Open Meeting: External Upper Limb Tremor Stimulator Therapy

Meeting Date & Time:	June 27, 2023, 10:00 a.m. ET
Facilitator:	Michael Hanna
Location:	Virtual Meeting

Dr. Sunil Lalla (00:00:08): Good morning everyone and welcome to our virtual open meeting. Thank you to our registered speakers and attendees on the phones.

Today we'll be soliciting public comments regarding the proposed new external upper limb tremor stimulator therapy local coverage determination otherwise known as LCD.

This is referenced in the Medicare Coverage Database as DL39591. I'm Dr. Sunil Lalla and I'm with CGS Administrators, the jurisdictions B and C, DME MAC.

Also attending from CGS is Dr. Robert Hoover. Representing Noridian Healthcare Solutions are Drs. Smitha Ballyamanda and Angela Jenny with jurisdictions A and D respectively.

Moderating our phone lines and keeping our speakers on track is Michael Hanna from Provider Outreach and Education at CGS.

Speakers, please take your queue to speak from him. Each speaker will have 14 minutes.

Michael will send a gentle reminder to the speaker when they have two minutes left in their time. We're looking forward to hearing your comments today regarding External Upper Limb Tremor Stimulator Therapy LCD. Please remember to put these comments in writing and send to them- send them to us via email at the EULTSTLCDcomments@cgsadmin.com.

Details for submitting comments are also available on the DME MAC websites. Please remember that we only respond to written comments.

These comments are due no later than Saturday, July eighth, 2023. Also, we will be recording the meeting today as Michael mentioned.

This will be posted on the DME MAC websites. By listening you are- and participating- you are giving your consent to the use of your recorded voice and comments by signing into this meeting.

Please be careful about sharing any personal health information in your verbal comments. Today we have five commenters who are pre-registered to speak.

We are only permitting registered commenters to speak at today's meeting, but anyone can submit written comments to the email address I mentioned earlier. For each speaker today we ask that you introduce yourself, the organization that you represent, and please disclose any conflicts of interest that you may have with this topic. For those listening in on the phone, please mute your phone line and computer.

Do not, again, please do not place this call on hold because we'll all be forced to listen to the wonderful background music.

Speakers should be prepared to begin their comments immediately after being called upon. I'll now turn the presentation over to Dr. Robert Hoover to go over the highlights of the proposed LCD. Doctor Hoover?

Dr. Robert Hoover (00:03:10): Thank you, Dr. Lalla. I also put in the chat the email address for comments and the due date. So if everybody wants to take a look at the chat, you'll have that information.

The DME MACs are proposing a new LCD today which describes coverage for a class of devices that stimulate nerve pathways in the upper extremity to control limb tremor.

The new LCD is titled External Upper Limb Tremor Stimulator Therapy. This therapy is sometimes referred to as TAPS or transcutaneous afferent patterned stimulation. Best- Based upon the best

available evidence at this time the DME MACs are proposing that external upper limb tremor stimulation therapy devices are not reasonable and necessary. Additional details regarding the evidence analyzed and the rationale for this determination may be found in the proposed LCD on the DME MAC websites and the Medicare Coverage Database using the policy reference that Dr. Lalla gave just a few moments ago and I'll also put that in the chat.

I'll now turn the microphone back over to our moderator Michael Hanna from CGS who will queue our speakers for today's meeting.

Michael Hanna (00:04:24): Thank you, gentlemen. The first commenter is Dr. Khemani.

Dr. Khemani, are you on the line today? You are welcome to raise your hand and we will unmute your line for you.

It appears that Dr. Khemani is not available this morning. As such, we will go through that individual's comments on the slide. They will be included.

And the second commenter this morning is Ben Duncan.

Ben, are you on the call this morning?

I see that name. I will now ask you to unmute your line, please.

Ben Duncan (00:05:18): Right.

Michael Hanna (00:05:20): Good morning, sir. We can hear you.

Ben Duncan (00:05:22): Hey, good morning. Can you hear me?

Michael Hanna (00:05:27): Yes, sir. Your audio is coming in fine. Thank you.

Ben Duncan (00:05:30): Okay. I know the video is not working, unless you just don't want to see my ugly picture that's probably posted on the post office wall.

Michael Hanna (00:05:54): You should be able to see that video now, sir.

Ben Duncan (00:05:57): Okay.

Yeah, that slide that's shown is the Archimedes spiral from a pre and post- post-test. Can everybody see that?

