14 68:4 offer 10:1 91:24 138:16 139:3 offers 67:5 offhand 24:9 office 25:5 67:2 officer 64:5 oftentimes 116:1 126:3, 7 139:15 oh 24:10 53:22 84:8 101:25 116:14 132:19 135:19 141:23 Okay 22:3 24:20 25:17, 19
--	---	---	---	--

26:5, 13 31:20 42:8 48:14 55:15 56:13, 19 63:17 70:3 79:19, 25 80:11, 16 85:15 88:8 89:25 90:1, 2 96:4 99:7, 9, 11 100:19 101:4 102:11 108:24 113:2, 25 114:10 124:19 125:2 126:21 128:12 133:7, 18 136:18 141:7 old 43:20 older 20:9, 12, 19 95:23 99:18 104:7 118:5 126:2, 10 141:5 once 96:5 102:22 137:19 ones 62:17 89:11 107:9 108:6 112:15 one-year 75:4 ongoing 27:23 28:4, 5 on-off 71:21 onset 60:19 Open 3:24 4:3, 9 7:13 9:4 32:5 48:15 80:12, 18 97:25 112:11 141:10 Opening 3:4 opinion 108:19 opinions 19:21 opportunities 93:17 opportunity 7:15 21:24 28:9 33:15 38:17 55:23 56:20 62:5 64:1, 13 70:19 75:23 80:19 93:20 130:8 139:10	opposed 26:8 48:22 50:8 84:23 131:4 optimization 35:5 optimized 50:8 option 129:6 options 27:19 28:19 29:13, 15 31:24 57:8 129:19 oral 60:22 order 5:2 103:11 132:25 133:1 organization 26:20 27:7 organizations 19:4 organized 107:3 oriented 25:4 133:16 original 19:14 OTD 2:11 OTR/L 2:11 Ott 29:4 outcome 52:19, 22 61:9 69:11 72:19 73:2, 18 75:12 77:2, 25 79:1 101:16 115:4 117:19 118:2 120:1 132:22 outcomes 16:10 17:5, 11, 14 18:12, 15 19:9, 12 22:17, 18, 23 31:1 34:5, 12, 13, 15, 16 35:3, 10, 11, 21 47:14 51:23 52:13, 14 53:8 64:21 65:15, 17 68:19 69:9, 24 71:17 73:17 75:4, 6, 10 78:4, 16, 17 79:11 81:4, 6 91:22 97:1, 23 103:25 104:3	106:19 109:13, 15 113:4 115:20, 24 117:13 119:8 133:11 140:14, 22, 24 outlined 22:15 128:23 outside 50:7 89:13 overall 43:21 47:17 50:24 51:5 73:23 111:11 113:18 116:19 121:13, 15, 21, 23 122:1 126:1, 15 141:1 overarchingly 122:11 overflowing 50:15 overlap 40:13 41:9 overlooked 31:11 overtaken 45:19 owns 6:18 < P > p.m 142:25 package 107:3 packet 48:10 Page 3:2 96:18 paid 137:24 pain 92:16 paired 18:5 Panel 4:3, 6, 9 5:1, 13, 17, 22 7:14, 17, 21, 25 9:6, 19 10:8 38:11 42:14 44:8, 13, 18 45:2 48:16 61:8 80:12, 18, 19 85:4 99:25 100:5 102:12 114:11 124:25 141:21 142:14 Panelists 2:1	panels 45:21 panel's 81:20 paper 53:6 papers 49:3 Parkinson 121:19 Parkinson's 1:15 5:12, 15, 25 6:20 10:4 11:7 12:4, 12 13:8, 15, 21 14:6 17:2, 22 18:17 21:21 22:16 23:14 24:11, 13 25:14 26:23 27:3 33:3, 18 34:10, 18 36:15, 17 37:11, 13 39:8, 22 41:8 42:22 43:2, 18, 25 45:3, 16 47:3, 6 50:2 53:2 57:10, 13, 15, 19 58:9, 11 64:15 65:1, 4 67:7, 24 68:7, 11, 12 69:23 70:9 71:6 73:7, 20 74:19 89:3, 13 93:10 99:18 101:15, 23 102:9 106:25 107:7 110:18 112:6, 14 113:10, 19 114:1, 21 115:8 116:15 118:4, 9, 20, 24 121:10 124:11 126:5 134:20 137:9 138:15 part 6:7 31:13 32:15, 20 49:6 52:7 58:12 71:24 72:25 73:18 76:24 84:3 89:3 92:10 94:3, 10 110:20 113:8	116:24 124:16 132:23 134:10 136:6 141:10 partially 109:24 participate 8:1 participated 142:14 participating 6:9 9:21 particular 10:7 21:19 62:15 67:19 87:2 97:11, 13 98:6 105:21 114:23 115:19 particularly 41:7 56:1, 23 65:1, 15 67:25 82:4 90:20 108:13 119:21 130:19 parts 18:3 passed 136:21 path 137:21 pathophysiology 138:11 Patient 2:14 20:16 22:25 23:5, 15, 18 24:10, 12, 14 25:8, 9, 13 27:8 31:6 49:23 50:5, 14 53:14 55:12 61:5 63:9 92:21 93:8 104:2 105:25 109:14 110:6, 7, 9 111:10 115:24 117:18 121:5 122:17 125:24 126:25 129:6 135:5 136:15 137:17 138:4 139:2, 11 140:3, 22 patient-reported 16:15 17:5 22:18 23:12 31:1 51:22
---	--	--	---	---

