CENTERS FOR MEDICARE AND MEDICAID SERVICES

Medicare Evidence Development & Coverage

Advisory Committee

Zoom Virtual Meeting

May 21, 2024

Centers for Medicare and Medicaid Services

7500 Security Boulevard

Baltimore, Maryland

Panelists

Chairperson
Joseph Ross, MD, MHS

Vice-Chair
Sanket Dhruva, MD, MHS, FACC

Voting Members
Brian Isetts, RPh PhD, BS-Pharm
Alexander Fanaroff, MD, MHS
Melissa M. Garrido, PhD, BS
Fred Kobylarz, MD, MPH
Joy H. Lewis, DO, PhD, FACP
Eric Wall, MD, MPH
Heather Young

HCFA Liaison
Tamara Syrek Jensen, JD

Patient Advocate
Naftali Z. Frankel

Industry Representative
Mark D. Carlson, MD, MA

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PANEL PROCEEDINGS

(The meeting was called to order at 10:00 a.m., Tuesday, May 21, 2024.)

MS. HALL: Good morning and welcome committee chairperson, vice chairperson, members and guests to our virtual MEDCAC meeting.

I am Tara Hall, the Medicare Evidence Development and Coverage Advisory Committee MEDCAC coordinator.

The committee is here to discuss the devices for self-management of Type 1 and insulin-dependent Type 2 diabetes. This meeting will examine the growing challenges associated with the decreased level of evidence of certain new and innovative technologies. By voting on specific questions and by their discussion, MEDCAC panel members will advise CMS about the ideal health outcomes and research studies of devices for diabetes self-management, appropriate measurement instruments, and adequate follow-up durations to help them provide clarity and transparency in future national coverage analysis.

The following announcement addresses

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

We ask in the interest of fairness that all persons making statements or presentations disclose if you or any member of your immediate family owns stock or has another formal financial interest in any company that is related to this topic, diabetes or insulin. This includes speaker fees, salaries, grants and other support.

If you require a financial disclosure statement, please email Ruth McKesson so she can send you the form for completion. Her email is ruth.mckesson@cms.hhs.gov.

We ask that all presenters please adhere to their time limit. We have numerous presenters and a tight agenda; therefore, we cannot allow for extra time. During each presentation presenters will receive reminders

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informing them how much time they have remaining to help them stay within their allotted time. Speakers will receive a prompt two minutes prior to their speaking time to insure they are ready to present.

During the open public comments, attendees who wish to address the will have that opportunity on a first come basis.

Please email Ruth McKesson if you want to address the panel by 8:30 a.m. eastern standard time -- excuse me, 10:30 a.m. eastern standard time.

For the record, voting members present for today's meeting are Sanket Dhruva, Brian Isetts, Heather Young, Melissa Garrido, Eric Wall, Alexander Fanaroff, Naftali Frankel, Fred Kobylarz and Joy Lewis. Nonvoting panel members are Joseph Ross and Mark Carlson. A quorum is present and no one has been recused because of conflicts of interest.

The panel, including nonvoting members, will participate in the voting dialogue but the nonvoting members will not participate in the online voting. The voting results will be available on our website

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following the meeting.

We ask that all speakers state their name each time they speak, speak slow and concise so everyone can understand, speak directly into microphones, and do not use your speaker phones to help achieve best audio quality. Ensure your devices are on mute when not speaking. While speaking, please place ring on silent, remove pets from the area and anything else that will minimize distractions and limit background noises.

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

In the spirit of the Federal Advisory Committee Act and the Government in the Sunshine Act, we ask that the advisory committee members take heed that their

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conversations about the topic at hand take place in the open forum of the meeting.

We are aware that meeting attendees, including the media, are anxious to speak with the panel about these proceedings. However, CMS and the committee will refrain from discussing the details of this meeting with the media until its conclusion. Also, the committee is reminded from discussing the meeting topics during the break.

I just want to remind everybody, if you want to speak, please send an email to Ruth McKesson by 10:30 this morning.

And now I would like to turn the meeting over to Steve Farmer.

DR. FARMER: Thank you so much. CMS remains committed to modernizing its coverage pathways to direct, efficient, predictable and transparent coverage. We are equally committed to covering items and services based on scientifically sound clinical evidence and with appropriate safeguards.

When developing premarket clinical studies, CMS believes manufacturers will be better positioned for multiple product

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development stages if they anticipate both FDA and CMS expectations.

For coverage decisions, CMS specifically requires evidence of benefit in the Medicare population, which is often older, has more complex medical records and is often inadequately represented in clinical studies used to obtain FDA market authorization.

As part of CMS' commitment to improve the transparency of the NCD process, CMS expects to finalize guidance soon about how we review bodies of evidence during national coverage analyses and our expectations for coverage with evidence studies.

We also expect to publish proposed guidance on fit-for-purpose study designs soon.

CMS is developing this clinical endpoints guidance series to improve to the predictability and transparency of our evidence reviews for treatments addressing these areas. These reviews will assist interested parties seeking Medicare coverage for an item or service such as a drug or device in understanding the typed of evidence CMS expects to review when making NCDs.

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Please not that clinical endpoint guidance documents do not review specific technologies and are not national coverage analyses or NCDs. Instead, they identify health outcomes of interest to CMS when reviewing technologies and considering reasonable and necessary NCDs.

For the current review, CMS engaged with a contractor to complete a clinical endpoints review of devices for self management of Type 1 and insulin dependent Type 2 diabetes. This topic was selected because of the high burden of diabetes in the Medicare beneficiary population, and because technologies are being developed to treat this condition.

This review compiles a succinct list of outcomes and instruments that represent the most relevant meaningful outcomes that will be used to evaluate these devices for Medicare beneficiaries. It also identifies any published evidence that defines clinically meaningful differences for each endpoint.

The clinical endpoints review and the input from this MEDCAC will inform the

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development of guidance for this therapeutic area. This guidance is intended as a reference for clinical investigators developing studies and for CMS staff who may review studies in this therapeutic area. CMS would consider endpoints other than those identified in this review and this MEDCAC if there is good reason to include them. Even so, CMS will strongly prefer endpoints that have been validated and for which an MCID has been established.

We hope that the MEDCAC will consider several important factors in this discussion today.

The appropriateness of each endpoint for the Medicare population. CMS recommends that investigators carefully consider the intended recipients of an item or service when designing clinical studies, such that the findings may be credibly generalized to the relevant Medicare beneficiary population, including important subpopulations.

Second, the ability of established clinically meaningful differences. CMS does not recommend any specific clinical endpoint or instrument identified in this review but

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generally recommends that the body of evidence address a range of outcomes that reflect multiple attributes of an item or service. And when choosing among the clinical endpoint options, CMS recommends that clinical studies prioritize validated endpoints and instruments, and those with well established or published minimal clinically meaningful important differences, because those study findings using those endpoints are more readily interpreted.

And thirdly, the appropriate duration of followup. CMS may have difficulty reaching conclusions regarding potential risks and harms associated with an item or service if the studies lack sufficient followup to demonstrate the durability of improved health outcomes.

CMS thanks the MEDCAC afternoon and the public for your thoughtful deliberations on this topic. I look forward to this meeting, and now I would like to turn to my colleague, Terry Rogstad to summarize the findings of the clinical endpoints review. Terry?

MS. ROGSTAD: Good morning. I'm trying to get my screen shared. All right. Is my slide showing okay?

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DR. YOUNG: You're not in presentation mode.
DR. ROSS: And Terry, we can't see you on video either.
MS. ROGSTAD: All right, okay. So I'm going to stop sharing for a second. All right. Is it still on in presentation mode?
DR. ROSS: No, it looks like you're working now, and we can see you on video.
MS. ROGSTAD: Great -- I will be presenting --
MS. HALL: Terry, can you stop sharing your screens? We're going to do all the slides.
MS. ROGSTAD: Stop sharing my screen?
MS. HALL: Yes, Leah will present the slide.
MS. ROGSTAD: I'm sorry, okay. That makes it easier. I'm a little confused. Do people see the slide?
DR. WALL: Not yet, we just see you.
MS. ROGSTAD: All right. Leah, are you ready to put that in presentation mode? All right.
I will do a very quick review of the

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clinical endpoints review which as Steve said, was a literature review that CMS commissioned to an outside contractor. There is an executive summary of the CER, it is a document that was posted online and if you haven't done so already, it would be helpful to open that document on your screen or have a hard copy on your desk to refer to during the meeting. There's more detail in that executive summary than what I'm going to present with the slides. Next slide please.
So the CER started out with some background information. There are two key measures of high blood sugar in people with diabetes. A1c represents the percentage of red blood cells with sugarcoated hemoglobin and it is usually averaged over the past three months. And since it is an average value, it doesn't give any information about glycemic variation, so other measures are taken to determine whether the blood sugar is in an acceptable range or whether the patient is under a condition of hyperglycemia, too much sugar in the blood, or hypoglycemia, blood sugar is too low.

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There is a good general consensus on the optimal blood glucose range of 70 to 180 milligrams of sugar per decaliter of blood.
Hypoglycemia is particularly an issue for older adults and accounts for more hospital admissions than does hyperglycemia. Hypoglycemia can cause dizziness, weakness, trouble speaking and confusion. With older adults that may be on medications not related to their diabetes that can also contribute to these symptoms, and of course risk of falling in older adults can make these symptoms more serious.
Hyperglycemia can cause ketoacidosis which happens when the body starts breaking down fat instead of sugar because of a lack of insulin, and this can lead to a dangerous buildup of ketones in the blood. Next slide please.
Devices for self managing diabetes may be appropriate for patients with Type 1 or insulin-dependent Type 2 diabetes. The three devices that were included in the CER were continuous glucose monitors, insulin pumps, and closed loop systems which included a CGM. Next

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slide please.
The CER involved a systematic search of the published literature between the years 2018 and 2023 and collected research reports on the three device types. Those reports could be systematic reviews, formal consensus statements or prospective clinical trials, which were defined as RCTs, nonrandomized studies and single-arm trial. Several study designs were excluded.
When the panel subcommittee met, they pointed out that the inclusion-exclusion criteria are a bit confusing. It is not readily apparent how a nonrandomized study or a single-arm trial is different from prospective observational studies which were excluded, and we never could figure that out, so we looked at the studies that actually made it into the CER.
There were mostly RCTs. There were several single-arm studies. There was one study that was labeled a quasi experimental study and another one that appeared to be a cohort study. So the selection criteria matter if it means that important endpoints or outcomes were missed because certain study

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designs were excluded.

So with that in mind, the panel subcommittee considered whether from their perspective there were any important endpoints missing from the one prioritized in the CER, and those were added and appear in the voting questions along with the important clinical endpoints identified by the CER itself. Next slide.

As I said before, there is a document called an executive summary of the CER. The Tables A1, A2 and B in that document include the information I'm about to present in greater detail. Next slide.

Six statements were identified that have been issued by professional associations with recommendations on the measures that should be used to monitor patients with diabetes. The most frequently recommended measures were A1c, hypoglycemia of any level, Level 2 hypoglycemia, time in range, and Level 2 hyperglycemia. Time in range refers to the percentage of time that a patient is in, that they have blood and glucose levels in an acceptable range.

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One of the six statements was restricted to older adults and they recommended three of the five measures recommended by other statements. None of these statements defined minimal clinically important differences, and there's a typo on my slide, that should be differences, not definitions. However, three of the statement agreed on target values that clinicians can use to monitor patients with diabetes, so target values for the various glycemic measures. Next slide please.

Then the CER looked at the clinical, the primary clinical studies that met its selection criteria and found that the most frequently investigated outcomes in those studies were time in range, Level 1 hypoglycemia, A1c, and Level 1 hyperglycemia. 27 of the 69 studies enrolled older adults. They were not, those studies were not limited to older adults but they had a good number of patients over the age of 65 in the study groups. And those studies, the same outcomes were frequently investigated, plus Level 3 hypoglycemia, the most severe level of hypoglycemia.

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In the executive summary you will find a table that lists all of the surrogate markers that were identified in the primary studies including the ones less frequently cited, so those don't appear on that slide but you can get the full list in the executive summary. No MCIDs were identified in the studies or in the published systematic review of glycemic outcomes. However, the National Institute for Health and clinical Excellence in the UK, otherwise known as NICE, and the American Diabetes Association agreed that an absolute change in A1c of .5 percentage points is accepted as clinically significant. Next slide.