Dr. Sunil Lalla (00:06:18): Yes, thank you.

Ben Duncan (00:06:19): Okay, well, why don't I go on and introduce myself? Good morning everyone. My name is Ben Duncan.

I am a Medicare recipient with essential tremor. I had been in very successful senior executive positions in 3 various careers in my life. My essential tremor developed over 16 years ago.

For a long time. I couldn't perform basic actions such as writing, keyboarding, eating, and dressing myself. ET forced me to retire early and it made me seriously depressed, angry, and frustrated.

I tried numerous treatments, including three very strong ET medications, which had serious debilitating side effects.

I was on the maximum dosage of all three of these for over five years, but the debilitating side effects forced me to have to use a walker or cane to get around because the balance and dizziness side effects.

Despite all three medications, I still had significant difficulty with basic tasks. As a military veteran, I obtained my Cala device through my local VA clinic. I've been using it for over two and a half years and it has been a Godsend. It really saved my life. Currently using the Cala device, I feel like I'm back to either 98- 99 percent of my past full functioning because of this device. I have weaned off all three of the expensive tier one and tier two ET meds and the debilitating side effects I used to have.

One thing I want to emphasize is the Cala device was clearly designed for tremor patients in mind, unlike other assessments and treatment devices that have leads and sticky electrodes and you have to remain still during the treatment. This is just something I would not be able to do by myself at home.

The Cala device avoids all of these complications and it has made a really important difference in my life. This means that I'm able to use the Cala treatment device most times a day with no preparation needed. For example, the stimulator and band are designed to fit around the wrist. So that all I need to do is wet my wrist for connectivity issues, put it on, tighten the band, and set my intensity treatment level when I need to use the device.

I can continue my normal daily activities while having a treatment session.

When I'm done with each treatment session, I place the band and stimulator back on the magnetic charger, which makes the device much more accessible for me.

If I don't have these treatments for my tremors, it would have normally taken me two to three minutes just to plug in my phone charger. If I had to use leads, electrodes, and sit calmly for treatment 40 minute sessions, three treatment each day, I'm not sure that I would use it so regularly.

The band has a three-month life expectancy and the stimulator tells me when to change the band.

The band is also self-regulating and I adjust the treatment to my treatment needs. Furthermore, anytime an adjustment is made, that information is sent to Cala Health. Then I can go to their website and I can review my own treatment progression. This is a great motivator for me to- to continue to use.

Without any effective treatment- tremor treatment- this disease since it's progressive strips a person of their self-worth, self-confidence, and robs each person's self-identity. As a person's world shrinks because you're not able to do the functions you use to, it can also lead to other problems like alcohol abuse, PTSD, or thoughts of "what is the use to continue through this." I know. I've been there.

That ends when an unpaid patient advocates so that other ET sufferers may not have to experience the harmful debilitating effects of ET like I did. I tell my story today so that Medicare and CMS can understand why the Cala system is uniquely suited to people with hand tremors just like me.

I hope this helps CMS understand the positive impact this device has on patients with essential tremor.

Thank you for taking time- pardon me- to listen to my story and my journey in dealing with essential tremor. I am open for any questions that folks may have. Thank you.

Michael Hanna (00:14:10): Thank you for coming on the call this morning, Mr. Duncan. We appreciate it and we appreciate you taking time from your schedule to add your comments.

We'll now move to the next commenter. Dr. Dhira Khosla, are you on the line this morning?

Dr. Dhira Khosla (00:14:30): I am. Thank you. Good morning everyone and thank you for the opportunity to present today.

Next slide, please.

My name is Dhira Khosla and I'm a board-certified neurologist.

I have served as a medical director at Cala Health for the past two years and I receive compensation in that role.

I completed my neuromuscular fellowship at Stanford University and practiced in the San Francisco Bay Area community for 13 years prior to joining Cala.

Cala Health designs, manufactures, and is the sole distributor of the Cala TAPS Therapy systems - the only non-pharmacological non-invasive medical therapy clinically validated to relieve upper limb tremor symptoms in essential tremor or ET.

As noted on the left, I will provide a brief review of TAPS therapy and then focus my comments on clinical evidence that we strongly believe supports Medicare coverage for external upper limb tremor stimulators that deliver TAPS therapy.

I will focus specifically on patients with severe ET who demonstrate improvement and therapy adherence in an initial trial period.

Next slide, please.