53:8 65:16 66:18 72:19 81:6 91:22 97:1 113:4 117:13 119:8 120:13, 16 133:11 patients 5:12 13:8 27:13 28:5 29:6, 16 30:2 33:21 34:24 36:8 38:9 40:15 48:20 56:1, 22 57:10, 15, 17 59:13 60:3, 25 61:2 62:23 63:1 64:11, 15, 21, 25 67:6, 20, 24 68:7, 10, 19 69:22 71:25 72:12 73:6, 11, 22, 24 78:13, 19, 22 86:10 88:25 108:22 111:9 112:5 115:6 118:5 122:7 123:2, 17 124:6 136:7 140:2, 6, 8 patient's 49:24 53:11, 18 114:19 115:9 117:3, 13 118:2 134:23 136:15 pattern 59:19 Paul 143:3 pay 137:23 payment 137:5 PD 38:2, 6, 9, 14 39:16 40:11, 19 41:2, 5, 10 64:22 73:24 74:7 75:1, 3 79:6 81:2 85:22 97:5 104:4 PD/ET 16:1	PDQ-39 66:21 72:19 114:6 119:10 peak 68:4 people 21:7 23:25 28:22 29:14, 20 30:3, 6, 13 31:9 41:19 47:3 48:22 52:20, 24 56:10 62:8 63:2 64:7 77:2, 6, 9, 18 79:7 80:4 81:9 100:15 119:12 121:16 128:6 129:3, 22 131:9, 16 137:6, 8 141:8 peoples 58:5 percent 46:4, 5, 12 52:23, 24, 25 57:17 60:22, 24 61:2 percentage 20:12 perception 53:11, 14, 19 perform 30:11, 17 31:6 34:24 60:13 132:2 performance 44:14, 24 49:24 54:18 72:9 75:16 performed 29:2 61:10 75:2 115:23 performing 45:17 132:13 performs 43:3 period 85:24 97:16 121:1 peripheral 34:1 37:20 57:22 59:19 periprocedural 76:16 77:1 115:20 125:23	permanently 105:2 125:24 persistence 41:17, 22, 24 person 10:25 43:3 45:2, 15 47:14 50:8, 11 102:14 103:11 personal 8:22 125:9 personally 8:20 10:16 57:20 81:14 persons 6:16 27:21 32:25 person's 55:2 perspective 15:11 64:14 81:20 82:6 88:20 91:25 114:19 117:4 122:9, 17 pertain 99:16 pertinent 95:20 pets 8:11 pharmaceutical 12:21 29:17 pharmacological 33:24 35:15 pharmacotherap ies 29:21 57:6 60:22 pharmacotherap y 57:4 phase 76:16 136:19 phases 44:9 PhD 2:12 3:17 Philadelphia 64:10 phone 8:8 43:4 physical 20:21 physician 23:16, 17 84:13 physician-rated 66:22 physicians 27:14 67:1 111:16 physician's 25:5	physiologic 75:6, 9 pick 85:5 118:11, 14 121:15 132:25 135:21 picking 60:1 picture 36:25 65:18 piece 92:13 110:21 122:6, 12 123:4 131:20 132:24 pieces 135:16 place 8:10 9:4 136:12 placement 69:15 86:2 platform 42:20 please 6:23 7:3, 16 8:10, 22 9:11 11:24 13:11 14:18 15:8, 21 16:4, 6 17:4, 20 18:7, 17 19:1, 16 20:2, 24 24:24 26:17 28:10 29:7 30:22 33:14 34:11 35:20 36:11 42:16, 19 44:1 45:14 46:20 47:9 48:9 49:16 59:3 64:16 66:14 67:11, 20 68:9 70:23 71:3, 8, 11, 14 72:20 73:1 74:13 84:8 86:16 96:4 100:23 113:13 plug 60:2 pocket 55:9 77:5 point 23:6 30:25 36:24 45:10 54:5 61:22, 23 76:18	92:14 97:22 98:6 105:11 117:13 120:18 121:6, 8 136:16 137:11 138:22 140:16, 19 pointed 20:17 117:2 points 38:12 46:6 50:22 78:1 104:16 109:6, 16 116:10 120:20, 25 122:2 policy 38:8 pool 49:14 poor 30:16 72:8 73:4 79:1 119:21 population 20:11 30:21 58:9 60:11 63:9 65:4 74:1 95:19, 21 121:5 122:20 141:4 portion 130:13 pose 130:20, 21 position 26:21 positive 60:8 106:2, 3 positivity 46:4 possibility 129:1 possible 12:10 75:19 115:3, 25 posted 15:17 postoperative 72:13 postoperatively 71:23 postsurgical 72:2, 4 postural 104:10 108:16 posture 23:21 potential 65:23 96:13 111:19 112:21 115:1 potentially 17:16 52:14
--	---	--	--	--

70:1 121:3 139:24 pouring 59:25 63:5 practicality 123:25 practice 14:11 18:20, 25 36:11 50:4 59:13 61:15 68:23 84:24 93:6, 19 94:3 130:11 practicing 33:22 Pravin 3:18 33:21 Praxis 27:1 preamble 99:14 precise 43:7 44:10 47:11 precision 53:18 pre-meeting 74:10 preoperative 71:25 preparation 24:1 preparatory 131:25 pre-post 90:20 pre-procedural 74:2 presence 77:10 present 7:12, 18, 23 23:16 38:17 40:15 55:16 62:5 75:23 Presentation 3:8 7:7 15:20 16:5 21:24 26:9 39:6 70:11 80:21 88:24 103:23 presentations 6:17 26:7 82:20 90:12 91:5 141:15 presented 29:10 47:14 70:20 84:14, 25	85:18 99:21 111:15 112:25 presenter 26:1 63:21 139:18 Presenters 3:16 7:3, 5, 7, 10 26:6 62:10 87:12 presenting 84:12 president 26:20 press 44:8, 10 45:5 presses 44:3, 19 45:4 presurgical 72:2 presurgically 72:7 pretty 79:25 141:13 prevention 127:20 previously 70:22 94:18 primarily 40:22 71:6 90:14 primary 52:19 65:19 110:11 111:22, 25 principle 37:19 39:19 140:5 principles 97:8, 10 printed 88:5 prior 7:11 15:17 62:9 115:12 117:19, 20 prioritization 14:24 16:17 prioritize 66:10 98:13 prioritized 21:18 86:20, 22 prioritizes 68:24 PRO 115:15 probability 69:25	probably 17:12 24:15 95:11 109:3 123:2 problem 73:14 problems 33:1 47:15 57:9 78:11 procedure 127:9 129:14, 16 136:10 procedure- related 127:4 procedures 36:1 38:3 130:11 proceed 29:18 74:5 96:23 proceeding 136:9 PROCEEDINGS 5:1 9:7 143:4 process 52:4 64:2 67:12 69:2 139:21 produced 143:8 professional 5:18 13:6 14:8 15:1 18:18 19:3 professor 21:5 26:22 42:14 53:23 64:8 profile 64:25 68:20 profiles 40:12 program 21:10 52:4 programs 28:2 progress 108:21 118:10 progresses 130:10 progressing 108:23 progression 43:25 47:8 53:24 68:7 73:15 79:6	111:19 136:13, 18 137:20 progressive 12:13 13:12 57:1, 9 progressively 45:6 prohibit 6:8 Promises 56:16 prompt 7:11 propose 32:18 proposed 78:9 PROs 114:20 PROSPECT 41:25 60:16 protocol 57:21 proven 106:21 provide 6:3 19:17 26:16 27:19, 22 28:6 44:11 105:19 139:25 provided 18:23 27:25 38:10 92:7 provider 43:9, 11 49:23 50:6, 14 51:5 54:19 provider's 50:16 provides 35:16 42:25 92:3 140:7 providing 21:16 95:6 prudent 36:4 psychological 69:9 psychosocial 123:1 Public 3:15, 24 7:13 21:6 25:24 26:6 70:5 80:9, 22 82:20 84:15 94:16 103:24 141:11, 15 142:15 publication 85:2	publications 43:16 published 14:1 18:2 28:16 54:11 59:15 90:9 pull 11:15 100:15 purpose 81:7 93:25 134:17 put 23:9 52:6 79:18 108:17 110:23 121:12 122:23 124:11, 13 141:17 putting 138:21 < Q > QDG 42:17, 20, 25 43:5, 7, 14 44:2 45:17 46:3, 24 47:2 49:5 53:7, 13 54:14 QDG's 47:10 qualify 121:21 quality 8:9 17:6 24:11 30:13 32:25 33:4 53:1, 3 66:20 67:17 68:10 72:18 91:23 92:21 98:3 110:20 113:19 114:2, 4, 8 115:7 116:11, 16, 18, 19, 22 118:7, 8, 20, 21, 22 119:1, 19, 22, 25 120:2 121:13, 15, 17, 24 122:1, 10, 23, 24 123:22 124:12, 13 134:5, 10 137:16 140:9, 10 141:1 quantitative 42:24 43:12
---	---	---	--	--