The other set of outcomes that appeared in the 69 studies were quality of life measures. That was the only type of patient-reported outcome that was frequently investigated and this was an endpoint in most of the studies, and in about half of the studies that focused on older adults.

Four quality of life instruments were identified and all have been validated. Three of them have been, or MCIDs have been

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identified or defined for three of those instruments. Two quality of life measures were added by the panel subcommittee and a search was made for MCIDs for those two additional instruments, but none were found. Next slide.

Adverse events were also sometimes investigated, either categorized as serious or any adverse event. However, the CER did not provide any detail on the specific events that were recorded, and no MCIDs were identified. Next slide.

The CER made some additional observations about these clinical endpoints. No studies evaluated more than three of the five endpoints most commonly recommended by the professional associations, and few studies evaluated as many as, even as many as three of those five endpoints.

The CER also observed that some of the frequently cited endpoints varied in frequency, varied in the frequency of citation according to the type of diabetes that was, characterized the patients in the study, or the type of device that was being investigated.

And perhaps the most pertinent

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observation was that time in range was the only endpoint to differ in frequency between studies that enrolled older adults than in studies that did not. The studies that included older adults were more likely to study time in range, and the difference between those studies and studies without older adults was statistically significant. Next slide.

Lastly, the CER identified four systematic reviews of studies of these devices and they focused on A1c, time in range, severe hypoglycemia and patient-reported outcomes. Next slide.

So that's the end of my summary. As I said, more detail is available in the executive summary document. Thank you.

DR. ROSS: Thank you, Terry. And Leah, you can stop sharing.

So my name is Joe Ross. I'm the acting chair, or the chair of the MEDCAC for this meeting. I want to just take a moment to thank everybody for their time and their participation. I think the biggest challenge ahead of us is the very tight timeframe in which these conversations and public comments

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will be made, and so I appreciate the CMS presentation on the clinical endpoints review holding right on time, so we are on track.

So just by short way of introduction, the MEDCAC is a group of experts that's been convened to provide advice and recommendations relating to Medicare coverage, specifically in this case the types of endpoints that should be addressed in a body of evidence regarding devices for self management of Type 1 or insulin-dependent Type 2 diabetes in older adults. And over the course of this meeting we're going to, towards the end specifically, our panelists are going to b using rating scales to indicate the importance they attach to each endpoint domain broken in to four groups that reflect the clinical evidence endpoint review that Terry just presented.

Surrogate markers, which are indirect assessments, using biomarkers, physiological measures or imaging intended to predict or act as a proxy for target outcome of interest, for example the percentage of time in hypoglycemia.

The second domain being health outcomes or direct assessments of a target

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outcome of interest, for example complications of diabetes.

The third domain being quality of life, patient-reported assessment of symptoms, burden or function, for example the diabetes distress scale.

And then device safety, for example hypoglycemia-related emergency department visits.

We will discuss the appropriateness of these measures, the ideal duration of followup that we would want to see these endpoints ascertained over, and any conventional or validated threshold for the minimal clinically important difference or MCID. And we will encourage our panelists to provide justification and rationale for their point of view when it comes time to actually use the rating skills and cast a vote.

At this point we're going to turn to the scheduled list of public comments unless any of our panelists have a specific question for CMS after the clinical endpoints review. Please just use the raise your hand function. Okay. There will be plenty of time for

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questions during deliberation.

We are going to turn to the public comments. We have a list of 13 speakers, each of whom has five minutes, and I have to just inform everyone that we will be very adherent to time, there will be no going over, and there will be an opportunity for questions and clarifications immediately afterwards; is that right, Tara?

MS. HALL: Yes, that's correct. And I Candace DeMatteis, I think I'm saying your name correctly, I apologize if I'm saying it wrong, you will be the first speaker.

DR. ROSS: Great. So I'm just going to use the timer, and Candace, the floor is yours.

MS. DEMATTEIS: Thank you. Good morning. I'm Candace DeMatteis, policy director for the Partnership to Fight Chronic Disease. We do not have any financial relationship with manufacturers of the products being discuss today or their competitors.

Diabetes, and more particularly Type 2 diabetes, is one of the most prevalent and most costly conditions for Medicare. More than 29

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percent of adults aged 65 or over in the U.S. have diabetes and diabetes is often one of a constellation of chronic conditions people covered by Medicare are managing on a day-to-day basis. Often the symptoms of Type 2 diabetes aren't discernible by the person affected until there's a major problem, leading many people living with Type 2 diabetes to go undiagnosed and under treated.

Being diagnoses with a chronic condition is an emotional event, causing frustration and a feeling of loss of control. Managing diabetes effectively means significant lifestyle changes involving diet, exercise, medication use, often including insulin and frequent glucose monitoring to minimize the impact of the disease on health.

The devices under consideration today provide meaningful tools that help people regain not only a sense of control but actual control over their blood glucose levels, control that decades of research have demonstrated is essential to prevent the predictable complications that poor diabetes control manifests. Behavior changes are best

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achieved when reinforced by regular feedback. That's an important consideration of these devices but one which I did not see mentioned within your considerations.

The substantial health disparities associated with diabetes should also be a paramount consideration. Black, American Indian, Alaskan native, Hispanic, native Hawaiian, southeast Asian and many other communities of color are significantly and disproportionately affected by Type 2 diabetes, both in terme of higher prevalence and in poorer outcomes. Those diabetes complications include blindness, amputations and premature death. Though your discussions include a focus on hypoglycemia that reality, the reality that hospitalizations for diabetes-related amputations are more than three times higher than hospitalizations for hypoglycemia should be noted. People with lower socioeconomic status and lower education levels are also affected disproportionately.

So where is the clinical, clinically relevant discussion about what imposing additional criteria on Medicare coverage will

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do for access for these people? These decisions don't happen in a vacuum without consequences, and have been used by CMS in the past to justify imposing coverage with evidence development requirements that by definition condition Medicare coverage and limit access. These are real-world consequences that impact Medicare and more importantly, the people Medicare covers. That should be considered.

In 2022 the American Diabetes Association released a study examining claims data on continuous glucose monitors, including Medicare claims. That study found that people with lower incomes and people living in states with the highest rates of diabetes, prevalence and mortality are the least likely to get access to a CGM. So the people experiencing the highest burden of disease had the least access to tools that your recommendations could make even more difficult to access.

So it's important to consider those life and death factors when you're discussing these questions. Those realities should factor heavily in your discussion and decisions today, and we urge you to consider the exercise you

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undertake not just as an intellectually or clinically interesting one, but one with real life potentially devastating consequences for some of the most vulnerable Medicare beneficiaries.

Thank you for the opportunity to share these concerns.

DR. ROSS: Thank you. Any questions from the panel? Okay. Our next speaker is Janet McGill, Dr. Janet McGill.

MS. HALL: No, the next will be Aaron.

DR. ROSS: Oh, okay. Tara, I will let you introduce the speakers because I may have an outdated list.

MS. HALL: Okay, thank you.

DR. ROSS: Aaron, whenever you're ready.

MR. TURNER-PHIFER: I think Susan was going to go next, but I don't want to jump her in line.

MS. PESCHIN: I saw that. Tara, am I going next, or is Aaron?

MS. HALL: I'm sorry, Susan, you can go. I apologize.

MS. PESCHIN: Okay, that's okay, thank

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you. Thanks, Aaron, for being willing to jump.

Hi everybody. I'm Sue Peschin, I serve as president and CEO of the Alliance for Aging Research. The alliance is the leading nonprofit organization dedicated to changing the narrative to achieve healthy aging and equitable access to care and we do receive unrestricted support from industry and others for our mission.

We're locking arms today with 25 other non diabetes organizations to oppose any efforts by CMS to restrict beneficiary access to FDA approved devices for self management of Type 1 and insulin-dependent Type 2 diabetes. We sent a letter signed by 26 organizations to Administrator Brooks-Lasure and to this MEDCAC, along with key congressional staff, and the letter is publicly available on the alliance's website at agingresearch.org and it was mailed to all of you, and I'll read just a few of the groups here so you can see the diversity of the organizations. American Kidney Fund, Melanoma Research Alliance, National Grange, National Hispanic Council on Aging, National Medical Association, Prevent Blindness and Voice of

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Alzheimer's.

And in part, the letter states we're increasingly disturbed by the CMS coverage and analysis group's creation and leveraging of research debates to justify utilization management of Part B items and services. This process of positioning this advisory committee to reevaluate clinical outcomes for an entire class of medical products that the FDA already legitimately determined to be safe and efficacious takes valuable time and resources away from researchers, clinicians and patient advocates serving people living with diabetes. No external organizations requested this evidence review or the endpoints for trials of diabetes devices, nor was the Agency for Healthcare Research and Quality consulted, and that's the HHS agency that's charged with conducting evidence reviews.

CMS instead convened a MEDCAC subgroup on its own in February of 2024 that was not publicly announced until about a month after it occurred. This subgroup reviewed a report written by an outside contractor on devices for diabetes self management and enlisted one guest

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endocrinologist to provide responses to CMS' questions. To us it raises questions about the Agency's judgment when it pursues this topic without reasonable justification in light of its struggles to manage resources.

To be clear, no one in the diabetes community asked for this. Here's where CMS' interests lie. Diabetes is the most expensive chronic disease in the U.S. That makes medical devices for diabetes self management a rich target for Medicare Part B coverage restrictions. This should not be done.

The standards of care established by the American Diabetes Association and American Association of Clinical Endocrinology unequivocally endorse the use of continuous glucose monitors and insulin pumps by people who are insulin dependent. These endorsements rest on the foundation of voluminous clinical data with scores of studies affirming th medical necessity of these technologies. The use of these devices is established science, and there is no basis whatsoever for calling them into question.

This exercise is similar to the one

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CMS staged in 2021 when mundane academic debate on targeting amyloid was leveraged to squash coverage for the entire class of FDA approved disease modifying therapies for the treatment of early Alzheimer's in April of 2022. The effectiveness of CMS' cost cutting strategy in Alzheimer's lies in the small number of Medicare related claims that have been paid for Leqembi, the second FDA approved therapy in the class. Since last July of 2023 based on claims data, only a scant four to 5,000 patients have been started on Leqembi with approximately 2,000 to 2,500 patients currently on treatment. This is a fraction of potentially eligible patients.

The federal statute authorizing Medicare starts with a noninterference clause that prohibits CMS from, quote, supervision or control over the practice of medicine or the manner in which medical services are provided, end quote. Clinicians should be able to help Medicare patients decide which interventions are best for them without complicating coverage barriers dictating care.

DR. ROSS: One minute.

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MS. PESCHIN: CMS is a payer. It's not a biomedical expert agency like the FDA or anybody's family doctor. The actions being taken by CMS on diabetes self care devices are an overreach of agency authority and undermining the public trust in the FDA, and more broadly in biomedical science itself. Ultimately the Agency and this advisory committee should not be staging research debates to vindicate itself on what's really happening here, a setup to the rationing of patient care. Thank you.

DR. ROSS: Thank you for your comments. Are there any questions for the speaker?

MS. HALL: Okay, Aaron, now you can go. Thank you.

MR. TURNER-PHIFER: Good morning everyone. Name's Aaron Turner, director of health policy at JDRF. I'm just background. JDRF is the leading global Type 1 diabetes research and advocacy organization. Our mission is to accelerate life changing breakthroughs to cure, prevent and to treat diabetes and its complications. I appreciate

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the opportunity to provide our perspective at today's meeting.

We don't have a financial conflict. However, we do work with the different manufacturers that are impacted, particularly around things like our charity walks and rides, so happy to complete documentation there, and we'll follow up afterwards.

So jumping into comments here, just as background, T1D is an insidious autoimmune disease that strikes children and adults, and is fatal without lifelong insulin therapy. Recent advances in technology have given people with T1D access to life changing devices that are allowing them to better manage their diabetes. These devices, pumps and the CGMs used with those monitors are the standard of care for everyone living with T1D and it's clear given the compelling evidence that their impact is having a positive one on folks' lives.