Let's take a moment to briefly review the external upper limb tremor stimulator of the peripheral nerves - code K1018, which delivers transcutaneous afferent patterned stimulation or TAPS therapy to relieve hand tremors in patients with ET.

On the left, you can see the neural circuitry targeted by TAPS. As noted, this is the same circuitry targeted by deep brain stimulation.

As noted on the right, Cala Trio and Cala kIQ are the only TAPS devices commercially available in the United States.

Both devices deliver the same TAPS therapy, with Cala kIQ cleared by the FDA as being substantially equivalent to the prior version of the device, the Cala Trio.

Next slide, please.

Before diving into the clinical evidence, I would like to briefly review recent updates from the Department of Veterans Affairs at a recent literature review that validates TAPS therapy as standard of care treatment for patients with medication refractory ET.

This policy and the evidence review were not referenced in the draft LCD, but we believe provide important context on the ET treatment algorithm and acceptance of TAPS therapy as an effective therapy option.

As noted on the left, the Veterans Health Administration established a national coverage policy for TAPS therapy in 2020.

This VA policy is structured similarly to the proposal I will discuss today, in that positive coverage is provided for disabling medically refractory ET.

The VA policy also includes a trial period and requires a follow-up evaluation in order to continue coverage.

On the right, the UpToDate guidelines evaluate and summarize a process to diagnose and treat a patient with ET.

The clinical evidence supporting the evidence of TAPS therapy resulted in a recommendation for the use of Cala Trio as a treatment option for medication refractory ET patients.

The consensus guidelines published by the International Essential Tremor Foundation discussed in the draft LCD support the use of TAPS therapy.

The VA policy and UpToDate recommendations discussed here, along with the IETF guidelines, demonstrate that TAPS is a recognized treatment in the neurology community.

Next slide, please.

Let me briefly summarize our response to the draft LCD. We strongly believe that when prescribed to relieve disabling hand tremors in Medicare beneficiaries with severe ET, the clinical evidence and generally accepted standards of care support a favorable reasonable and necessary determination for TAPS therapy systems.

We request that Medicare reconsider the draft LCD and instead establish coverage for TAPS therapy devices for Medicare beneficiaries with severe ET that restricts their ability to perform upper limb related activities of daily living such as eating, drinking, and writing, who have failed medication therapy and who are not candidates for deep brain stimulation.

Finally, as the evidence we will discuss also shows, patients who meet minimum symptom improvement and device use criteria in the first 30 days of use are highly likely to continue using consistently and achieving long-lasting tremor relief.

We believe these data are consistent with this establishing coverage under a trial period process consistent with a national coverage policy adopted by the VA and standards of care for other neuro-stim devices and items of DME.

Next slide, please.

As I mentioned, previously published and forthcoming data demonstrate TAPS provides consistent tremor relief in Medicare age ET patients who meet the severe ET subgroup criteria in the panel on the left.

These criteria include patients age 65 or older who are diagnosed with ET, are severely impacted in their ability to eat, drink, or write, and have failed at least one first line ET medication.

For the Bain & Findley Activities of Daily Living, a score of three indicates that the patient can only perform eating, drinking, or writing tasks with a lot of effort and a score of four indicates that the patient cannot perform a task at all. Over the next few slides, I will review results from several existing and forthcoming publications listed here.

First, in the double-blinded sham-controlled RCT published by Pahwa et al, I'll discuss how sub analysis of patients meeting the severe ET subgroup criteria met the primary as well as additional endpoints.

Second, I will present data from an RCT that will be published by CVS Health Clinical Trial Services and show how TAPS outperforms standards of care tremor relief during one month of home use.

After that, I'll discuss findings from several studies supporting the duration of tremor relief provided by TAPS therapy, in response to the draft LCD's question on the duration of treatment effect.

Lastly, I will highlight data from the PROSPECT trial, as well as forthcoming evidence from the ongoing real world evidence study, both of which show that severe ET patients who met certain criteria in the first 30 days of use showed consistent improved tremor outcomes and device adherence out to three and 12 months.

Next slide, please.

Let's turn to the trial by Pahwa. As a clinician, I can understand the comment from the draft LCD observing that the study missed the primary endpoint and evaluated a heterogeneous patient population, but there are two other observations that I believe are important in the consideration of this study.