44:12 54:20 55:11 QUEST 32:14, 21, 22 33:2 34:21 58:17 59:5 62:13 63:13 question 22:20 23:24 25:3 32:6, 12, 20 40:8, 9, 23 41:13 51:9, 18 52:11 76:13 78:6 83:1, 4, 16 84:7, 10, 16 90:25 99:13 101:10, 11 103:1 113:11 117:11 126:24 127:1 138:8 questionnaires 92:3 Questions 3:12, 15 4:6 5:21 10:10 22:1, 3, 14 23:13, 16 24:20 25:7, 10, 19, 21 26:8 32:10 33:11 38:18 39:2 42:8 48:16 49:9 51:13 52:1 62:6, 8 63:16 69:5, 6 70:3 76:1, 6 79:20, 22 81:11 85:19 90:10 96:2, 3 99:4 101:23 102:2 103:16 130:4, 20 quick 25:3 90:16 91:3 quickly 41:21 62:11 91:9 99:11 125:12 quite 19:15 28:19 50:3 58:18 82:9	84:21 quorum 7:23 < R > RAC-CT 2:15 raise 90:5 range 17:14 47:22 70:20 83:2, 13 85:21 86:2 131:18 rank 107:9 108:19 116:12 117:20 118:15, 16, 19, 25 120:3 127:7 ranking 91:10, 11 rare 77:9 rate 45:8 60:3 rated 60:25 127:15 rates 73:24 112:23 Rating 17:22 23:14 24:14 25:15 34:22 46:18 53:2 89:4 100:3 rationalize 103:13 raw 45:21 RCTs 67:22 read 23:2 49:3 99:14 reading 24:1 103:23 ready 7:12 26:10 29:19 100:17 real 43:2, 8, 12 93:24 realize 116:6 125:17 realized 28:17 really 28:8 30:5 35:5 41:11 50:3 67:12 68:16 75:8, 23 84:16 85:23 88:24	92:14, 17, 20, 22 93:20 95:5, 13 104:6 106:13 107:15 110:13 117:15 119:9, 17, 24 121:24 134:5, 6, 23 141:14 142:2 reason 62:15 73:16 107:6 109:9, 23 113:20 reasonable 21:12 54:7 71:22 112:24 125:14 reasons 56:3, 24 119:20 128:1 recall 24:16 receive 7:7, 10 86:11 105:25 received 43:14 52:2 71:1 100:20 receptors 12:23 Recess 80:15 recognition 72:9 recognize 38:11 58:21 84:20 recognized 37:24 recognizes 46:10 64:18 recommend 36:10 51:21 61:7 recommendation 15:5 recommendation s 18:21 98:15 recommended 15:7 17:25 19:22 24:8 29:15 59:9, 10 61:16 62:13, 17 record 6:7 7:18 138:21	recorded 102:13 114:12 125:1 recovery 129:16 recruit 28:4 recused 7:24 red 16:18 44:16, 23 46:6 reduce 13:20 30:9 Reducing 42:2 reduction 59:22 104:15 reevaluated 61:23 refer 16:4 referred 17:2 82:19 referring 82:10 88:15 refers 13:1 refill 80:4 reflect 22:24 53:10, 18 58:25 80:20 81:23 97:7 99:6 100:11 103:14 131:6 133:19 reflected 15:20 119:16 reflecting 92:7 111:8 123:20 130:9 reflection 138:17 141:8 reflections 81:10 96:1 refractory 12:4 refrain 9:8, 11 regard 17:15 18:8 regarding 14:9 27:2 76:17 130:15 regards 51:20 regimen 47:20 regular 44:25 regularly 63:1 121:4	regulatory 51:15, 17 52:4 93:15 139:21 Reiling 29:4 reimburse 137:12 reiterate 70:21 109:6 reiterating 67:8 relate 18:10 85:20 101:7, 15 108:3 related 6:20 20:20 25:16 27:11 35:11 42:23 60:13 72:16 78:6 81:8 107:23 108:4 112:3, 13 114:1 118:4, 20 119:1 129:25 131:2 133:15 134:4 relates 84:17 121:7 129:13 136:6 138:7 relationship 22:13 relative 96:10 relatively 36:4 83:19 release 44:9, 10 45:8 releases 44:3, 19 relevant 5:18 63:9 83:23 93:12 106:2 137:22 reliable 31:3 78:13 138:13 reliably 22:24 140:13 remaining 7:9 Remarks 3:4 4:11 remember 31:16 72:14 remind 21:7 31:8 52:10
--	---	---	--	---