Closed loop systems comprised of a pump and CGM working together to deliver insulin directly to the wearer with limited input by the person represent the latest

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advancement in care. Evidence indicates that these systems are having an even greater impact, positive impact on wearers of all ages.

And now for JDRF's perspective. 20 years removed from our first grant funding a closed loop system prototype, there are multiple closed loop systems available in the market, with a growing rate of adoption by those in the T1D community. Both CGMs and closed loop are directly impactful and in a significant way in the wellbeing and livelihood of those living with T1D.

Given our decades of experience advancing care and technology, JDRF has funded and/or supported many of the studies and consensus statements cited in the endpoints review report. We're pleased to see such a thorough review be completed, happy to see all the positive data years of work and investment from the community has had. We do believe the endpoints set up by CMS to review are all relevant and important to everyone living with T1D.

We want to call attention to two endpoints in particular, time in range and

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level one hypoglycemia, level one defined as 70 milligrams per decaliter. Those are important to the delivery of care, particularly for folks with Type 1. The growing body of evidence continues to link time in range to clinical outcomes, including the development of retinopathy and further complications of T1D.

A JDRF funded 2020 study on T1D glycemic outcomes showed adults with T1D review or -- excuse me, sorry -- showed adults with T1D were avoiding one to five, on a level of one to five, only one hypoglycemic event per week to be five times as important than being .5 percent above their target A1c.

I mangled that. Basically what our study showed was that avoiding hypoglycemic events was more important to people with Type 1 diabetes than an improvement in their A1c.

As such, any consideration of endpoints should include both the time in range metrics and level one hypoglycemic metrics in addition to the other endpoints utilized by the FDA such as A1c levels and level two hypoglycemia, which is defined as 54 milligrams per decaliter.

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As highlighted in the endpoints review, MCIDs are an important metric that warrant consideration. While the prepared report notes that there is a lack of clear definition at present for MCIDs, at least a universally accepted clear definition, this currently allows care to focus on the unique patient needs at any given moment.

We caution against CMS action to establish its own MCID definition that would in any way restrict the ability of physicians to tailor care to the unique needs of the individuals living with diabetes.

We further caution against any suggestion as implied in the prepared documents for this meeting, that there is a lack of clear evidence regarding the impact of diabetes on older adults living with T1D. We do not believe that there is a fundamental difference in the physiology of older adults that warrant separate data relative to those who are younger, such as is the case that may be required for pediatric populations versus adult populations.

As shown in the data provided by

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CMS --

DR. ROSS: 30 seconds.

MR. TURNER-PHIFER: -- benefits of devices remain constant across adult age groups. For example, JDRF has supported several studies demonstrating the use of CGM in older adults, and showing statistically significant reductions in hypoglycemia relative to the standard relative to standard glucose monitoring.

A final note of caution. Here after years of research and direct advocacy by JDRF in the broader T1D community, we applauded CMS' final expansion of coverage for all approved CGMs in 2022, but we appreciate that Medicare --

DR. ROSS: Wrap up.

MR. TURNER-PHIFER: -- now covers CGMs for all people with T1D. Yet we remember with concern that it took CMS nearly a decade to provide initial access to CGMs.

DR. ROSS: Aaron, I've got to stop you. You're over time.

MR. TURNER-PHIFER: Okay. Thank you very much. I appreciate it.

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DR. ROSS: Any questions for the speaker? And I do apologize for not giving a one-minute advance, but only 30 seconds.

MR. FRANKEL: Yeah, one clarification question.

DR. ROSS: Yes, good. Go ahead.

MR. FRANKEL: To your points that you just made regarding not differentiating between the younger and elderly population, do you view that across the board in terms of when you were viewing the materials in terms of clinical outcomes and concerns for example about hypoglycemia? Is that your position as an organization, that that should not be specifically focused on for the elderly population, which may have more concerns regarding those specific clinical outcomes?

MR. TURNER-PHIFER: I think -- I'll respond two ways. The first is that organizationally our position is that you know, we've seen both in study data, but also real world evidence that the impact of these devices is a positive one across population demographics. And we also know, and I think the ADA standard of care reflects it, that

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older adults have different concerns than younger adults with respect to outcomes, particularly around avoiding hypoglycemic events.

And so there may be, as you're considering what's more important, I think we would expect those considerations to be weighted more heavily, what a person values and what their physician may value. But with respect to the underlying data about the impact of the devices, I think that we would consider it to be positive across the board.

DR. ROSS: Thank you. Tara, who's next?

MS. HALL: Laura is next.

MS. FRIEDMAN: Hi everyone. My name is Laura Friedman. I'm the vice president of regulatory affairs at the American Diabetes Association, I appreciate the opportunity to share our remarks with you today.

We do not have any specific financial disclosures to share, but we do receive funding from industry for various aspects of our operation, and we're happy to follow up if needed as well.

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A little background. ADA is the nation's leading voluntary health organization fighting to bend the curve on the diabetes epidemic. Founded in 1940, the ADA has been driving discover and research to treat, manage or prevent diabetes while working relentlessly for a cure. We review and author the most authoritative and widely followed clinical practice guide recommendations, guidelines and standards for the treatment of diabetes, and publish the most influential professional journals concerning diabetes treatment and research.

In our chapter on diabetes technology, ADA standards of care states that when coupled with diabetes self management, education and support, diabetes technology can improve the lives and health of people with diabetes, and has transformed the management landscape by improving outcomes and making the condition easier to live with. People with diabetes who have been using CGM insulin pumps and/or automated insulin delivery systems for diabetes management should have continued access across third party payers, regardless of age or A1c

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levels.

We acknowledge the troubling trend of the time delay between when a device is approved by the FDA and the period of time it takes to receive Medicare coverage, and note that the ADA broadly supports measures that will expand access to technology for beneficiaries with diabetes, whether this refers to technologies on the market today or in the future.

We urge that CMS take extra care to avoid making choices that would limit access for people with diabetes, especially once the device has already been thoroughly tested and proven safe and effective, like CGM, insulin pumps and automated insulin delivery systems where CGM informed algorithms modulate insulin delivery, as well as diabetes self management support software serving as medical devices.

We are grateful to the DME MAC medical directors for expanding access to technology for Medicare beneficiaries by making important coverage criteria changes to the LCD for glucose monitors. We appreciate specifically the elimination of the four or more times a day

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blood glucose monitoring testing requirement in 2021 as well as the 2023 expansion allowing all insulin dependent people with diabetes and others who have a history of problematic hypoglycemia to have access to this important technology.

Each of these changes has removed significant barriers for beneficiaries with diabetes, and we respectfully caution the Agency against directing additional barriers to devices and technology that have been rigorously tested in people with all types of diabetes and at all ages.

The ADA recommends that CGM devices should be offered for diabetes management in adults with diabetes on multiple daily injections, insulin pumps, AID systems or basal insulin who are capable of using the devices safely, as well as for youth with Type 1 diabetes or Type 2 diabetes on multiple daily injections.

Based on the Agency's comments in the MEDCAC issue brief about diabetes technologies in older people, we draw your attention to a recommendation that older individuals with

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Type 1 diabetes benefit from ongoing insulin pump therapy and access to insulin pump therapy including AID systems, and should be allowed or continued in older adults as it is in younger people. Multiple randomized control trials have been performed using real-time CGM devices and the results have largely been positive in terms of reducing A1c levels and/or episodes of hypoglycemia as long as participants regularly wore the devices.

The initial studies were done primarily in adults and youth with Type 1 diabetes on insulin pump therapy and/or on multiple daily injections. The primary outcome was met and showed benefit in adults of all ages, including seniors. Real-time -- randomized control trial data and real-time CGM use in different --

DR. ROSS: One minute.

MS. FRIEDMAN: -- types of diabetes on MDI, mixed therapies and basal insulin have consistently shown reductions in A1c levels and increases in time in range. The benefits of intermittently scanned CGM for adults with Type 2 diabetes not using insulin were recently

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reported in a randomized control trial showing that the use of intermittently scanned CGM plus diabetes education versus diabetes education alone showed decreased A1c levels and increased time in range as well as an increase in --

DR. ROSS: Sorry, we've reached the five minutes. Does anyone have any questions for this speaker? Okay. Thank you for presenting. Sorry I had to cut you off.

Tara, who is the next speaker?

MS. HALL: Next we have Jessica Castle.

DR. CASTLE: And will you be pulling up my slides or should I start sharing my screen? Perfect.

Good morning, everybody. I'm Jessica Castle, VP of medical affairs from Dexcom. We can go to the next slide in presentation mode if we can. So I am an employee and shareholder of Dexcom. Next slide please.

I'm going to speak to three different items, one on trial duration, one on A1c, and finally on time in range.

So the DCCT definitively showed that improving A1c results in reduction of

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microvascular complications in people living with Type 1 diabetes. The UKPDS similarly showed improvements in A1c reduced microvascular complications in people living with Type 2 diabetes. The EDIC study and the UKPDS follow-up study demonstrated a reduced risk of cardiovascular disease in people living with Type 1 and Type 2 diabetes respectively. And therefor, A1c has been shown to be an appropriate surrogate outcome for diabetes-related complications, and A1c can be measured after 12 weeks. Requiring trials longer than 12 weeks increases participant burden, as well as an increased risk of participant dropout. Also, requiring trials of longer duration delays the length of time that therapies reach patients and would be prohibitively expensive in the development of technology, and therefore recommend a minimum trial duration of no longer than 12 weeks. Next slide please.

A1c, so the magnitude of A1c improvement is correlated with baseline A1c levels, and therefore with patients as they approach the typical target of seven percent,

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that these lower baseline levels typically result in a lower magnitude of improvement, which is important to keep in mind. An A1c change of .3 percent is clinically meaningful and has been associated with reduced risk of retinopathy. Guidance from both the FDA and the European Medicines Agency uses this .3 percent threshold when evaluating drugs to improve glycemic control, and therefore, we recommend establishing a minimally clinical difference in A1c of no higher than.3 percent. Next slide.

Time in range is the time in which the blood glucose is between 70 and 180 milligrams per decaliter. CGM allows for the measurement of time in range, which has significant advantages over A1c. The time in range derived from the seven-point finger stick testing in the DCCT was strongly associated with the reduced risk of microvascular complications. A 10 percent increase in time in range correlates with a .6 to .8 percent reduction in A1c, and so logic would indicate that a five percent increase in time in range would correlate with .3 to .4 reduction in A1c, which is clinically

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meaningful. A five percent increase in time in range correlated in a case control study recently published in the Diabetes Technology and Therapeutics Journal, with a significant reduction in risk of retinopathy, a clinically meaningful vascular complication.

Two international consensus statements, one in 2019 and one in 2023, indicated that a time in range improvement of five percent is clinically significant, and therefor we recommend establishing a minimum clinically important difference for time in range of no higher than seven percent, or no higher than five percent.

And that is my last slide. Happy to take any questions.

DR. ROSS: Thank you, Jessica. Any questions from the panel?

MS. HALL: Okay, Gregory, you're up next.

DR. FORLENZA: Yes, so thank you. Good morning, and thank you for inviting me to present today. My name is Greg Forlenza, I'm a pediatric endocrinologist and technology researcher at Barbara Davis Center in Denver,

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Colorado. Next slide.

And our team here at University of Colorado and Barbara Davis Center conducts research on all the devices currently on the market in the United States to help people with Type 1 and Type 2 diabetes improve blood sugar control, improve their quality of life and improve their care. Next slide.

So our group conducted an analysis of Medicare and Medicaid beneficiaries who had started a novel closed loop system or automated insulin delivery system, and that's what I'm going to be sharing with you in a moment. You guys obviously know what Medicare and Medicaid are all about, but the reason that we conducted this analysis was everything in the field that you look at shows that both older adults and low income individuals, particularly low income children, have much lower rates of technology use than the general population, and that there is some provider bias and coverage barriers that contribute to that. And so what we aimed to show in this analysis is how beneficial these technologies can be in these groups that are currently under utilizing them.

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In my sharing it with you today, I wanted to share with you how experts in the field who are actively doing clinical care and actively conducting clinical research are evaluating the use of these technologies and how these evaluations could contribute to us determining whether or not these should be used, and thereby showing you that they should be covered. Next slide.