First, it's notable that the study demonstrated statistically significant improvement in patient-rated Bain Findley ADL scores. The ability to perform these tasks, is how I would evaluate the patient in the office. So if TAPS there can result in an improvement in ADLs, that is what is meaningful to patients.

Second, the data here- that's shown here on the slide- focus on the treatment effects seen in a more homogeneous population who satisfied the severe ET subgroup criteria mentioned earlier.

Within this population, the study met the primary endpoint as well as additional endpoints, demonstrating that severe ET patients have a greater and more consistent improvement in tremor relief than sham.

Next slide, please.

Another study strengthening the evidence supporting TAPS therapy's effect include the new results just recently announced by CVS Health Clinical Trial Services. This 276-patient randomized study enrolled 188 Medicare Advantage patients and 88 commercial patients from AETNA's managed care database.

Patients were randomized, one to one, to one month of treatment or standard of care in a home use environment.

The study met its pre-specified primary and secondary endpoints with patients in the TAPS treatment arm showing a statistically significant reduction in tremor power and clinically significant improvement in their ability to complete upper limb ADLs than patients who continued standard of care without TAPS therapy.

Next slide, please.

Furthermore, amongst the 160 severe patients of Medicare age, the effect size in the treatment arm was even larger when compared to the standard of care arm, both with respect to improvement in tremor power and ADLs.

We believe this new analysis, which we expect to be submitted for publication in the very near term, addresses multiple questions raised in the draft LCD.

Next slide, please.

On this slide, we summarize data across several studies demonstrating that patients can achieve periods of tremor relief both during and after stimulation sessions.

In PROSPECT, patients self-reported an average duration of benefit of 94 minutes. This result is consistent with the objective measurements in the Yu et al study with relief both during the 40 min stim session and for 60 min afterwards as shown here.

Analysis of real-world usage also indicates that patients can use successive simulation sessions to obtain extended tremor relief.

Next slide, please.

Collectively, we believe the studies and data presented on the prior slides show that patients with severe ET who use TAPS therapy achieve very consistent improvements in their tremor related symptoms.

These improvements are shown both in reduced tremor power, but much more importantly are demonstrated by patients reporting that they are better able to complete ADLs like eating, drinking, and writing following stimulation.

This newfound ability to complete their ADLs with TAPS therapy is something these patients were

not able to achieve with medication.

On this slide and the next, we summarize additional data analysis to identify the patients who have been clearly shown to maintain this clinical benefit over longer term use of the device.

The box on the left lists the criteria we use to define the group of patients with a high degree of response to therapy and adherence in their initial month of TAPS therapy.

Data collected at the baseline visit was used to identify 138 patients from the PROSPECT study who meet the criteria for severe ET subgroup.

In PROSPECT after the first baseline visit patients were asked to use TAPS twice daily at home for 30 days and then return for visit two. These one-month data were used to identify patients who had average uses of TAPS therapy at least five days a week, showed at least 50 percent reduction in median tremor power, and at least 1 point improvement in their severely impacted ADL task. 54 out of the 138 patients in the severity subgroup met this criteria.

After the second visit, patients were asked to continue daily home use and return for a final visit at three months.

Next slide, please.

This figure shows the three months result among the subgroup of severe ET patients who met the trial criteria.

All of the patients showed tremor power improvement. 94 percent of them showed at least 50 percent improvement at three months with a median 68 percent tremor reduction.

Additionally, at the three-month time point, 84 percent of these patients improved by at least one category of severity in their eating, drinking or writing ADL task.

These results highlight the utility of a one-month trial in identifying patients who will consistently use and obtain clinical benefit from TAPS therapy.

Next slide, please.

The study presented on this slide shows that this effect lasts and extends out to at least 12 months.

In the Medicare age population of an expanded RWE by Lu, that is currently under review, 96 percent of the patients meeting this suggested trial criteria showed tremor power improvement at 12 months with four out of five patients experiencing at least 50 percent improvement. This shows that Medicare age patients who met the 30-day trial criteria continue to receive benefits for at least one year in real world usage.

Next slide, please.

Based on these strong outcomes, we believe adopting coverage through a trial period is consistent with clinical evidence along with coverage of other items of DME and neuromodulation devices.

Adopting coverage of TAPS therapy through an initial trial period is supported by clinical evidence just reviewed and enabled by the TAPS Physician Portal. Based upon the analysis of TAPS and patients with severe ET, we believe the evidence supports an initial trial period.

Next slide, please.