reminded 9:11	124:4	113:23 139:21	Rogstad 3:9	120:9 122:3
reminder 22:6	requires 44:14	141:17	10:5 11:13, 14,	123:7 124:19
reminders 7:7	requiring 75:14	reviewed 14:17,	17 23:6 24:7	125:2 126:21
remote 42:21	research 5:18,	19 22:21 61:4	25:12, 22 41:1	127:13, 24
47:24 49:13, 25	24 17:24 26:22,	reviewers 16:9,	82:8 85:5	128:12 129:8
52:18, 21 53:16	23 27:11, 22, 23	20 17:15, 25	86:14, 17 87:5,	130:12 132:4
93:17	28:1, 4 52:9	18:16 19:8, 12,	7 88:1, 8 89:1,	133:3, 18
removal 75:14	59:16 71:1	20, 24 20:17	10, 25	134:16 136:3
Remove 8:11	75:8 81:19	24:8 85:7	role 10:19, 22	138:7 139:7
removed 105:4	138:18	reviewing	67:23 84:10	141:2 142:7, 19,
repeat 75:1	reserve 19:1	15:23 36:18	room 50:13	23
78:2	25:20	reviews 14:5,	Rosenow 3:22	roster 103:12
repeatable	resource 28:17	20 17:13 19:20	70:6, 8, 12	routine 71:24
74:12	resources 27:21	20:7, 10, 15	75:25 76:5, 17	75:1 94:3
replacement	respect 40:17	62:20 138:9	78:15 79:13, 17,	routinely 35:5
47:16	137:14	revision 18:1	20, 23 114:24	58:13
report 10:6	respectively	rich 67:14	Ross 2:4 3:6,	rule 14:24
11:18, 19, 21, 25	45:24	right 24:9	13 4:4, 7, 10	Ruth 6:23 7:16
13:25 14:7, 16,	responded	25:20 36:12, 25	7:22 10:13	r-u-t-h 7:1
18, 19 15:1, 9,	15:16	44:7 45:21	21:3, 4 23:24	ruth.mckesson@
15, 19, 24 16:8,	response 61:25	62:9 75:7 76:9	24:20, 23 25:18,	cms.hhs.gov 7:1
18 17:10, 12	responses	87:23 89:10	23 26:2, 5 32:3,	
18:19 19:7, 11,	51:11 59:14	90:20 91:4, 21	12 33:10 38:22	< S >
17 82:11, 12, 19	responsive	92:6 94:1, 11	39:1 40:5	safe 32:1
87:21 125:17	71:11 73:9	97:18 98:20	41:12 42:7	safety 17:10
reported 11:18	responsiveness	101:1, 12 103:1	48:14 49:16	22:19 33:16
14:21 19:19	71:19	108:18 109:25	51:10 53:20	34:15 35:10, 21,
24:10, 13, 14	rest 12:17	110:16 135:18,	55:15, 20 56:7,	23, 25 41:14
25:13 109:14	22:2 142:24	19 139:21	13 62:7 63:16,	67:7 69:8
124:18	result 65:2	141:20	20 69:4, 7 70:2	75:12 81:8
reporting 110:8	68:20 140:22	right-hand	75:25 77:22	83:8, 24, 25
reports 20:5	results 8:2	18:12	78:5 79:9, 14,	84:2 97:2, 23
represent 20:11	24:12 36:11	rigidity 12:16	19, 25 80:11, 16	124:22 125:6, 7,
Representative	59:22 68:8	45:12 46:15	81:22 82:24	10, 19 126:1, 25
2:17 20:13	reverses 42:3, 5	51:2	83:15 86:16	127:11, 15, 21
47:2	reversible 36:3	ringers 8:11	87:3, 6, 20	128:8, 11, 14, 21
represented	41:21	rise 89:21	89:15 90:2	129:6, 25 130:4,
20:10 46:5	Review 3:8, 11	rises 120:1	91:18 92:25	10
49:12	5:17 11:19, 20	risk 57:3, 5, 7	93:23 95:8, 25	safety-related
representing	14:4, 22 21:10	58:25 72:8	96:21 98:20	69:11 125:12
51:1 64:4	22:2, 8 23:3	73:22 74:6	99:4, 9 100:19	127:22
84:11	24:6 28:21	78:25 104:11	101:7, 13, 22, 25	safety's 129:11
represents 64:7	29:1, 8 32:14	115:1 128:20,	102:7, 14 103:2,	Sage 27:2
reproducible	51:17 59:11	21, 22 129:2	5, 8, 9 104:17	salaries 6:21
86:13	61:18 69:2	Robin 2:11	106:5 107:21	Sally 2:12
request 20:3	78:8 80:22	7:20 24:23, 25	108:7, 24	7:20 53:22
require 6:22	82:1 83:18	130:24 133:23	109:20 110:25	77:23 81:12
84:19	89:8, 18 94:16	robustly 45:11	113:1, 13, 21	87:20 96:4
required 45:13	95:5 96:2	Rocky 142:20	114:6, 14 116:8	101:3 102:16
	99:21, 22		117:5 119:3	

136:3 140:20 141:23 San 39:4 51:13 Sanket 2:7 7:19 10:20, 21 39:3 51:12 76:4 92:25 93:23 94:14 103:19 satisfy 52:21 saw 42:1 102:18 139:25 saying 128:16 133:23 Scale 17:22 18:3 23:14 24:8, 14 25:15 33:2 34:22 53:2 58:13 59:2, 6, 10, 12, 15, 23 60:18, 24 61:5, 9, 13, 16, 23 62:12, 16, 21, 22 63:12 72:25 74:16 85:9 89:4 90:9 100:3 111:11 113:6 124:22 scales 17:9 22:11 33:4, 8 34:23 39:25 46:18 59:4 62:20 63:15 66:22 79:14, 15 133:10 scalp 77:21 schedule 50:16 130:19 141:9 Scheduled 3:15 25:24 80:9, 17 Scheupbach 68:9 scholarships 28:7 scientific 27:16 score 43:21 47:21 50:19, 22, 25 51:3, 5 53:7 71:23	scores 53:3 132:15 screen 56:9 87:18, 24 88:2 91:3 102:3, 17 screening 74:2, 25 75:1 90:17, 22 script 10:12 scroll 88:9 se 89:14 90:4 search 14:1 searched 14:4 second 29:20 34:7 52:10 76:24 80:5 108:3 113:3 138:8 139:18 secondary 12:6 seconds 44:5 section 20:4 33:6 130:14 Security 1:23 see 13:6 16:22 19:8 23:2 30:15 31:5 32:6 41:21 45:9 46:7, 8 47:1 54:15, 17 72:15 74:1 77:7, 9 80:13 86:21 87:10 88:8, 10 97:17 99:7 101:25 103:4 119:9, 16 120:6 122:18, 23 131:7, 12 138:19 139:5 141:3 seeing 53:17 90:15 seek 63:2 seen 42:2, 5 47:25 65:5 69:12 89:18 94:18 95:22 112:24 select 60:10 selected 15:1	62:24 102:23 self 50:11 send 6:24 101:2 senior 11:17 seniors 31:9 sense 35:14 40:3 49:4 79:12 116:12 120:12 sensor 18:24 54:13 sensors 88:14 sent 15:10 101:1 102:19 separate 82:11 100:8 101:23 102:2 113:18 114:4 119:25 127:2 130:20 135:25 separately 18:4 46:12 series 40:24 serious 17:16, 19 server 43:6 service 21:11 SERVICES 1:11, 22 session 100:21, 24 set 18:21 19:3 43:17 126:9 sets 96:24 141:13 setup 96:22 seven 102:4 severe 37:10 61:1 severity 20:14 98:4 108:15 112:2 134:19 Sharan 3:21 63:24 64:4 69:4, 14 share 88:1 shared 76:10 106:11 shares 42:18	sharing 9:19 87:18, 24 Shill 29:2 shocker 122:5 shoed 54:17 short 46:9 90:16 shorter 105:5 short-term 77:1 show 19:5 45:21 52:18 89:25 124:7 128:3 showed 35:20 54:14 showing 68:6 shown 35:18 43:17 44:7, 16 47:22 50:3 53:6 100:3 102:2 shows 16:16, 19 44:13 45:15 47:1, 4, 5 87:14 side 17:17 18:12 36:4 42:6 47:7 57:5 71:16 77:19 92:17 128:8 129:24 135:24 sign 32:9 100:18, 20 signature 45:20 46:2 signatures 45:6 significant 29:24 30:6 35:13 58:23 75:8, 19 78:23 90:21 110:19 significantly 60:12 sign-on 100:16 signs 12:15 43:2 silent 8:11 similar 36:17 37:20 39:24, 25 40:1, 2, 8 41:7	73:16 74:18 106:10 111:23 similarities 36:13 similarly 40:19 74:20 116:24 132:8 simple 43:4 62:25 simplicity 91:2 simply 74:24 Sinemet 47:16, 20 single 47:19 123:23 sit 22:9 site 57:18 six 50:10 56:18 62:2 75:22 102:4 105:5, 8 115:16 118:1 121:1 size 83:9, 20 86:5, 25 skills 72:24 skin 42:1 128:5 sleep 17:6 24:4, 9 72:22 77:12 88:15 91:23 114:3 116:11 118:8, 21, 22 119:19, 21 120:2 124:12 140:10 sleeping 77:19 slender 77:6, 15 slice 52:14 slide 11:23, 24 12:11 13:11, 17, 24 14:18 15:8, 20, 21 16:6, 23 17:4, 17, 20 18:6, 17, 21 19:1, 5, 16 20:2, 23 26:17 27:4 28:10 29:7 30:21, 22 33:14 34:10, 13, 15 35:20 36:11 37:22, 24 38:19,
--	---	--	--	---