So in this analysis we looked at users who were six years old and older, which was on label use of the device at the time of analysis, and had at least 12 consecutive months of data available in our industry partner for this analysis, Tandem, makers of the control IQ pump, in their online database, and participants had to have at least 30 days with greater than 75 percent available CGM data after initiation of the technology. And for our analysis, this group, some of whom we're going to be presenting in some of the other talks today, we're looking first at time in range, time in target range which we've heard about today, percent of time the blood sugar is between 70 and 180. We all were in universal

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agreement that was the most important metric.

The second metric is one I actually haven't heard folks talk about today, is glucose management indicator or GMI. GMI is a mathematical abstraction of average sensor glucose to determine what your hemoglobin A1c would be based on that blood sugar. During the pandemic when we couldn't draw blood on participants, that was a very valuable tool to sort of approximate hemoglobin A1c and for data driven analysis where you can't get biological samples, that's also a very useful indicator. And then we looked at the standard blood sugar rate, which is for Level 1 and Level 2 hypoglycemia and Level 1 and Level 2 hyperglycemia. Next slide.

So this is the baseline data for whom we were looking at, and what we're seeing here is about 4,000 Medicare beneficiaries, about 1,300 Medicaid beneficiaries, and within that about 500 people who are currently using the device off label with Type 2 diabetes, and here we see the baseline statistics for each of those groups, including looking at GMI, sensor glucose and time in range statistics and those

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are folded in to the next data set. And just as an FYI, most of the people that we're analyzing here, we're currently using a system that minimized hypoglycemia, and so we're seeing a transition from a hypo minimizing system to a system which minimizes both hyper and hypoglycemia. Next slide.

And so this is the payoff slide, this is the data that we were looking at that we were so excited as clinical researchers to be seeing. We were seeing among the Medicare population, we saw a GMI, which is again that mathematical abstraction for a hemoglobin A1c, a reduction from 7.3 to 7.0 percent, and supporting what Dr. Castle said on the last slide, we all felt this was clinically meaningful. It's obviously statistically significant. For the Medicaid population we saw a .4 percent reduction in GMI.

For time in range we saw a 10 percent improvement among the Medicare population and --

DR. ROSS: One minute.

DR. FORLENZA: -- a 14 percent improvement among the Medicaid population.

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And in Type 2 we saw similar data, and you can see that for hypoglycemia, that was maintained, severe hypo was reduced, and time above ranges were all reduced. Next slide.

And so in summarizing this data, what we can conclude, I just want to go to the last slide here, is that existing data on over 5,500 Medicare and Medicaid beneficiaries, demonstrates individual and group level improvement with AID systems. An understanding of this baseline comparison is important because hypo was already reduced, and at a group level, the percentage meeting ADA goals, which is the slide I'm not showing but I can go over it if there's a question. It's also of high interest, because as a clinician that's what you see and that's what makes a difference for payers.

And so we recommend both individual and group level analysis of people meeting ADA goals and of the standard CGM metrics being presented today.

And just to wrap up, as a clinician conducting this research --

DR. ROSS: Thank you, Dr. Forlenza.

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DR. FORLENZA: Thank you guys for listening, and thank you for your advocacy.

DR. ROSS: Thank you. If I could just ask one question, I'm sorry about the slide.

The post CIQ data, was that 12 months, if I understood?

DR. FORLENZA: Yes, 12-month data, correct.

DR. ROSS: Great. Any other questions for this speaker from the panel? Okay, thank you.

DR. FORLENZA: Thank you guys very much.

MS. HALL: Next we'll have Davida.

MS. KRUGER: Thank you. Next slide please.

These are my financial disclosures. I work at Henry Ford Health division of endocrinology. I have been in this position for more than 42 years as a clinician and a researcher. Next slide.

So this is just general comments about diabetes technology in terms of the ADA guidelines. They clearly state that real-time CGM and insulin pump therapy should be

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available for all individuals with Type 1 diabetes or insulin-requiring Type 2 diabetes. The clinical benefits of these technologies, they're not in dispute, we've been using them for years, they're FDA approved, we know how to use these devices. Glucose control as evidenced by current standards of care improves outcomes. Glucose control is best achieved currently through CGMs and insulin administration devices, notably we believe insulin pumps. I manage more than, in our clinic, 2,000 individuals on insulin pumps, both Type 1 and Type 2, from all walks of life. We use all devices that are on the markets and do clinical research on them as well.

The benefits of diabetes technology is consistent across people with diabetes, regardless of the type of diabetes and the age. And I wanted to make a comment about the age. Since I've been in this position for more than 42 years and started using pumps in 1982 when I was the national chairperson of the Diabetes Control and Complications Trial, all of our clinical patients of course were also offered insulin pumps. So I've got all of these

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individuals who have aged into the Medicare population, both Type 1 and insulin-requiring Type 2. I've got several people in their 90s, many people in their 80s and in the 70s, and they use them effectively. When they turn 65, there's no way I can say you're no longer going to be able to use this, and we offer those patients as they pass Medicare who will benefit by it if they've not been seen in our practice before that. So it's across all people with diabetes regardless of the type of diabetes and age and education, although I hope we do better than the data my friend Greg just showed you, in making sure all people in all walks of life get to use this technology. Next slide please.

And the general, the Diabetes Control and Complications Trial conclusively demonstrated that good glucose control directly reduces the rates of several significant complications. This is a landmark study that I believe you're all familiar with. At 6.5 years we showed an A1c of less than seven percent reduced the risks of complications to our patients. The primary consideration should be whether a device demonstrates the capacity to

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move patients to their target glucose range. And of course, in our clinical practice we absolutely believe that. Next slide please.

And then clinical trials. I've been doing clinical trials in Type 2 diabetes. They are very much beholden to the FDA, and so I heard one of the speakers also say that, how do we live to the needs of the FDA and the needs of CMS. But clinical trials for diabetes technology are needed to demonstrate the accuracy and utility of the these devices, which I believe are being done, and I believe shortly you will be able to see the outcomes of two trials we recently completed in Type 2 diabetes, and the current device trial compares new technology to recently available technology.

Clinical benchmark and study outcomes must be tailored to real world considerations. Our control groups may be using diabetes technology, CGM or current pumps. Accuracy and utility can be demonstrated in clinical trials of three months, that's what we did in these recent clinical studies. The FDA believed that to be enough, and we certainly saw differences

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in our patients. And while you talk --

DR. ROSS: One minute.

MS. KRUGER: -- about MCI, it's an important metric, should be in the specific clinical trial design and population study.

And I'll conclude, and then I know Janet will be behind me and she will go on.

I want to say a quote my friend Henry Anhafe (phonetic) said. Living with diabetes doesn't mean sacrificing a vibrant and fulfilling like as we age. In fact it's quite the opposite. With the right tools, mindset and support, individuals can navigate to their golden years with grace and vitality, and I hope you grow to remember that so that we can get what we need to continue to manage people in clinical practice. Thank you.

DR. ROSS: Thank you for your comments. Any questions for the speaker? Thank you very much.

MS. HALL: Next will be Laurel.

DR. DHRUVA: Joe, I think we have a question from Melissa. Sorry.

DR. ROSS: Oh. Please jump in. Thank you, Sanket.

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DR. GARRIDO: Thank you. Did you say anything about the MCID and how that might, the optimal MCID might differ with age? You mentioned it might differ with a population study. Would it be different for someone in their 90s, say versus in their 70s?

MS. KRUGER: Well, you know, I think that we have to keep that all consideration, but I don't think it should dictate anything, that it should be the only dictation. I think we have to look at the individual sitting in front of us. We are concerned about their education, making sure they get all of the clinical support. I think certainly the person who's starting the pump before 65 versus the pump patient that we give it to them in their 80s, their educational needs, their hypoglycemia, they may need different family support. All those things I think are very very important.

One of the things we noticed in clinical practice is the individual who got a pump, say in their 40s, 50s and 60s, when they're in their 80s they're so used to owning their own diabetes and managing their own

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diabetes that we need to be able to help support them as they age. So I'm not negating that. I just don't think that's the only thing, and I don't think that as a person ages we should say they can't have these technologies, because I see every day, both in clinical practice and research, how well they do. And we prevent hypoglycemia, we keep them in time in range, and I can't do that on injections alone.

DR. ROSS: Great, thank you very much. Next speaker. Tara, who is next?

MS. HALL: Laurel Messer.

DR. MESSER: Hi. Is Janet on before me?

MS. HALL: We're having an issue, so we need you to go first.

DR. MESSER: Oh, okay. Thank you, everyone, for your time. I thank the panel for convening and listening. My name is Dr. Laurel Messer. I'm senior director of medical affairs at Tandem Diabetes Care. I am a nurse, nurse scientist, and have been in practice working with insulin dependent people with diabetes using diabetes technologies for over 20 years.

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Next slide please.

I am currently an employee and shareholder of Tandem Diabetes Care. Next slide.

So, I appreciate all the comments so far in calling out the unique vulnerabilities of older people living with diabetes. First of all, this is a highly heterogeneous population with wide varieties in life expectancy, baseline health, comorbidities and cognitive function. Cognitive function is particularly called out by the American Diabetes Association as an important characteristic in this population, and because of this heterogeneity there's high individualization that occurs in clinical care as well as glycemic targets. So for example in a population like this, there's no agreed upon hard stop of what a glycemic target should be because of high risk for hypoglycemia and other heterogeneous factors, and so it's really important to consider individual needs in older people living with diabetes. Also of note, they are at higher risk for hypoglycemia for a variety of reasons, including erratic meal intake, progressive

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renal insufficiency, and treatment with other hypoglycemic agents and polypharmacy. Next slide please.

So looking at the domains that the panel is evaluating, our opinion is to prioritize surrogate markers and device-related safety, which I will talk about in the next two slides. While health outcomes are important, they are expensive, they are complicated by comorbidities, and the long duration of study required may prevent getting the devices into the hands of individuals who need it. And quality of life, while also very important, has a wide variation in how it is measured and no agreed standard. Next slide please.

To keep this simple, our recommendation is to prioritize time in range and hypoglycemia measures using CGM derived measures. We agree with Dr. Castle and others that a three-month study is sufficient to determine safety and efficacy for these measures.

One thing that's important to call out, especially for time in range, two things: Number one, the within person change of five

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percent has been endorsed by a clinical international consensus to be clinically meaningful, so a five percent within person change would be a recommended MCID for time in range. This is important for the fact that there's individualization needed within this group, so it would not be appropriate to look at a fixed glycemic target of, say 70 percent time in range and look at the percentage of individuals who achieve this. It's more important to look at within person change.

And then the other reason to look at this is that every randomized clinical trial has a different control group. So if you're looking to evaluate a change compared to a randomized clinical trial, it's important to consider that that control group may include in class devices. Typically RCTs are designed to look at one particular device compared to other treatments, but this may not get at the class effect and importance of one device over others, which is why we endorse a clinically meaningful time at five percent time in range with an individual.

And hypoglycemia, of course, is

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important for older adults with diabetes and needs to be taken within context of CGM derived metrics, and any percentage of hypoglycemia reduced, we believe, is an MCID. Next slide please.

DR. ROSS: One minute.

DR. MESSER: All of the other ones are best captured in the 70 to 180 in time and hypo. A1c is also important. However, as Dr. Castle brought out, lower baseline means lower magnitude of improvement, and this may not be the best metric. Next slide.

Finally, for safety and efficacy, device discontinuation rates and adherence to device use indicate that older adults can use these devices safely and effectively, and are easily measured with clinical trials. Next slide please. Next slide.

So in summary, our recommendation is let's keep it simple. Let's look at improvement in time in range as well as hypoglycemia as the most important metric for approval of diabetes devices. Device continuation and adherence rates directly indicate whether older adults can safely

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tolerate these therapies. We ask that CMS does not require long costly trials or stringent MCIDs, which would inappropriately deny coverage for a variety of older individuals affected with diabetes. Thank you very much for your time.

DR. ROSS: Thank you, Dr. Messer. Any questions for the speaker? Okay. Tara, who's next?

MS. HALL: Next we have Janet.