Michael Hanna (00:27:44): You're coming up on the two-minute mark Dr. Khosla.

Dr. Dhira Khosla (00:27:47): Okay, thank you. In conclusion, I strongly urge you to reconsider offering coverage in the narrow segment of patients with the greatest unmet need. We have outlined our recommendation here as it relates to proposed initial coverage and then proposed reevaluation following the trial period. Thank you for your time and time permitting I'd be happy to take any questions. Thank you.

Dr. Sunil Lalla (00:28:22): Thank you, Dr. Khosla-

Michael Hanna (00:28:22): Thank you so much, Dr. Khosla-

Dr. Sunil Lalla (00:28:22): I was just-

Michael Hanna (00:28:24): Go ahead, Dr. Lalla.

Dr. Sunil Lalla (00:28:26): Yeah, I was just gonna say thank you, Dr. Khosla. I don't have any questions.

Kip Ludwig (00:28:38): Hello, can you hear me?

Michael Hanna (00:28:41): Yes, sir, is this Mr. Kip Ludwig?

Kip Ludwig (00:28:43): This would be Mr. Kip Ludwig. Am I ready to roll?

Michael Hanna (00:28:45): Wonderful. You have the floor, sir.

Kip Ludwig (00:28:48): Thank you very much. So my name is Kip Ludwig and I am currently an associate professor in the departments of biomedical engineering and neurological surgery at the University of Wisconsin-Madison and co-director of the Wisconsin Institutes for Translational Neural Engineering.

My lens specifically is doing work on understanding how invasive and noninvasive neuromodulation therapies can induce both wanted and unwanted changes over time at the biomolecular cellular and network levels. I previously served as the program director for neural engineering at the National Institutes of Health where I co-led the translational devices program at the neurology institute, including the deep brain stimulation portfolio. I also led the trans NIH programs under the White House “Bring Initiative” and a trans NIH planning team to develop the “Spark Program”, an initiative to fund advances in neuromodulation therapies. I am not currently compensated by Cala Health, but was previously a consultant to the company serving on their scientific advisory board and received compensation in that role.

I’m here today to share my perspective on TAPS therapy and encourage the Medicare contractors to support access to TAPS for Medicare patients. Two areas particularly stood out to me in the proposed LCD’s description of TAPS and what seemed to be the remaining questions important to Medicare’s- Medicare’s coverage decision, the duration of benefit following stimulation and potential long-term effectiveness of TAPS therapies without habituation or loss of effect.

I thought I could bring my experience in neural modulation, both implanted and noninvasive, to provide the scientific basis for the clinical evidence demonstrating that TAPS therapy continues to be clinically effective for long-term users and provides primary symptom relief extending 60 minutes or longer after stimulation.

Based on results from deep brain stimulation or more simply DBS, it’s reasonable to ask if a noninvasive treatment targeting the thalamus might have habituation over time.

To address this concern, I’m going to outline the leading theories on why there is habituation to DBS causing the treatment to be less effective over time. I will then outline why I believe, and I think the data supports, that the Cala Health TAPS therapy is very different than DBS in terms of potential habituation.

Essential tremor is characterized by a slowly progressive action tremor usually affecting both upper extremities. Unfortunately, this pathological oscillation does not emerge from a single oscillator in the brain, but from an oscillatory network, including a little cerebellar system, the thalamus, and cortical motor regions.

The thalamus is an attractive target for interrupting this oscillatory network as it is a relay of information from cerebellum to cortex. Delesioning of the thalamus, known as thalamotomy, has been performed to control tremor in ET since the 1950s. The thalamotomy has a significant risk of creating new neurological deficits. DBS was proposed as an alternative to thalamotomy in the 1980s ultimately being approved- FDA approved in 1997. DBS directly stimulates neurons and thalamus continuously, twenty-four seven, at high frequencies between 100 to 200 hertz. These high rates are fundamentally required to cause a general inhibition of thalamic relay neurons which disrupt oscillatory activity.

Although DBS of the thalamus has shown a significant benefit in treating tremor, The decreased efficacy of DBS to treat tremor over time is well documented.

There are several potential players causing this change in efficacy over time. First, DBS is an acute symptomatic treatment for oscillatory neural activity resulting in tremor instead of solving the underlying problem causing the oscillatory activity.

DBS of the thalamus does not prevent the disease itself from progressing and over time this progression leads to increased tremor severity ultimately limiting the impact of DBS.