20 42:16, 18 43:17 44:1, 17 45:13, 15 46:19, 25 47:1, 9 48:8, 9 56:8 58:1 59:3 61:6, 21 64:3, 16 65:10 66:14 67:11, 20 68:8 69:8 70:22 71:3, 8, 10, 12, 14 72:20 73:1 74:13 75:4, 11, 20 slides 11:15 63:23 97:25 slight 41:9 61:1 92:15 slimmed 77:17 slow 8:5 slowed 45:8 slowness 12:16 45:7 small 47:12 48:5 88:17 126:12 138:1 smaller 77:14, 15 94:21 99:10 snapshots 140:1 social 30:17 socialization 58:6 socially 30:5 Society 18:3 59:11 61:17 72:24 95:17 soldier 128:14 somebody 65:11 129:13 someone's 132:25 134:5, 10 somewhat 72:3 120:12 soon 50:2 soreness 77:3 Sorry 24:25 48:4 49:18 52:10 56:7 61:22 102:20	106:4 108:5 116:14 137:20 sort 51:22, 23 69:11 89:21 91:21 92:7, 17 93:7, 24 94:11, 24, 25 97:8, 10 98:1 99:24 107:4 108:17 118:2 119:16, 24 130:14 131:4, 8, 19, 20 138:8 141:16 sorts 72:11 sounded 88:23 90:21 sounds 85:10 139:20 soup 59:24 63:4 sources 19:14 66:12 south 57:14 space 110:4 138:18 spatial 44:11 72:10 speak 8:5, 6 9:6 33:15 41:15 42:10 49:1 69:10 78:14 79:10 speaker 6:21 8:8 26:6 33:12 42:11 55:21 58:18 70:6 92:1 138:12 139:25 141:15 speakers 8:4 80:23 94:17 97:19 105:13 142:15 speaking 7:11 8:10 135:23 speaks 69:15 86:24 special 6:8 specialist 57:11 82:4	specific 5:21 10:3, 9 17:1, 8 21:11 22:3 23:3 25:15 32:23, 25 33:7 41:1 79:10 90:3 96:6 97:13 103:14 107:17 109:8 111:17 114:4 121:19, 20 123:13, 23 124:1 130:15 133:8, 15 140:4 142:5 specifically 37:2 80:24 96:4 101:15 106:20 112:4 124:4 139:22 141:5 specifics 85:3 88:21 spectrum 47:3 83:3 speech 35:23 66:1 73:16 78:3, 9, 21 87:11 98:5 110:17 speed 44:21 spent 10:14 138:10 spirit 8:24 64:3 spoken 66:16 spoon 59:25 63:5 133:2 spoons 128:5 squeezed 75:21 stability 108:16 stacked 94:22 staff 9:22 102:13 114:12 125:1 stage 68:11, 12 staged 38:3 stand 80:5 standard 47:15 69:22 80:3 86:12	standardized 34:20 35:4 Stanford 42:15 start 45:25 48:17 54:20 56:17 64:1 80:12 103:17 104:13 111:3 114:15 128:15 136:24 138:5 started 56:18 87:17 starting 67:15 state 8:4 24:24 66:9 stated 128:1 statement 6:23 41:3 54:7 65:4, 10 statements 6:16 14:9 states 43:23, 24 66:7 statistical 50:25 53:6 statistically 51:6 statutes 6:8 stay 7:9 32:5 50:8, 14 132:23 142:19 Stearns 2:12 7:21 53:20, 21, 22 77:22, 23 78:7 81:13 87:17, 23 88:3, 18 96:5 98:14 99:3 100:25 101:4 102:17, 25 103:3 108:25 109:1, 23 113:11, 14, 25 114:10 120:10, 11 123:21 127:24, 25 136:5 140:15, 25 141:24 142:21 steering 57:21 step 93:7	stepping 125:25 stick 62:8 sticks 110:5 stigma 136:17 stimulate 12:22 stimulates 59:19 stimulation 13:23 34:1, 3 37:8, 20 38:5 42:3 54:13, 21 59:19 64:7, 12 67:17 71:5, 12 72:16 73:19 stock 6:18 stop 61:21 80:2 87:23 128:6 stopped 48:6 strategy 31:5 strengthening 134:8 stress 13:7 strike 45:23 strikes 46:2, 10, 16 stripes 45:9 strong 50:17 107:11 strongly 110:1, 6 Stroop 90:15 struck 113:14 114:23 Stuart 3:20 55:22 stuck 56:8, 9 92:23 students 28:7 studied 86:19, 22 87:15 studies 5:14, 24 12:2 14:10, 22 20:10, 13 53:16 60:10 61:14 65:20 67:22 69:19 71:21 82:14, 18, 22 87:15, 16 88:12, 14, 16, 17 89:22, 23 92:5 94:10
--	---	--	---	---