DR. ROSS: Dr. McGill, are you ready?

DR. MCGILL: Thank you very much, and I want to thank MEDCAC for holding this meeting, for inviting us to participate. I'm professor of medicine, I'll go to the next slide, at Washington University School of Medicine.

I've been in this role for 37 years, similar to Davida. Consequently, my patients are getting older, they're very older. I see many patients with Type 1 and Type 2 diabetes who are insulin requiring as a result of both insulin deficiency, duration of disease. I use these devices, I use every single device on the market, and have done studies in these devices.

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Okay, next slide.

So, general commentary. ADA clearly states that real-time CGM and insulin pump therapies should be available for individuals with Type 1 or insulin-requiring Type 2 diabetes. And I might add that those are patients who require physiologic replacement of insulin, not just insulin therapy or basal insulin therapy or other newer therapies that have limited this group, now to people who really need physiologic replacement. The benefit of these technologies is not in dispute, as was mentioned, as has been mentioned by other speakers. Glucose control improves, time in range improves. The benefit is consistent across people with diabetes, regardless of type of diabetes and age. Next slide.

We've talked about the Diabetes Control and Complications Trial, that and the UKPDS, and other trials have now, now it's settled science that improved glucose control improves outcomes. This does not to be revisited. We need, simply need to know the best ways for achieving excellent glucose

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control. Next slide.

So clinical trials for diabetes technologies are needed to demonstrate accuracy and utility of the device, whether CGM or insulin administration, whether pumps or smart bands, they should compare new technology to available technology. When that is done, then we need to modify our expectations, for this minimally clinically important difference depends on the control group. If your control, the control group is using older therapies, such as injection therapies, we expect to see an improvement in A1c, reduction in hypoglycemia, improvement in time in range.

So the accuracy and utility is commonly demonstrated in a clinical trial of three months duration, such as the recent clinical trial for the Islet Beta Bionics insulin pump system. Using CGM, it was a three-month trial, and significantly limits user input functions, is available for people who have difficulty with clinical decision making achieve, achieve outcomes that are really quite remarkable.

MCID is an important metric, but needs

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to consider the trial design and population studied. Next slide.

Across all domains, a three-month followup for devices is adequate and appropriate. It reflects changes in A1c should there be any, average blood glucose levels, time in range, and rates of hypoglycemia, and --

DR. ROSS: One minute.

DR. MCGILL: -- may determine device safety. And there is no data that suggests that longer follow-up periods are necessary for quality of life or health outcomes, there is a complete lack of data. What we need is safety. Next slide.

That's the end of my slides.

So endpoints should be specific to the types of technology studied, the study population, Type 2 diabetes, we see reduction in hyperglycemia. Type 1 diabetes it's hyperglycemia and hypoglycemia. Non inferiority should be considered when a current device is compared to recent technology with respect to glycemic controls including hypoglycemia. The MCID for surrogate markers

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is detailed in the written response, and we advise no worsening quality of life with respect to the current assessment tool scores, which --

DR. ROSS: Dr. McGill, I'm sorry, that's time.

DR. MCGILL: Yes, thank you.

DR. ROSS: Thank you very much. Any questions for this speaker?

MS. HALL: If no questions, Medha, you're next.

DR. MUNSHI: Hello. I am Medha Munshi, a professor of medicine at Harvard Medical School. I lost my slides.

DR. ROSS: Don't worry, Dr. Munshi, I'm not taking this against your time.

DR. MUNSHI: Thank you. This is what happens to geriatric patients. Sometimes it just takes a little time.

DR. ROSS: Just a reminder for all members of the panel to try to keep your camera on, and for speakers, when you finish speaking, then turn your camera off. Thank you very much. Okay.

DR. MUNSHI: Thank you again. Hi, I'm

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Mehda Munshi, professor of medicine at Harvard Medical School, director of the Joslin Geriatric Diabetes program, I'm a primary care geriatrician at Beth Israel Deaconess Medical Center and the founding president of the International Geriatric Diabetes Society. My area of research and primary clinical interests are the technology and care of older adults with diabetes. Here are my disclosures, and I have no financial interest in the outcome of this meeting. Next slide.

So I would like to comment the clinical endpoints that are important for consideration of older adults with diabetes. Next. The time spent?

So time spent in hypoglycemia, both Level 1 and Level 2, is a primary concern in this population. Next.

Older adults have hypoglycemia unawareness that results in lack of adrenergic warning symptoms and lack of recognition and reporting of hypoglycemia, as well as failure of prompt treatment, as seen in our study published in 2011. Next.

The consequences of hypoglycemia are

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catastrophic -- next -- in this population, resulting in higher risk of falls, fractures, cognitive decline, cardiac events, emergency room visits and hospitalization, as well as long-term care facility admissions. Next please.

Thus, the recognition of asymptomatic hypoglycemia by CGM has significant clinical implications and benefits in this frail population. Next. Next slide please. Next slide please.

Hypoglycemia thus, should be considered as health outcome of interest in older population with diabetes. The goal for hypoglycemia duration should be really aimed at near zero percent, as a risk of any amount of hypoglycemia will outweigh the benefits of controlling hyperglycemia in this population and the MCID will depend on the sample size and study characteristics of the study cohort. Next slide please.

The time in range, next please, is usually between 70 to 180 milligrams per decaliter, but that may need to be adjusted based on overall health status in this

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population, next please, the same way as A1c goals in the older population are currently recommended. Next please.

CGM targets of clinical significance including time below range, time in range and time above range should be considered based on healthy, intermediate and poor health overall status of the older individual. Time in hyperglycemia, both Level 1 and 2, thus should be adjusted based on health of an older adult as well as quality of life concerns with increasing complexity of the treatment that might be needed. Next please.

The high coefficient or variation or CV percentage reflecting glycemic variability correlates with the risk of hypoglycemia in older adults and is an important outcome, as shown in our study published in 2020. Next please.

Hemoglobin A1c is typically considered a clinical endpoint important for individuals with diabetes. However, clinical conditions that impact RBC lifespan and impact A1c measurement occur frequently, especially in frail older adults, making interpretation of

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A1c unreliable in many instances. Next please.

In addition, hemoglobin A1c does not correlate with hypoglycemia as seen in our study. Next please.

As shown here, next please, A1c values less than seven percent, eight percent, eight to nine percent, or more than nine percent did not correlate with risk of hypoglycemia as measured by CGM.

DR. ROSS: One minute.

DR. MUNSHI: Next please.

A1c doses not identify glycemic excursions and the same hemoglobin A1c can have a variable pattern as seen on CGM. A1c thus should be deemphasized as outcome of older adults in diabetes. Next please.

Distress about hypoglycemia, next please, and its feared consequences lead to fear of hypoglycemia and important quality of life issue, as well as limiting factor for improved glycemic control in the older population. These qualify of life parameters improve with CGM use in our studies. Next please.

So in summary, the priority for

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clinical outcomes in older adults should include the risk of hypoglycemia as the first priority followed by decreasing glycemic variability, individualizing optimal time in range, and finally control of hyperglycemia.

Thank you for this time.

DR. ROSS: Thank you. Any questions for the speaker.

DR. WALL: Joe, I do. Dr. Munshi, I appreciated your slides and your talk. You know, a number of presenters have addressed the MCID as depending on the population and also on the, basically the clinical trial design. Could you elaborate a little bit more as to what that actually means, how that translates in practice or in doing studies?

DR. MUNSHI: Yeah. Thank you for the question. I feel like it's important with the outcome of interest, and that was my point about the hypoglycemia. Many times we consider less than one percent as the goal for hypoglycemia. However, you know, one hypoglycemic episode, one fall, one hip fracture and nursing home admission makes it really irrelevant whether the MCID is, you

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know, in those studies. So I feel like basically depending on the population that is being studied, if it is high risk in older adults in intermediate or poor health versus healthy population, that might actually end the outcome, primary outcome, that may actually affect the MCID in those instances. I don't know if that answers you.

DR. WALL: No, that's great, thank you.

DR. ROSS: Dr. Munshi, if I may, could you talk about how you measured variability, which you emphasized in your comments?

DR. MUNSHI: Yes. So with continuous glucose monitoring, we are able to actually identify the CV percent, the coefficient of variation percentage, and again, that is known to be, have 36 percent as the optimal level.

But when you get to the appropriate population, it's the variability that causes the highs and lows, and an important variable which is not really measured unless continuous glucose monitoring is done. So it's one of the biggest, big fallibility of the other measures, of the A1c.

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DR. ROSS: I may ask one last question. You're the only speaker thus far that's talked about the distress scale. Could you just remark upon its utility and how you've used it?

DR. MUNSHI: Yes. So many times, and diabetes-related distress, again, is different for different populations. We have sometimes a hard time taking the validated surveys because they are meant for the younger population, you know, what kind of distress that causes. What we have found is that the biggest distress in older adults are about the hypoglycemia and fear of hypoglycemia, and having a technology that warns them and prevents the hypoglycemia is of tremendous comfort to them. So even beyond the control of glycemia, which is important, I'm not putting that down, but the ability for the patient to feel reassured that they are not going to be hypoglycemic and passed out and no one will find them, is of tremendous comfort to them. That's what we have seen repeatedly.

DR. ROSS: Thank you for those comments. Okay. We should move to the next

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speaker. Tara, who would that be?
MS. HALL: Robert is next.
DR. VIGERSKY: Good morning. My name is Bob Vigersky. I'm an adult endocrinologist and currently the chief medical office for Medtronic Diabetes. I'm also a Red Cross volunteer at Walter Reed, where I spent 27 years in the Army Medical Corps, and I still see patients, and speaking of seeing patients for long periods of time, some of my patients have been seeing me for 20, 25 years, and have aged into Medicare or in the case of the military, into TRICARE. I also am the past president of the Endocrine Society. Next slide.
I'm, as I mentioned, I am an employee of Medtronic. These are my disclosures. Next slide.
I'm not going to read this, but I think it's clear from certainly the last four speakers and I support this, that we don't want Medicare to impose further restrictions on these technologies which have really been supported by enormous amounts of evidence, and have been adopted by the medical community. We

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do recognize that there are important endpoints that we have to identify, and I think I would agree with the other sneakers that A1c plus time in range are the really important endpoints, but time in range as a composite of time in range and time below range. We all know that we can give more and more insulin and get better time in range, but without the devices that we're discussing, CGM, insulin pumps and automated insulin delivery systems. They are giving you low time below range in addition to time, increased time in range. And this is really a composite endpoint in a sense, so the key would be as high a time in range as possible without exceeding the goals for time below range. Next slide.
Now you have heard allusions to this paper by Tony Bedalino. This has been adopted by the American Diabetes Association and other professional organizations around the world. And you've heard about what the goals are of time in range greater than 70 percent for Type 1 and Type 2 diabetes but what you haven't heard, at least not directly, except from Dr. Munshi, is the goals are different for our

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older adults in high risk and the guideline development committee recognized that time in range between 70 and 180 may not be 70 percent but perhaps somewhat lower, like greater than 50, and importantly, the time below range of less than 70 shouldn't be less than four percent, but rather less than one percent, and as Dr. Munshi said, maybe it should be zero percent.
On the right is the relationship of time in range to A1c. This was also alluded to and directly, this is a study, one of two studies, this one is mine, that shows the relationship of time in range to A1c, basically saying that for every 10 percent change in time in range, there's a .8 percent change in A1c on average.
And so that gets back to the clinically meaningful change in time in range, which would be five percent, which is equivalent to .4 percent A1c. Next slide.
Now I thought it would be instructive to show a case, because this really tells you what's going on in the clinic with our patients. This is a 69-year-old gentleman.

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He's had diabetes for 58 years and his A1c is 6.3. And before we had these technologies we would say this gentleman is doing great. But he had 16 percent time below range when he was on an insulin pump that didn't have automation. And then when he transitioned to the 780G, which is a Medtronic device and automated insulin delivery system --
DR. ROSS: One minute.
DR. VIGERSKY: -- he actually got 93 percent time in range but three percent time below range, which is too high for his age per those guidelines I just showed you. Next slide.
And this is my next to last slide, and the daily reports I think are instructive. So you can see there are days here where this gentleman actually became hypoglycemic to Level 1 and some Level 2. So this really aids in analyzing the patient's case and making changes in the settings of this device to keep the person safe. Next slide.
And we've for this meeting, we've -- next slide please. We have mined data from -- next slide please.