Second, the targeting of the ventral intermediate nucleus and thalamus with DBS electrodes needs to be very precise. Unfortunately, as the brain pulsates within cerebral spinal fluid, with each heart beaten breath, DBS electrodes have been shown to migrate out of position over time. Movement of these electrodes limits the impact of DBS on tremor activity over time. Finally, and perhaps most importantly, DBS directly applies an electric field to thalamic neurons continuously and stimulates at non-naturally high frequencies. This unfortunately creates multiple potential

sources of habituation. Similar how you stop feeling your clothes after you put them on, it is well known that your brain tends to filter out continuous input over time. This is because continuous, unchanging stimulation, there is no new information that is physiologically relevant over time, so your brain learns to ignore it. The same is true for this constant stimulation to thalamic neurons in DBS.

In addition, by directly applying electrical stimulation within the brain at frequencies that are well beyond sustained natural neural firing patterns It forces neuronal and non-neuronal cells to adapt over time to this changed environment.

Honestly, it's like asking me to run a marathon right now with you. Given my lack of exercise the last eight months, I might try to keep up with you for the first mile or two, but by mile five I'm either walking, keeling over dead or grabbing an Uber home. This is where the Cala Health TAPS therapy is very different than DBS in my view, and therefore unlikely to experience the same problem with habituation.

The TAPS therapy device measures the speed of each patient's tremor and then applies bursts of stimulation that alternate between the median and radial nerves at the frequency of the tremor to acutely disrupt it. The median and radial nerves project to the thalamus and when stimulated at the wrist, send naturally occurring signals that eventually reach the thalamus instead of blasting thalamus directly with a high intensity electric field at non-natural frequencies. The natural inputs to the thalamus are being activated only intermittently and at the low natural frequency of the tremor. There's also no long-term electrode movement to be concerned about as the device is non-invasive.

Taken together, these design innovations should dramatically limit the habituation and support the long-term effectiveness of TAPS therapy compared to non-natural, continuous direct stimulation of the thalamus at high frequencies used in DBS.

Second, I also want to discuss why I believe the evidence shows TAPS therapy reduces tremor for a sustained period after active stimulation is completed. TAPS therapy putatively works by fundamentally changing thalamic behavior through a mechanism known as Coordinated Reset introduced by Peter Tass.

As I mentioned before, tremor is in part due to neuronal cells unnaturally oscillating together. The median and radial nerves connect to different neuronal cell populations within thalamus. By stimulating first the median nerve, and then the radial nerve separately and out of phase, this causes the two different cell populations to activate at different times instead of in sync. This is intended to retrain neurons within the thalamus to learn to activate separately from each other over time. In this way, the Cala Health TAPS therapy is not only working as an acute disruption to tremor circuits like DBS, but alters the pattern of neurons within the thalamus after stimulation ends. We see the sustained effect is reported by patients in the studies of TAPS therapy and there is notable recent evidence that shows a similar post-stimulation duration of effect when Coordinated Reset strategies are attempted through traditional DBS electrodes. When Coordinated Reset is employed, a change in the response in neurons isn't a bug for TAPS therapy, it's an intended feature designed to provide durable tremor relief after stimulation is completed. I hope my explanation helps to clarify why I believe the TAPS therapy effect will not decrease over time, unlike DBS.

To wrap up my comments, I strongly encourage Medicare to reconsider your initial proposal to find TAPS not medically reasonable or necessary, as I believe its effect is supported by the clinical evidence and underlying science.

I would be happy to answer any questions or expand on these or any other areas in my written comments.

Michael Hanna (00:37:01): Thank you, Mr. Ludwig. I appreciate your comments this morning. We will re-mute your line. And our final speaker today is Dr. Kelly Lyons. Kelly, we should have your line open momentarily.

Dr. Kelly Lyons (00:37:13): Hey, can you hear me?

Michael Hanna (00:37:15): Yes ma'am, your audio is coming in clear.

Dr. Kelly Lyons (00:37:18): Okay, thank you. Well, good morning. My name is Kelly Lyons. I'm a research professor of neurology at the University of Kansas Medical Center. I obtained my PhD in 1993 from the University of Kansas and have been researching essential tremor Parkinson's disease and other movement disorders for over 30 years. I currently consult for several companies that develop medications and surgical procedures for ET. However, I do not and have not received payments from Cala Health.

Next slide, please.

Oh, we never got my slides.