99:16 106:12 116:2, 5 128:3 study 39:15 53:13 54:11 66:11 68:6, 9 69:1 84:4, 22 92:10 97:5 101:19 117:24, 25 128:7 132:5 stuff 133:4 Subcommittee 3:11 subdomain 98:9, 10 114:9 118:19 subdomains 91:21 100:11 106:23 107:24 subject 15:10, 15 subjected 14:23 75:7 subjective 74:11 submitted 24:3 131:1 subscale 74:17 subscore 62:14 subscores 43:21 subscribed 143:9 subsection 71:20 subset 21:20 subsets 108:18 substantially 115:9 subthalamic 69:17 successful 9:23 successfully 61:14 suggested 61:16 67:4 68:22 99:15 suggesting 39:14 40:11 69:20 suggests 76:10 suicidal 73:25 76:21	suicidality 73:22 76:9, 12 78:2 115:1 116:10 suicide 74:6 76:11, 22 115:2 sum 95:18 summarized 40:25 Summary 3:11 16:1 21:1 30:23 61:7 87:6, 7, 21 Sunshine 9:1 supplied 18:16 support 6:22 27:11, 22 28:3 68:16 131:16 supporting 60:10 supports 64:22 supposed 80:2 91:7 sure 10:22 52:19 53:16 56:14 63:19 83:12 106:14 112:15 134:14 140:18 Surgeons 70:17, 18 surgery 13:23 29:18, 19 68:14 71:16 72:15 73:10, 12 74:5 75:10 76:22 78:16, 17, 20, 21, 24 79:3, 4 surgical 28:23 29:12, 13 35:17 37:15 38:3 57:7 77:13 78:13 surprised 78:11 surprisingly 18:10 surrogate 138:11, 24 139:13, 15, 24	surrogates 139:4 survey 24:12 117:24 survive 139:12 swallowing 73:16 78:3, 10, 22 110:15, 21 134:7, 10 Sydney 64:9 symptom 64:25 65:18 68:20 87:13 98:2, 4 108:15 112:2 symptomatic 75:15 symptoms 12:6, 18 13:16, 19 24:4 35:22 40:14, 18, 20 41:9, 10 51:19 60:12 66:4, 5, 6 88:10 89:23 104:5, 24 105:7, 12 107:4, 8 108:3 112:12 124:17 129:21 131:3 140:3 141:5 Syrek 2:21 3:5 9:14, 17 142:12 system 42:22 65:9, 24 systematic 14:1, 5, 19 17:13 19:19 20:7 99:20 systemic 57:4 systems 73:23 < T > TABLE 3:1 4:1 16:16 35:18 46:23 47:20 81:13, 23 86:17, 18 87:3, 5, 9, 14, 18, 19 88:9 89:16, 18 tables 15:22, 24 88:5	tablet 43:5 47:17 tag 78:6 tailored 83:23 84:4 126:19 131:19 take 9:2, 3 29:25 34:25 38:18 56:14 67:4 83:12 106:25 134:2 takes 46:8, 11 67:1 talk 22:11 83:24 84:20 97:19 134:7 talked 32:14 49:2 92:1 116:25 127:19 talking 21:11, 14, 20 84:22 107:17, 22, 23 126:2, 4 133:25 138:10 Tamara 2:21 3:5 9:14, 16 142:9 tapping 46:19 TAPS 28:24 29:16 34:1 35:13 36:3, 5 37:18 38:8 41:20 54:24 57:22 59:17 60:9, 17, 25 61:11 62:21 131:22 Tara 2:24 3:5 5:7 11:11 25:23 32:4 38:24 42:11 55:20 63:20, 24 80:8 100:15 101:1 target 37:4 38:5 104:20 105:14 112:7, 9 targeted 37:9, 13 55:6 targets 69:16	task 43:4 44:2 45:17 tasks 29:25 34:25 58:5 60:4 61:3 63:1, 2 TBD 94:11 tea 60:1 63:5 team 95:14 96:3 tease 118:8, 12 122:24 techniques 77:14 technology 42:25 49:10 67:9 132:1 teed 107:2 telephone 60:1 tell 18:14 48:4 77:10 temporal 44:11 ten 28:6 80:4 ten-second 45:10 tensioned 44:4 Teresa 3:9 11:12, 17 term 20:6 31:18 112:13 terms 35:21 41:17 51:24 75:12 77:12 81:18 83:4 87:1 93:17 96:11 97:3 104:23 106:13 107:10, 13 109:18 112:19 113:7 115:12, 14 116:10, 15, 21 120:17 124:13 130:1 131:6 136:7, 22 137:5, 24 138:19 terrific 113:1 Terry 10:5 21:3 22:15, 20 25:20 32:13
---	---	--	--	---

40:25 80:21 81:12, 22 84:7, 15, 17 87:3 89:15 95:4, 14, 18 96:2 125:18 141:16 Terry's 21:23 97:25 103:23 test 44:14 67:9 90:16 140:23 testing 71:24 72:2, 4 74:23 75:2 90:19 91:25 tests 62:23, 24 TETRAS 32:21 33:5 34:21 58:17 59:5 62:14, 21 63:11 74:15, 18 thalamus 36:22, 25 37:2 71:13 thank 9:18 10:16, 21 11:3, 9, 14 21:2, 3 26:14 30:23 32:2, 3 33:10 36:25 38:16, 20, 22 40:4 42:7, 9, 13 48:8, 11, 14 49:9 51:10 52:16 55:16, 18 56:19 62:4, 7 63:17, 19, 24, 25 69:3, 4 70:3, 7, 18 75:22, 25 79:18, 19, 20, 23 83:16 85:15 99:3, 8 101:4 102:11 106:9 107:2 108:6, 7, 24 109:20, 22 114:10 117:5, 7 119:3 120:9 122:3 124:19 126:21 127:13 130:12 141:22 142:12, 17 thanking 9:20	Thanks 39:3, 5 40:6 49:18 51:12, 25 76:4, 5 77:22 93:1 95:10 103:19 106:5 107:21 114:17 116:8 125:5 142:23 therapies 28:23 29:17 35:22 41:15 63:3 69:8 112:18 123:24, 25 therapist 29:5 therapy 25:2 27:19 28:23 29:13 30:8 35:15 37:6 41:18 43:24 48:5 55:5 57:22 58:25 59:14, 17 60:9, 25 61:24, 25 62:3, 21 63:3 68:3 112:19 131:1, 13, 24 THEREOF 143:9 thing 23:20 31:17 61:22 74:8 102:18 126:12 129:23 132:16 136:21 things 23:22 25:15 54:25 63:4, 11 71:18 72:7, 8, 11 74:3, 15 75:13 78:18 79:7 91:24 100:9 107:25 118:6, 23 124:10 131:15, 19 134:3 135:9 137:6 142:4 think 22:12, 22 33:1 39:7, 12 54:9, 16, 25 55:4 56:3, 22 58:2, 14, 17 62:1, 15, 19, 20,	21 63:5, 10, 11, 13 66:15, 17 70:5, 19 71:15, 18 73:3, 17 75:21 76:25 77:6, 25 79:2 80:24, 25 81:13 83:8 84:19 85:18 86:3, 5, 6 91:19 92:6, 22 93:12, 25 95:3, 13, 19, 20, 22 96:7 103:22 104:4, 17, 18, 22, 23 105:3, 4, 6, 8, 9, 17, 19, 22 106:11, 18, 25 107:15, 18 110:3, 8, 12, 13, 17, 19 111:6, 14, 21, 25 112:10, 15 114:18 115:3, 13, 16, 22 116:6, 15, 16, 21, 23 118:17 119:17 120:12, 20, 21 121:2, 22 122:8, 10, 11, 12, 16, 19, 21, 25 123:12, 13, 15 124:1, 2, 3, 20 125:8, 9, 10, 13, 15, 22, 25 126:15, 23 127:18 128:1, 3, 14, 16, 17, 22, 25 129:5, 11, 14, 17 130:24 131:11, 24 132:11, 15, 22, 23 133:14, 23 134:3, 9, 12, 20 135:4, 5, 8, 11 136:11, 21, 23 137:19 138:24 139:6, 17, 23 140:19 141:14 142:4 thinking 48:1 53:25 54:21 76:21 85:16	86:7 93:5 95:12, 13 97:11, 14 104:5 120:14 125:7 132:19 138:25 ThinkPad 101:8 thinks 134:4 third 110:24 124:20 139:18 third-line 29:20 thorough 95:5 141:13 thoroughness 95:10 thought 34:7 92:11, 13 94:16 111:4, 14 141:25 142:1 119:4 three 11:23 15:10 16:20 17:14 19:8, 20, 22 47:17 58:15 62:2, 19 65:11 96:24 102:3 105:7 125:13 141:13 threshold 14:25 16:18 100:14 thrilled 119:8 tie 110:24 tight 7:5 tightly 110:13 time 7:4, 6, 8, 10, 11 8:5 9:19 11:4 21:8 26:3, 4 28:19 31:19 32:9, 11 38:16, 18 41:22 42:9 43:2, 8, 10, 12 45:5, 10, 23 46:7, 12 47:8 49:24 50:7 52:24 53:25 54:15 55:16 56:15 63:8, 18 66:19 70:4 73:6 75:2, 20 76:14 79:21	80:1, 3 83:11, 17 85:24 86:1 92:12 94:7 101:12 105:8 112:5 130:6, 7 133:21 134:2 137:21 138:10 141:23 timely 28:2 times 47:17 83:19 timing 44:9 93:2, 3 136:12 137:19 titrate 93:7 titrations 93:21 today 5:10 9:21 10:12, 13, 25 11:4, 6 15:20 21:8, 20 28:9 30:24 33:16 38:11, 17 42:10 55:17 70:10, 19, 20 132:8 today's 7:19 8:21 10:3 11:22 15:5 16:2 21:5 told 32:4 38:23 tool 47:24 49:21 51:18 52:9 53:18 86:9 90:22 91:1, 3 tools 12:7 35:2 64:14 66:12, 24 90:17 93:6 106:20 117:17, 21 top 52:4 89:21 120:1 123:17 topic 6:20 9:3 10:3, 9 26:16 36:20 70:10 topics 9:12 10:3 70:20 83:13 totally 51:14
--	---	--	--	---