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We have mined data from our database and looked at in those of us aged 65 and greater, over 5,000 individuals, and we found that in this population 84 percent had a time in range greater than 70, and 95.8 percent maintained a time below range less than four percent, and 97 percent kept the time below range of 54 less than one percent. So these automated insulin devices are very effective in reducing time below range and increasing time in range. Thank you.

DR. ROSS: Thank you, Dr. Vigersky, right on time. Any questions for this speaker?

MR. FRANKEL: One question. What are your thoughts about what Dr. Munshi mentioned about the deprioritization of A1c? What's your vantage point on that one specific point, because you also mentioned A1c on your slides.

DR. VIGERSKY: Yes, so I think A1c still has value, because it is the one metric that is generally related to complications. But there are, and I didn't show this, there are a number of papers now that show the relationship of time in range to complications. So I think we're in a transition point where we

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really need both A1c and time in range.

DR. ROSS: Okay, thank you. I think we're going to our last presentation; is that right, Tara?

MS. HALL: Yes. We've got Sethu next.

DR. REDDY: Good afternoon. Thank you for this opportunity to present to this group doing very important work, and the topic is very close to our hearts. If I could have the first slide up?

I'm Dr. Sethu Reddy, past chief of endocrinology diabetes at the Cleveland Clinic, past chief of adult diabetes at the Joslin Diabetes Center, currently finished my term as the past president of AACE, if we can have that in the show mode, and being en endocrinologist for 40 years plus, and hopefully I'll express some of those sentiments in the next couple of minutes that we have.

I'm not seeing the slides up, but can you hear me?

DR. SCHULMAN-ROSENBAUM: Yeah, we can hear you, but the slide's not up.

DR. REDDY: And my pleasure to also introduce my partner for today, Dr. Rifka

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Schulman-Rosenbaum, who is one of our leaders of our diabetes state network at AACE, and also has had much experience dealing with pump patients and CGM as well.

And certainly we realize that CGM is the real safety blanket no matter what we decide on managing peoples diabetes. CGM offers a great safety blanket, security blanket for our patients and their relatives.

They're not showing up in the show mode. I have no control over them.

MS. HALL: Give us one second please.

DR. REDDY: But we have no conflicts to report, neither myself nor Dr. Schulman-Rosenbaum.

I do want to highlight two references for you that AACE has published, our diabetes guidelines. One of the highlights, I think, is that we recommend that anyone on insulin therapy is deserving of potentially using CGM, and we've just seen so many behavioral changes from using CGM on patients lifestyle and nutrition and control. We also published in 2021 on the use of advanced technology in the management of people with diabetes.

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We want to get to the heart of the matter and I'm going to hand it over to Rifka to go over the surrogate markers that the committee has proposed, and she will express our opinions about those.

DR. SCHULMAN-ROSENBAUM: Thank you, Dr. Reddy. And you know, just as a little bit of background, we're giving our input from the standpoint of clinical endocrinologists. We acknowledge that there is a paucity of studies focused solely on older adults, even fewer studies focused on Type 2 diabetes older adults, which is a large portion of Medicare. And so we have to do the best we can to come up with what makes the most sense clinically, especially when there is a paucity of data, and we wanted to really highlight the importance of avoiding hypoglycemia in the elderly, as has been mentioned by many other speakers, which can contribute to altered mental status, cognitive impairment, falls, motor vehicle accidents, hospitalizations and immediate quality of life issues which we think are really important, and some other factors that are more longer term may be less appropriate to

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focus on in the older population.

So starting with the surrogate markers, we felt that number of hypoglycemic episodes was extremely important, appropriate, and that's five. Now we did put six months here for duration, but to acknowledge that three months could be also acceptable. It really depends on the incidence of events, but let's say three to six months. And we were suggesting for the MCID a reduction by 25 percent from baseline, so an incidence of four percent hypoglycemia going to three percent would be clinically meaningful.

A few words about hemoglobin A1c. You know, we acknowledge that the MCID standard is the 0.5 percent which is reasonable in most cases. Of course it does matter what the baseline hemoglobin A1c is, which can affect what percent drop would be meaningful. But you know, a hemoglobin A1c has accuracy limitations. For many older patients they have comorbidities, they may have anemia or chronic kidney disease which can affect the accuracy of hemoglobin A1c. And as mentioned earlier, you know, it's an average, and so it doesn't

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account for hypoglycemia or glycemic variability, which is very important, avoiding hypoglycemia in the elderly. So we gave that a four.

In terms of time in range, we also agree with many of the other speakers of the importance of valuing the time in range with the relatively shorter studies of three months and as mentioned earlier, the five or 10 percent difference as a suggested MCID. You can go to the next slide please.

In terms of health outcomes, you know, for restoration of hypoglycemia awareness, we thought this may be a little difficult to quantify so we didn't put as strong of a grade on that one. We do think cognitive function change is a very important variable. We would rely on our colleagues in geriatrics to identify what the standard would be, but we do think that that would be an extremely important measure for cognitive function, especially since cognitive function can be cyclically involved with hypoglycemia, leading to further cognitive function or further hypoglycemia.

DR. ROSS: One minute.

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DR. SCHULMAN-ROSENBAUM: We believe that hospitalizations, both ED and admission, are extremely important, so we put those at level five, looking for a 50 percent reduction. And we didn't not want to put the priority on the longer term outcomes. While very important for an elderly population, this should not be the focus. Next slide.

We did put some comments on the quality of life indicators. We agree with Dr. Munshi that focusing on the fear of hypoglycemia is really the most important one, and left some comments on suggestions for MCIDs for these. Next slide.

And in terms of device-related safety, I know we put four here but it could be also a five, four to five for hypoglycemia-related emergency department visits. We're not aware of any tissues damage typically from these devices so that was rated low, and you know --

DR. ROSS: We're out of time, Dr. Schulman-Rosenbaum.

DR. SCHULMAN-ROSENBAUM: Thank you.

THE COURT: I'm sorry to interrupt, Dr. Schulman-Rosenbaum. Are there any

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questions for the presenters?

DR. SCHULMAN-ROSENBAUM: I see a question.

DR. FANAROFF: Yeah, so this is Alexander from the panel. You know, you and a lot of the speakers have indicated a three-month duration for hemoglobin A1c or time in range would be appropriate, which makes sense because that's how long it takes to see a change in the parameter.

The question is, you know, it seems like you would have to have changes in A1c or time in range that were sustained to reduce the risk of microvascular complications. In your experience clinically, I guess, once patients start on these devices and they lower their hemoglobin A1c or they change their time in range, is it maintained over a long time, and do patients continue using the devices over a long period of time.

DR. SCHULMAN-ROSENBAUM: So obviously there's variation between patients, but I would say that in most of the patients they really enjoy the devices and do very well using them compared to the time before they used the

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device.

And obviously, again, there are exceptions for different circumstances, individual reasons, but most patients, I think, would continue, and so the three month would be a surrogate for a longer term control.

DR. REDDY: It's hard to put in words the safety psychologically that they feel. It's really like riding a bicycle with training wheels. They know that they can go about their life without worrying about severe hypoglycemia, so they're more likely to stay on, I think.

DR. ROSS: Thank you. Any last questions? Great, thank you. I want to thank all of the public speakers who submitted comments to consider to this committee.

It's 11:45 or so, so we're a little bit behind schedule, but there has been no one who volunteered to present during the open public comment period. Rather than taking a ten-minute break, I'm going to give us 20 minutes, so those of us on the east coast can try to eat lunch quickly. And we will reconvene and then go forward with discussion

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beginning at ten minutes after 12 on the east coast. So that's now 17 or so minutes, whatever it is, it's about 20 minutes, okay? So we'll start at ten minute after 12 p.m. eastern time. And you can leave yourself logged in, so just go off video and make sure you're muted. Thank you.

(Recess.)

DR. ROSS: Thanks everybody for coming back so we can get started pretty close to on time.

Tara, I have one quick question for you. In past virtual meetings as we've entered into the open panel discussion, you've asked us to state our name because someone who is dong the transcript is working off the audio recording, not with the video. Do you want us to continue to do that, so for instance, say this is Joe Ross?

MS. HALL: Yes, please say your name each time you talk.

DR. ROSS: Okay. And I'm sorry I didn't clarify that beforehand, during the first part of the meeting. So keep that in mind everybody.

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So now we have, thankfully actually, a good couple of hours to talk about this clinical evidence endpoints review and the presentations that we heard over the course of the morning.

We have -- I thought it might be helpful just to start by talking through the domains and just thinking a little bit more in general about what we've heard, what we've read, and we reviewed the clinical endpoints review that was prepared, potential things that arose in your mind that were or were not discussed or should be points of emphasis.

And I just want to remind folks that in terms of device-related safety, we are going to work under the assumption that accuracy of the device has been confirmed by the FDA as part of the authorization process, and so inaccuracy on its own is not a safety-related domain, unless we're talking about accuracy as it may apply to an older adult. For instance, if there isn't information around the device's accuracy for an older adult as compared to the general population in terms of false positives, false negatives, but we're going to work under

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the assumption that accuracy has been confirmed as part of the FDA authorization process.

So I'm just going to open it up for now, and I'll try to keep us on time. I think we'll try to move towards the discussion of the actual voting questions to see if there's any points of clarification at around half past the hour, but for the next 15 minutes, do people want to reflect on the domains, the endpoint domains and the material you heard and what has or has not come up. Please just raise your hand, and state your name. Dr. Isetts, that's how you come up.

DR. ISETTS: Yes, thank you, Dr. Ross. Isetts, University of Minnesota, a professor and a pharmacist. Dr. Ross, are we able to comment on some of the presentations at this point or from earlier in the morning?

DR. ROSS: Oh, we can, and we can talk about them. And if you have questions that have come up over the break, sometimes the presenters stay on and we can ask them questions, but there's no guarantee that they're still there.

DR. ISETTS: Thank you, because I'd

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like to address the letter from the 26 non-diabetes organizations. They characterize, with all due respect, characterized our work as similar to rationing of medicine, and I'd like to turn that from an adversarial discussion more to a collaborative discussion.

And the fact that, you know, sure CMS is the evil payer and they want to stop payment on things, and that is a common concern that many of us have had over the years, tongue in cheek sometimes, and the reasoning they were using is that if the FDA approves, in this case a device, or a drug, CMS should cover it, no questions asked, although they used the discussion of the amyloid agents in which there was this push and pull FDA, particularly the FDA advisory panel, in terms of they did not support coverage of the agent, all right? So there was this, almost a rare discrepancy between CMS and FDA in terms of FDA doing their work, as many of the panelists resigned from the advisory panel, and so it was almost counterproductive to that discussion.

So I want to turn this into a positive in terms of, let's look at this as a

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collaboration of stewards of the Medicare trust fund, all right? So you conduct clinical trials, there was a set of patients that may not be the patients we care for, and so a lot of the discussion we heard today was very helpful in terms of tailoring our work to real world considerations. How can we work together to make sure that the devices are out there, can be used with both safety and effectiveness in the populations that may not have been tested in FDA work. And so I really found many of the discussions and the other, particularly the clinical endocrinologists to be very helpful in helping us figure out how can we enable this to used in a more effective and safer way.

DR. ROSS: I appreciate that. If I could just briefly comment, I just want to remind us that we are not here to discuss the authorization or payment for any specific technology regardless, and public commenters can say anything they want in there allotted time. We are really here to help advise and recommend to CMS what they should be looking for in the body of evidence regarding devices

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for self management of Type 1 or insulin dependent Type 2 diabetes in older adults.

And so I did, also found that the comments that addressed that question were of far greater utility to me in advancing my understanding. Dr. Wall?

DR. WALL: Yeah, this is Eric Wall in Seattle. Joe, I'm just trying to -- there was one of the speakers and I should have written this down, that suggested we missed a domain, because I think we were initially supposed to address the domain issue right now which is, are we missing anything in the domains. But I didn't make a note of it. Did anyone remember what was suggested that we were missing?