Michael Hanna (00:37:50): That's correct, Dr. Lyons. We did not receive them.

Dr. Kelly Lyons (00:37:54): Okay. Anyway, I serve as the president of the International Essential Tremor Foundation or IETF. The IETF was founded 35-years ago in 1988 as a nonprofit organization dedicated to meet the needs of patients with essential tremor and the physicians who care for them.

I've been involved with the IETF since 1997 as a board member, served as vice president from 2002 to 2008, and have served as president since 2008.

The IETF is the largest organization of its kind, providing a singularly focused voice for ET patients and the providers who care for them. We focus on increasing awareness, supporting research and providing education for persons with ET, their caregivers and healthcare professionals.

ET can be debilitating and significantly worsen quality of life, making it nearly impossible for some persons with ET to perform basic daily activities such as eating, drinking, writing, using a computer.

Unfortunately, ET is often overlooked as a disease that does not kill you and consequently many patients do not receive treatments that could dramatically improve their health-related quality of life and help them to remain independent.

One goal of the IETF is to increase awareness of all beneficial treatment options, knowing that each individual has different concerns and may respond differently to various treatments. For example, some may not be able to tolerate available medications due to side effects or their tremor may not respond to the medications.

Many patients are not candidates for surgical- for a surgical procedure to improve their tremor and therefore noninvasive treatments such as TAPS could be the only beneficial alternative for these patients. Furthermore, as an organization devoted to awareness, education, and the treatment of ET, the IETF strongly supports access to effective therapies and technology that can relieve ET symptoms.

Over the years, the organization has evaluated and provided recommendations for use of therapies that enable ET patients to perform activities that ET otherwise prevents them from accomplishing, allowing these individuals to regain their ability to live independent lives. For instance, when payers, including Medicare, were determining whether to provide coverage and access for MRI guided focus ultrasounds, the IETF engaged with payers to highlight the need for patients to access that alternative treatment option to deep brain stimulation.

Our goal and purpose is treatment agnostic. We only seek to ensure that people suffering from debilitating ET have access to effective treatment options. In addition to myself and our staff, the IETF has a board of medical and scientific advisors who are thought leaders in essential tremor through years of experience in treating and researching this disorder, often as practitioners and directors of some of the most well recognize movement disorder clinics and research centers throughout the United States. That 30-member board is responsible for reviewing research grants, writing articles for our publications, speaking at IETF events, answering patient questions and advising the board on research and treatment related issues.

Next slide, please.

It's long been recognized by the IETF that these expert clinician- and these expert clinicians that there's a significant unmet need in their treatment of ET patients, particularly those who cannot tolerate medication, or for whom medication is no longer working. The IETF conducted an online survey of about3,000 patients to better understand their treatments and the treatment gaps that remain.

Over 30 percent of the respondents could not tolerate or received no benefit from medication, and less than four percent had undergone a surgical procedure for their tremor.

It was concluded that additional treatment options are critical for the effective treatment of ET. In 2021 I worked with two other colleagues to develop a standard guide that could summarize ET diagnostic considerations currently available, medical and surgical treatment options, and currently available assistive devices.

Based on our review and clinical experience, a treatment algorithm of available treatment options was created. I'm a researcher with more than 25 years of experience with ET and I work with a multidisciplinary set of authors, including Dr. Holly Shill and Dr. Kelli Reiling-Ott. Dr. Shill is head of our medical advisory board and a movement disorder expert practicing at Barrow Neurological

Institute. She's been seeing movement disorder patients since 1999 and has treated over1,000 ET patients. Dr. Ott is an occupational therapist experienced in movement disorders and worked in a movement disorder clinic at the University of Kansas Medical Center for over ten years.

As part of our review we conducted a literature review related to all available therapies for ET including the Cala Trio, which incorporated studies available at that time while also considering the realities of the treatment gap that existed at the time between drug therapies and surgical procedures like DBS and focus ultrasound.

Though this evaluation did not follow a formal grading methodology, it was a rigorous review and evaluation of clinical evidence across ET therapy options to develop a uniform set of treatment recommendations.

Based on the review we arrived at the decision that the Cala Trio or TAPS therapy can be considered when a patient has severe tremor, has considerable difficulty in performing tasks such as eating or drinking, and has failed a first line oral therapy.

Due to its effectiveness and because it is not invasion- invasive or permanent we recommended TAPS therapy before progressing to the surgical procedures that carry greater risks of adverse effects.