touch 81:15 97:25	86:24 87:2 93:7, 8, 9 107:16, 17	134:19 137:10 138:14 140:10	19:4, 23 20:18 44:5 46:5 56:6, 23 57:3 58:12	understand 8:6 22:24 62:23 67:23 79:9 90:23 96:12 112:17 140:16 141:18
touched 92:13 134:9 135:8	treatments 13:10, 22 37:9, 15 85:22 86:23 88:13 96:12 105:14	tremor- dominant 38:2 45:16	63:15 67:18, 22 71:11 82:5 89:3 92:23 98:24 99:23 103:15 105:6 108:6 111:21 118:15 120:20 122:25 130:20	understanding 39:13 66:11 91:17 105:24 108:21 114:19 137:13
trace 44:18 45:1 46:11	Tremor 1:16 5:11, 13, 15, 16, 25 6:1 10:5 11:8 12:5, 17 13:12, 13, 17, 20 14:6, 7 18:8, 10 21:22 23:21 25:16 26:15 27:2, 5, 8, 12, 13, 15, 22, 25 28:6, 8, 13, 15 29:6, 14, 23 30:3, 7, 9, 14, 16 31:4, 13, 17 32:23 33:1, 7, 9, 17, 24 34:7, 9, 10, 16, 17, 22, 25 35:4, 6, 11 36:6, 14, 16, 18, 23 37:4, 9, 14, 25 38:1, 9 39:9, 15, 21 40:18, 23 41:7 42:23 43:3 44:12 45:20 46:2, 7, 11, 13, 16 54:23 56:5, 24 57:16, 19 58:9, 10, 14 59:9, 22 60:12, 20, 21 61:11, 20 64:21 65:7, 12 66:5 67:16 68:18 71:6 74:14, 22 85:23 89:22 99:17, 19 101:24 102:10 104:14, 15 110:19 113:10, 15 114:22 115:8 116:21 118:10, 25 119:1 126:5	tremor- predominant 33:18 36:14 37:11 38:6, 14 39:22	60:16, 18 67:10 68:22 86:13 113:8	understood 36:18 39:17 78:1
tracers 44:16		tremor- prominent 38:1	type 19:23, 25 62:2 66:2 83:18 86:24 97:11, 17 107:15 125:21 126:19 138:14	undertreatment 48:3
traces 47:2		tremor-related 32:1, 16 51:19 62:14 120:6	types 13:23 20:2 22:13 91:14 98:24 101:18 116:2 129:20, 21 130:2 131:6, 8 133:5 138:17	unfortunately 48:12 75:7
track 82:21 111:23		Tremors 1:15 13:15 33:20 34:24 35:8 37:18	73:8 74:23 75:3 77:9 78:21 79:2	Unified 53:2
tracking 13:7 139:25		trial 41:25 45:5 50:1 52:18 53:5 60:16, 18 67:10	typically 69:16 77:8 79:2	unilateral 38:4
trained 67:3		trials 28:5 57:20, 22 59:4, 5 61:10 66:25 68:22 86:13 113:8	78:21 79:2	unintended 111:20
training 121:11		trick 136:2	typing 30:1	unique 46:2 47:5 94:17
transcribed 143:4		tried 29:16	< U > UCSF 39:4 51:13 76:5	United 17:21 23:13 24:13 25:14 89:3
TRANSCRIBER'S 143:1		trouble 50:12 100:22	ultimate 132:13	University 25:2 26:25 53:22 70:14 77:24
transcript 98:25 143:7		troubled 66:19	ultimately 30:10, 12	unlocking 60:2
transcriptionist 8:15 143:16		true 35:11 82:2 143:7	ultrasound 28:23 29:12 34:2 37:7 38:4	Unrelated 49:15 51:14, 18 76:6, 12
transcutaneous 33:25 37:19 59:18		truly 58:8 64:3 74:12	uncomfortable 77:11	unusually 101:5
transformed 49:13		try 32:8 70:21 82:21 129:4	undergoes 129:13	unwieldy 98:9
translate 140:23		trying 22:23 41:3 91:2 102:19 109:10	undergoing 94:8, 9 125:24 139:20	update 28:21
translated 93:19		ttpoll.com 100:21	underlying 132:18	updated 28:14, 18
translating 93:5		tunneling 77:3		updating 95:7
transmitted 43:5, 8		turn 9:13 25:23 124:20		UPDRS 43:21 46:19 48:24 50:20 65:12, 25 66:23, 25 71:20 72:23, 25 133:4
transparency 6:3		twice 52:25		upper 44:7, 18 59:22
treat 14:6 57:8 74:4 85:22 93:10 107:7 112:14		two 7:11 12:25 15:7, 12 18:20		UPS 43:20 51:3, 7, 8 55:8