DR. ROSS: This is Joe. I'm curious what others heard. A handful of the earlier speakers I thought, you know, really emphasized, actually I thought kind of equitable access, particularly inequities, and I didn't know if they were suggesting that as a domain of endpoints that should be looked for. They kept talking about equity and inequity, but I didn't get, I didn't think that that's what they were suggesting, that we should be

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looking for evidence of equitable use or equitable outcomes.

There was an endpoint that was raised, that was the GMI endpoint, which I believe would be considered a surrogate measure in our, you know, in this framework that CMS has developed, as it was a proxy for hemoglobin A1c. Is that what you mean?

DR. WALL: Yeah, okay. Great.

DR. ROSS: That came from Dr. Forlenza.

DR. WALL: This is Eric Wall. One more time I'm just going to use my question on here. I've not seen data, maybe I missed it. There's been a recurring theme of hypoglycemia in the elderly, which I think we all might agree to, but the prevalence of hyperglycemia, in other words really ketoacidotic hyperglycemia in the elderly, I'm just not sure of the prevalence of that in this population. Does anyone know that, or can anyone comment on that?

DR. ROSS: This is Joe Ross. I don't have those numbers at my fingertips, but I did also find it interesting that none of the

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speakers really emphasized hyperglycemia so much as they focused on hypoglycemia.

Fred, you're on mute.

DR. KOBYLARZ: I think Melissa had her hand up before me.

DR. ROSS: Oh, I'm sorry. I thought it came up earlier. Dr. Garrido?

DR. GARRIDO: This is Melissa Garrido. Just back to the point about the equity concerns in the beginning, I think the concern wasn't that it was a missing endpoint or a domain, I think the concern was that additional endpoints that CMS may or may not require could lead to inequities.

DR. ROSS: Thank you. Fred, you want to go now, or no?

DR. KOBYLARZ: Yes. Fred Kobylarz, Rutgers, Robert Johnson Medical School, you know, geriatrician. Let me just start with the, you know, the domains regarding, I think there was one comment in the -- I'm just sorry here -- the surrogate markers, you know, regarding minimally, you know, clinically important differences. And just given this, you know, older adult population, you know,

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there are healthy adults, you know, that have few coexisting, you know, chronic, you know, medical conditions, they're cognitively intact. And then you have more complex individuals that have more chronic illnesses, and there may be some, you know, cognitive impairment.

So I think what struck me here was in terms of just trying to establish like minimally clinical important differences in this population may be challenging.

DR. ROSS: Dr. Fanaroff, I think your hand came up first.

DR. FANAROFF: Alex Fanaroff from University of Pennsylvania. I think the other thing about MCID is that, you know, when thinking about an MCID from like a clinical trial statistics perspective, I think that there's the difference between groups, the average difference in the groups, and then there's also the change within any one patient, and those numbers may not be the same, you know, and I think that, so when we think about what the MCID is, you know, to me it makes more sense to think about it as the change that any one patient might need to have, and that might

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not reflect between group changes in a clinical trial. I think it's important to keep that in mind.

DR. ROSS: Dr. Lewis? You're on mute.

DR. LEWIS: Sorry about that, thank you. Joy Lewis, and I agree with Fred and Alex regarding the MCID and the fact that we need to look at the individual changes and the individual studies and what they're uniquely looking at.

And I wanted to speak to what Eric brought up before about a potential different domain. I too remember hearing that, but I never wrote down those words but I did, looking at my notes I see that Candace from the chronic disease group talked about the sense of control versus actual control that people might feel when they are using these devices, and that the regular feedback can lead to behavioral changes. That led me to think about the quality of life indices and that some of them might not capture what we're really intending, so this sense of freedom and ability to enjoy life might not always be measured, depending on what metric is used. And then that ties in to

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what some of the endocrinologists brought up in terms of the psychological safety and the decrease in fear of hypoglycemia. So it just leads me as I start thinking about these measures that we can call it health-related quality of life, but that encompasses in my mind all of these factors and not necessarily limitations of current measures that we listed on the -- of the current validated health-related quality of life metrics that we have right now. Thanks.

DR. ROSS: Thank you. Naftali Frankel?

MR. FRANKEL: Yeah, I think that Candace DeMatteis also had mentioned, I guess this goes along with health outcomes under that rubric of, that she noted that there was no reference to amputations, so I know that was also noted in that presentation. So you know, I know that we listed some different examples, I don't think it was an all inclusive one, but that was one she did note that wasn't specifically mentioned in the packet.

DR. ROSS: Dr. Young?

DR. YOUNG: Yes, thank you. Heather

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Young. I was really struck by the comments that related to the heterogeneity of older adults and the heterogeneity within the 65-plus population that we all know is actually three generations of people. And so given the comorbidities, given the different histories of diabetes experience, time of diagnosis and all those kinds of issues, that the potential for a great deal of variability in outcomes could be there. And I think the more we can focus in on the most proximal outcomes to the technology that's under study, the better we will be as the further we go out to more distal indicators and health indicators, the more difficult it is to sort out what's confounding those outcomes. And so the presenters really reinforced, particularly those with a geriatric perspective, really reinforce the importance of staying very proximal to both the population of interest as well as the devices under consideration, what's actually being studied. Thank you.

DR. ROSS: No, thank you. If I can just riff on that a little bit, I also thought that there was kind of an offhand comment made

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that related to familiarity with the technology and how starting it when they were younger was obviously easier, because then to continue it when they were older when some of the cognitive function may be more challenging, or the need for a caregiver to assist, I just thought that was an interesting comment.

Fred? I'm sorry, I always say Fred instead of Dr. Kobylarz. I'm always concerned I'm going to misstate your last name.

DR. KOBYLARZ: So, Fred Kobylarz. Again, I just want to piggyback on what you're saying, and this came out in one of the presentations regarding cognitive function. And this also ties in to other geriatric syndromes, polypharmacy, depression, falls, and this can all significantly affect diabetes management. So you know, I do think that, you know, there should be some screening, you know, for cognitive impairment for older adults, and then the issue is, you know, if there is cognitive impairment, you know, if you're, you know, let's say in the older group, if you're older it might be more challenging to reach glycemic, you know, control and just make it

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more difficult to monitor and adjust for example, your insulin or you know, or your medications that you're taking. So you know, I think cognitive function here is, you know, and other geriatric symptoms are very important to consider.

DR. ROSS: Dr. Dhruva, and Mark, I did see your hand go up. I'll call you next.

DR. DHRUVA: Thanks. Sanket Dhruva, San Francisco. I wanted to -- this has been a great discussion, I really agree with those points. I wanted to, a lot of the comments talked about in terms of the time duration, that about three months was sufficient, and we know obviously that that's the timeframe for an A1c change that can be captured.

I did wonder and I think Joe, one of your questions to one of the endocrinology presentations, you know, the changes that we see, though, overall sometimes often take longer. For example, the University of Colorado presentation, the results were changed at one year. So I did wonder, I understand three months is a minimum to see a change in A1c, but I also did wonder around issues with

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the comfort of the device, the continuing use of the device, if a longer time period -- three months just felt a little bit too short in my view.

DR. ROSS: Dr. Carlson?

DR. CARLSON: So a question for Heather. I just wanted to make sure I understood correctly what you mean by proximal and more distal outcomes. I think I know but I want to make sure. Could you be more precise?

DR. YOUNG: Thank you, yes, I can. I think some of the health outcomes that are sequelae of problems with glycemic control are more distal, whereas the time in range is more proximal, and even hemoglobin A1c is an average running over three months, and so if you start a therapy on day one, you may start to get benefits day 15, 20, into that time and the average wouldn't be as accurate as when you're looking at time in range over time. And so just thinking about what really it's measuring is what you're indicating, what you're looking for, rather than lagging and potentially confounded.

DR. CARLSON: We're on the same page,

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and I agree with you, violently agree with you.

DR. ROSS: Mr. Frankel?

DR. FRANK: Naftali Frankel. I just want to quickly reference a point that was made earlier just on a very high level that, my understanding of course, and I think that this was understood in advance of this meeting and during this meeting, is that all our conversation is not in any way, when we're talking about equity issues, which of course was raised repeatedly amongst the speakers, that there is no guidance at all that we're providing to create any sort of obstruction or impediments towards physicians and patients access to these devices.

And you know, obviously as the patient representative on this panel, that's of course important to note, that that should be a presumption. And when we're talking about rationing, you know, I'm not going to get into that really in depth, because I think it's also a given, that we're not looking at all in terms of trying to identify determinations of whether to provide access or not, but collection of data. And if there's any mistake in that

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assumption, then that would be great to have that clarification on record.

DR. ROSS: And just to clarify, you are right, we are not making any advice or recommendations about, you know, the technology itself or themselves. It's all about what body of evidence we would advise CMS to ask for when making a coverage decision.

MR. FRANKEL: Okay. So I just thought it would help just to put that on the record.

In terms of A1c, that's something that I referenced before, after Dr. Munshi's presentation, and I think it might be helpful if it's possible to go back to that and ask for further input from her given her expertise in the area, because there was obviously a divergence on that specific point from a lot of the other presenters and other data that we reviewed. It would be helpful, I think, to have a little bit more clarity in terms of Dr. Munshi's perspective on deprioritizing that.

It sounded like in a very substantial way that that was, there was some emphasis over there on the lack of reliability, particularly

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because of the heterogeneity in the population we're talking about. So when we're talking about an elderly population where there's multiple comorbidities that can have a very broad spectrum and range, it seems that particularly in that population, she felt that this was something that should be deprioritized. And I just thought it would be helpful if maybe we can get a little bit more clarity on that specific point, given the fact that we're specifically mentioning that as one of the metrics.

DR. ROSS: Tara, are we able to invite Dr. Munshi back into the presenter so that we could ask for clarification? And maybe while that's happening, I can ask Dr. Isetts to --

DR. ISETTS: Dr. Fanaroff was first.

DR. ROSS: Oh, thank you. That's my Dutch panel. Sorry.

DR. FANAROFF: Thanks. Just in response to one of the things that Dr. Dhruva said, I was going to ask the question about, you know, whether a three-month change in A1c would be sustained and if, you know, continuous, continuation of using these

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devices. And actually Dr. Forlenza had sent me a message in the chat that I'm going to just like read it into the record so you guys can hear it too because it was sent to me.

So he said that when they looked at continuation of CGM and AID systems at their center, with 4,000 cases and 500 adults with Type 1 diabetes, they have a 99 percent continuation rate when they exclude coverage loss.

So it does sound like, at least in that one center's experience, that people tend to remain, you know, continue to use these devices.

DR. ROSS: That's helpful.

DR. ISETTS: Okay, Brian Isetts, University of Minnesota. I want to just address one of the comments that were submitted that was not covered in any of the presentations or discussions today. We had a colleague from the University of Washington introduce the measure that he characterized as being dormant over the last 20 years of the high glycation index, and that there's a greater risk for hypoglycemia in patients where

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there's a high glycation index and a greater risk for cardiovascular disease. Now I recognize that this, you know, high glycation index may not be ready for prime time in terms of our evidence review, although I want to make sure that we get it in the record for possible future considerations, that we acknowledge that it's out there, that the research is building, and we include that in our report.

DR. ROSS: Thanks. Actually, the other endpoint that was measured, although it wasn't described explicitly as a surrogate endpoint in addition to the GMI, which I thought Dr. Munshi spoke about, was this issue of variability and whether that's measured at the individual level during the course of treatment and its implications for hypoglycemia. So again, I didn't see in our evidence review, maybe others -- oh, I guess it is. The coefficient of variation was also mentioned, so I'm mistakenly speaking.

Was Dr. Munshi able to be rejoined into the meeting, Tara?

MS. HALL: I just sent her a message, I'm waiting for a response.

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DR. ROSS: Oh, okay. I believe Dr. Wall was next. Please correct me if I'm wrong.

DR. WALL: Yeah, this is Eric Wall. Just a quick clarification, Joe. When we get to the voting, we're voting on ranking or whatever it is we're doing, it's actually domains. We're not really ranking within a domain, we are not ranking measures, you know, the suggested measures. Let's say the surrogate markers, we're not prioritizing those measures one over the other. Am I correct?