Given the IETF's leading role in evaluating and disseminating treatment information for ET providers and patients, I respectfully ask that you consider the recommendations of the International Essential Tremor Foundation. Our organization serves as a resource for other organizations with a wider focus such as the American Academy of Neurology, which specifically sought out the IETF's endorsement when they conducted their last substantive update to their ET treatment guidelines in 2011. We did provide our endorsement at that time. Unfortunately, these guidelines from 2011 are now quite out of date despite the AAN reaffirming them in 2022 without any main material update.

Much has changed in ET treatments since 2011 including the availability and proven efficacy of MRI guided focused ultrasound which is not referenced in the AAN guidelines as well as the availability and efficacy of TAPS therapy devices we're discussing today.

This is in part why we developed our own treatment guide, which we can regularly update to take account of new treatment and evidence on a more rapid basis and provide information to providers and patients. In closing, I would emphasize again the very negative impact that untreated ET has on patients' ability to lead independent lives.

People unfamiliar with severe tremor can often take for granted the ability to get dressed in the morning, use utensils to eat or drink, or write or type- write or type a letter.

People with ET don't take these things for granted, and any treatment that's been demonstrated to help them regain their function and health related quality of life has value and should be accessible to ensure a non-invasion- noninvasive, nonmedication treatment option can be available to the subset of ET patients who need it.

We urge that Medicare coverage be granted for TAPS therapy devices, consistent with the IETF ET guideline recommendations.

Thank you for giving me time to speak with you this morning.

Dr. Sunil Lalla (00:45:42): Thank you, Dr. Lyons, and thanks to all members of the public and stakeholders for your thoughtful comments today.

Dr. Robert Hoover (00:45:50): Dr. Lalla, this is Dr. Hoover.

Dr. Sunil Lalla (00:45:51): Yes Dr. Hoover?

Dr. Robert Hoover (00:45:54): I actually had a question for Dr. Lyons if she would. Dr. Lyons, any speculation on why the American- they sought out the endorsement of the International Essential Tremor Foundation for their other guidelines, any speculation or any feedback from them about why TAPS therapy and deep brain stimulation were not included, and I believe you said deep brain stimulation were not included in their 2022 guidelines?

Dr. Kelly Lyons (00:46:21): Yeah, it was actually the MRI guided focus ultrasound that was not included.

Dr. Robert Hoover (00:46:27): Excuse me. Yes, correct.

Dr. Kelly Lyons (00:46:29): And I do, we actually did question them on this, I think it has a lot to do with the process for creating guidelines, it's a very drawn-out process. The literature review is often done a year or two prior to the actual publication coming out and my understanding is

that at the time that the literature review was done, the focused ultrasound and the Cala Trio publications were after their cutoff date for the update to the guidelines. And we have asked when the guidelines would be updated again and we have not received a response on that.

Dr. Sunil Lalla (00:47:15): Dr. Lyons, is that- is that pretty typical, once a decade sort of thing? I would think that they would be updated on at least an annual or a bi-annual basis.

Dr. Kelly Lyons (00:47:27): Like I said, the process is extremely time consuming, a very long process to do the complete literature reviews, all of the grading systems that they use and the academy and neurology is focused on all neurologic disorders. So I think given the number of disorders and the- the time and- and manpower required to do these they just, unfortunately, do not get updated as- as much as- as we would like to see them updated as providers and researchers.

Dr. Sunil Lalla (00:48:04): Certainly. Does- do any of the other medical directors have any questions, Drs. Jenny, Ballyamanda, Dr. Chan-House, any other questions for Dr. Lyons? Hearing none, again, thanks to all the members of the public and stakeholders for your comments today.

Once again, please do remember to send your comments in writing and if you have any full text, peer-reviewed articles to help support your comments, that are not already included in the bibliography, please send them along as well.

As noted earlier, the comment period will end on Saturday July eighth. Once we've collated and considered all of the comments received during the open period, we'll make any necessary changes to the proposed LCD content that are needed as a result of the comments received and then post a final LCD along with the response to comments document.

The final LCD will take effect a minimum of 45 days following the posting of the final LCD. For any updates, please refer to the DME MAC websites.

Thank you to Michael Hanna for moderating and for- and to everyone who participated in today's meetings. We look forward to your written comments and we'll go ahead and adjourn the meeting at this time. Thank you so much.

Dr. Robert Hoover (00:49:40): Thanks everyone.