58:12	14, 18, 22 122:8, 17	103:13, 18	123:12 128:21	142:18
upside 79:5	variable 13:1	106:8 109:4	129:4, 17 131:5, 6, 7 133:19	weekly 48:23
use 8:7, 16, 19	65:3 68:21	113:5, 25	134:24 135:3	weeks 53:4
12:24 18:11, 23, 25 37:18 41:19	varies 86:23	114:15 117:6	136:3 138:6, 20	weight 121:12
50:4 51:7	variety 84:14	120:10 124:21	141:3, 8, 21	weirdly 128:5
52:20 55:8, 11	85:17 86:23	125:4	142:11	welcome 5:4
58:13 59:12, 15	various 13:22	voted 102:12, 15 103:6, 7, 20	wanted 10:11, 12, 16 28:21	80:16
62:17 63:13	91:24	106:9 108:9	32:5 52:18	well 6:1 10:23
72:11 77:16	vary 97:17	109:1, 10, 22, 24	56:13 84:11	13:23 25:20
81:18 84:25	vast 22:15	111:1, 2, 5	86:4 130:21	31:9 33:6, 17, 24 39:8 55:2, 4
94:4, 24 100:2	81:24	114:11, 14, 17	138:16 142:9	57:10 59:1
101:8 108:23	ventral 37:2	117:9 119:6	wants 93:8	61:4 67:2
131:16 132:6, 21 133:8, 17	verbal 72:9	120:11 122:4	water 35:2	71:23 79:20
135:21, 22	version 15:15, 16 18:1 59:24	123:8 124:25	80:4	80:22 81:8
136:18	62:25	125:3, 5 126:22	waters 94:25	85:21 92:14
useful 62:20	versus 49:6	127:25 128:13, 14, 17 129:3, 9, 10	way 32:2 50:4, 13 60:18 74:13	93:18 97:14
63:14 86:9	84:6 91:4	votes 102:12	77:12 79:18	99:9 100:13
94:10 98:22	97:21 98:5, 18, 19 111:22	103:9 114:11	87:17 95:21	104:2, 13
133:20 141:15	114:3 117:18	124:25	111:3 115:4	105:13 107:3
142:2	118:16 123:22	Voting 3:12	117:12 118:11, 20 131:21	111:18 114:21
usefulness 61:11	127:4 136:17	4:6 5:21 7:18	132:14 133:9	116:4 119:6
user 62:22	142:5	8:1, 2 10:9	135:20 136:25	125:6 127:15
101:5	vertical 45:25	22:8, 14 85:19	137:4, 13	140:5
usually 17:18	Veterans 38:7	96:3, 9, 14, 20, 22 99:13	141:19 142:22	went 32:13
utmost 127:16	vice 5:5	100:16, 20	ways 65:11	we're 21:10, 13, 20 25:25 31:12
< V >	Vice-Chair 2:6	101:11 102:5	66:17 125:8	52:3, 5 53:12, 17 56:11 63:22
valid 61:9	video 45:15, 17	109:11 114:13	wearable 18:23	79:25 80:1, 17, 24 82:10 83:16, 24 84:21 85:17
validated 18:4	46:1	117:8 130:13	28:24 29:15	86:7 90:2 91:1, 6 94:1, 12 97:9
39:10 43:1, 13, 19, 20 49:2	view 97:22	< W >	54:4, 12, 13, 14	98:15 99:9, 10
55:11 58:12	98:7 117:14	waiting 63:22	59:16 83:2	101:11 102:25
61:13 63:7, 12	138:22	wall 129:4	88:14 105:3	103:10 107:17
74:13 75:9	VIM 37:17, 22	want 7:16	125:9 127:4, 6	111:6, 12, 18
82:20 92:8	38:6	9:18 21:7, 24	131:18 135:18	113:5 124:3
validating 139:3	virtual 5:6	26:3 29:18	136:14 138:5	130:19 132:19
validation	virtually 8:14	30:10, 23 31:7	wearables 36:2	133:9 137:18
46:24 49:11	visits 49:22, 23	58:2 62:4	37:18 40:21	138:25 141:9, 11
82:14, 17, 21	50:7, 9	64:24 67:13, 19	98:18 127:18	we've 27:25
84:20 85:13	visual 72:10	68:15 69:24	128:5 137:22	28:1 34:18
94:9 138:19	voice 8:18	78:16 86:9	wearing 13:2	43:17 49:9
141:3	volume 14:25	91:24 97:16	weather 142:22	50:17 53:15
validations	voluntary	98:11 107:7	Weaver 68:6	54:10 57:18
139:14	13:14 45:18	109:24 111:13, 22 115:10	website 8:3	62:9 65:5
valuable 62:16	46:15	121:6, 24	15:17 16:2	77:13, 17 80:20
134:3	vote 96:25	122:13, 18	Wednesday 5:3	
value 91:17	97:3, 7 98:10, 22 99:5 100:11, 18 101:14, 17		week 53:4	
97:14 121:3, 13,				

94:24 95:22
 103:16 112:24
 141:12
whatnot 111:8
white 135:13
wholeheartedly
 135:15
wholly 65:21
wide 17:14
 83:2, 13
willing 128:19,
 20 129:2
wire 77:18
wires 77:4
wish 7:14
WITNESS
 143:9
wonder 48:18
 130:18 139:8
wonderful
 142:18
wondering 24:5
 87:24 90:18
Word 15:25
 21:1 130:24
work 51:2
 55:3 95:4
 122:6 134:25
 137:14
working 52:3, 8
 110:18 122:19
world 131:23
worldwide 64:8
worn 59:20
worry 56:14
worse 12:17
worsening 70:1
worst 115:3
worth 92:7
 112:10
wrist 59:20
write 133:1
writhing 68:1
writing 30:1
 35:1 60:2 63:4
written 125:19

 < Y >
Yahr 72:22
Yale 21:6

Yeah 51:25
 52:16 88:1, 3
 89:1, 14 91:18
 93:23 95:8, 12,
 25 96:5 123:9
 125:16 132:11
 135:11 139:7
year 105:10
 115:17 118:1
years 10:14
 19:23 20:11
 26:19 33:23
 44:1 49:11
 57:12 60:19, 21
 70:14 90:9
Yi-Fen 2:10

 < Z >
ZIP 16:3