DR. ROSS: This is Joe. That is correct, although for instance, like the presentation that came from Dr. Reddy and Dr. Schulman-Rosenbaum, I thought that was actually useful. They talked about individual measures within each domain, and I would encourage you that if you do have an opinion about one measure versus another within a domain that when you do vote, you can talk about that.

Because again, just for a point of emphasis and for the public record, it is our spoken comments that are then used as part of

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the transcript that CMS then relies on more so than the votes themselves. So that for instance, if you were to vote on, I don't know, the quality of life or patient-reported outcome domain, you might think that's very important and rate that a five, but you would say if it's really this measure that you value highly, and these other measures that were listed there's much less evidence for, or something to that effect, so just to speak openly as to how and why you're making that vote. Does that help?

DR. WALL: Yeah, thank you.

DR. ROSS: Dr. Kobylarz?

DR. KOBYLARZ: Again, just to piggyback on what you, Dr. Ross, were just talking about, I think looking at the surrogate markers, emphasizing, you know, primary secondary type of endpoints, and at least what I was hearing, time in range, hypoglycemia were much more towards the top of the list, and just given the variability in things like A1c, maybe that could be a little bit lower or some kind of secondary endpoint.

DR. ROSS: Dr. Lewis?

DR. LEWIS: Thank you. Joy Lewis, and

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I think regarding -- forget it. And I appreciate Joe's comments that we can prioritize, agreeing with Fred that we can prioritize within each of the domains to which surrogate markers are mentioned.

I raised my hand because I just wanted to address the question that was raised regarding the duration of the studies, and the way I'm looking at this is that we're looking at devices that have been approved by the FDA, so they've been studied for a duration long enough to get FDA approval to measure the safety and effectiveness of the devices. But then we're tasked with looking at what studies need to be done or what needs to be considered, not necessarily a new study, but what needs to be considered to look at these for this Medicare population. And so for me, not wanting to add additional burden, I would say the three months, there was good evidence and there were compelling arguments made for the three-month minimum time period rather than a longer time period, given that these are already approved devices.

I recognize that the FDA approval

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might require some longer timeframes to show some of the safety and effectiveness, but that's not at the realm that we're operating in. In my mind, we're operating on what is the minimum for us, for an approved device that's already been FDA approved.

DR. ROSS: Other comments or questions about the domains or information that we've heard? Dr. Kobylarz?

DR. KOBYLARZ: Just another comment regarding device-related safety. At least what I heard here from one of the presenters, what would be key here would, at least what I heard was device continuation and adherence, you know, to the actual, you know, technology might be something here to think about.

DR. ROSS: Yeah, I think that's an excellent point. I also heard someone talk about specifically the capability of using the device safely but there, that wasn't defined in any way. You know, it's just an interesting challenge with medical devices in terms of both the individual user and the caregiver, how to assure, you know, that that's what's happening. I'm not sure that came up very much in the

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evidence, the endpoint review of the evidence in terms of sort of adverse events or safety seem to be much more related to device malfunction as opposed to device use or misuse, so that might be something that we might want to think about more.

But Dr. Young, I saw your hand coming up first I believe, but if I'm getting these wrong, because I'm juggling multiple things, just please correct me. Who was up first?

DR. YOUNG: I think Joy Lewis was up before me.

DR. ROSS: Joy?

DR. LEWIS: It's really okay, but thanks. Speaking directly to what you just talked about, I too wrote down that device discontinuation and patient preferences regarding use, which we hadn't initially discussed as part of safety, but that came up in the comments and in the presentations.

And I'm also just curious where the panel members would place cognitive function, into what domain. It's not necessarily measured in quality of life, it might be but not in all of these markers. It is a health

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outcome but it's, but we have talked a lot about these long-term health outcomes and deemphasizing those as measures of assessment for shorter term, and the unnecessarily complex nature and length of trials for really hard and fast health outcomes. So I'm just curious what others think about where they would put the cognitive function.

DR. ROSS: Yeah. I'll just note that there was a discrepancy in term in the table versus the question, where the table used the term patient-reported outcomes of the life impact domain, whereas the questions say quality of life, but then define that as patient-reported assessments of symptom burden or function. So I think I probably would have put cognitive function as an endpoint there, as opposed to an outcome per se.

DR. LEWIS: Yeah, that's how I put it in my notes as well.

DR. ROSS: Yeah. Dr. Young?

DR. YOUNG: Yes, thank you, Heather Young. I'd like to address the issue of the cognitive function. I think that cognitive function includes both dementia and delirium,

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and is looking at an outcome of treatment that the delirium aspect is probably more relevant than the dementia status. I would say that the cognitive ability, executive function and ability to engage with the device is a precursor to whether it's going to be successful or not, but I'd like to call attention to the fact that family caregivers provide about 80 percent of all long-term care or chronic care for older adults, and they in their capacity are acting on their behalf. And so assessing the individual who might be using the device may not necessarily link to the outcomes that are possible for that individual with the assistance of others. So I wouldn't want to see discrimination against people who have cognitive impairment based simply on their status because they're often aided by other people.

And related to the safety aspect, I was a little puzzled to actually see preferences and discontinuation as a safety issue, because there are many different reasons people discontinue that may or may not be safety related. And so as we think about that,

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it's in a domain of perhaps patient preference and also efficacy for that person and using a particular device. I'm not sure I would categorize it as safety per se, unless there was a discontinuation that was related to some kind of a skin reaction or some element that was very specific to the use of that device.

So it gets to this issue, again, of distal, proximal. Something that is discontinuation has multiple explanations. And so I would urge us to be more precise if that's a safety factor.

DR. ROSS: Those are all excellent points. Dr. Dhruva?

DR. DHRUVA: Thanks. I was going to make a similar point around the device discontinuation. I think that it matters as to why the device is discontinued. We know with a lot of medical devices, they might be discontinued, explanted for a safety indication, but it might also be related to a parent preference and the patient not wanting to continue.

I also wanted to, just to Dr. Lewis' good point around cognitive function changes, I

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think that, I think that I'm, I do I think place greater value on health outcomes like cognitive function changes, hypoglycemia that requires intervention from a caregiver or someone else than the surrogate markers. I know that it's easier to measure obviously Level 2 hypoglycemia, Level 1 hypoglycemia but to me what's important is the consequence to patients, less so the number, and sort of what happened to the patient, did they need a caregiver to intervene, did they have a fall, did they have any other adverse sequelae?

DR. ROSS: Mr. Frankel?

DR. FRANK: Yeah. You know, I think in some ways I'm echoing what Dr. Lewis as well as Dr. Young had mentioned before with cognitive function. You know, one of the things that I am a little bit concerned about, though, when listening to the conversation in terms of really what the substance is, in theory it all makes a lot of sense. You know, it was mentioned before in terms of potential screening mechanisms to be able to identify, but the problem is that of course when we're dealing with a national population and you're

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going to have different access to care and different clinicians involved, and different screening mechanisms potentially and different expertise amongst the physicians that are performing those screening mechanisms, there is a concern of a slippery slope which leads to the side of less access to patients in inappropriate ways.

You know, it was mentioned before by Dr. Young specifically with caregivers for example. There's a lot of different points of the equation which can extremely be in variance from one patient to another, depending on where the patient is receiving their care. And because of that, my thought process at least is to take a step back and say this is a device that was shown to be safe and effective by FDA and when we get to a certain point of granular data we have to in some way be trusting that physician and patient relationship is really crucial over here. And when we're starting to put metrics in that may be a little bit arbitrary and perhaps misused if it's not used completely effectively across the board, then it can potentially cause a creep of more

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problems than solution.

DR. ROSS: Dr. Fanaroff?

DR. FANAROFF: Yes. So thinking about cognitive function as an outcome of a study or something you'd want to see, I didn't see any data presented that would suggest that, you know, that the proximate outcome of better glucose control would lead to measurably different cognitive performance. And so you know, just thinking about that as an outcome, I'm not sure that it makes sense, unless there's somebody that knows something about, you know, whether better glucose control or avoiding hypoglycemia should affect cognitive function as would be measured on some kind of cognitive function test.

DR. ROSS: I would just say, if I could just jump on that point, which I also -- no one presented data on that, although several of the endocrinologists instead talked a lot about the distress scale. This is not about cognitive function per se, but about, almost like cognitive stress about hypoglycemia, and I thought that was actually quite interesting.

DR. WALL: Joe, this is Eric Wall.

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Just, I'm sorry, but I thought I was hearing that repeated episodes of hypo, repeated hypoglycemic episodes does have a long-term effect on cognition. I didn't see any support for that, but I thought I heard that in at least one or two of the speakers.

DR. ROSS: That is what I heard too, but there wasn't subsequent data presented by any of the speakers. Dr. Garrido?

DR. GARRIDO: I'm just going back to Dr. Dhruva's point about prioritizing health outcomes that require intervention. I completely agree that those are important, but I think what was important to note about the materials presented today is there's a really strong association between those surrogate markers and the health outcomes. I was concerned that measuring meaningful outcomes, meaningful differences in health outcomes might require large lengthy trials. It's not clear to me that the benefit of that information outweighs the cost, time or patient burden that would be involved in a big randomized trial. I mean, we could use real world evidence and use observational data, but then it's. I don't

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have a good sense of how accurately we can attribute a hospitalization or an ED visit to diabetes, and not to any one of the many confounding factors that Dr. Young was mentioning earlier.

DR. ROSS: Dr. Lewis?

DR. LEWIS: Thank you. Just getting back to the -- and I think those are great points, Dr. Garrido, thank you for that.

And getting back to the discussion around the cognitive function, I agree with Dr. Ross regarding what was highlighted most was the psychological safety, any changes in fear of hypoglycemia, feeling of reassurance and ability to do more in your life and feelings of freedom from having to do the continuous monitoring and less fear, and that can be related to cognitive function. We also know if you fall from a hypoglycemic episode and break a hip and are in the hospital, then a lot of older adults ends up having, you know, as Dr. Young mentioned, some delirium, it could be more of an acute onset from other things that are happening or from the fall, from being hospitalized, et cetera.

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And so I'm saying all this to just make sure that, just to share that the way I'm looking at this is if we include these measures it's not, I don't believe in making a recommendation that you need to see an improvement in cognitive function. And I agree with Mr. Frankel that we don't want to set limits on what cognitive function one possesses prior to obtaining these devices, but instead showing that if you can show an improvement or perceived cognitive function, a person feels better about their abilities in their life, then that's a bonus.

And to me, that's as much of a bonus as some of the other measures that we've already discussed. So I'm not trying, I don't believe in setting this as a requirement, but just to invite inclusion of these other domains so that the people studying these devices have the best ability to show the real world benefits in people using them.

DR. ROSS: Very helpful, and good level setting. Before we go into talking about the specific questions that we're going to vote on, does anyone have any -- I want to leave us

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an hour to go through them, because I think people are going to have things they want to say as part of the vote, which is what I really want to encourage. But does anyone else have any -- this is Joe Ross speaking. Does anyone have any last questions or point of clarification that they want to make for the panel members, or issues to surface? Mr. Frankel?

MR. FRANKEL: Yeah. The only thing I'd mention is that before it was asked about the hyperglycemia, because there was little focus on it. I just noticed, and again, I didn't have a chance to actually look up the paper, but one of the materials that were provided to us by the diatribe foundation, it references a specific piece of literature regarding hyperglycemia and how it has been shown to improve mood. Again, I can't speak to the validity of that paper, I didn't even look it up, but I'm not sure if anyone else here has anything to add on that specific point regarding that intersection between hyperglycemia and an improvement of mood for that patient population.

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DR. ROSS: Dr. Fanaroff?

DR. FANAROFF: I don't have anything to say to that particular question. I think one thing that just in general worth saying is that Dr. McGill talked about how the MCID for a given measure changed based on site design and comparators. I think that that is, you know, I wanted to raise that flag, I think it's important, I think in some of the studies the technology advancements almost certainly will compare, you know, new technology to already very good technology, potentially with not inferior devices, you know, where they're the same for measures of A1c and time in range, but better from a patient satisfaction standpoint.

And I think that, you know, in that case maybe the MCID becomes the non authority margin, I don't know exactly how that will be designed, but I think it's an important consideration to raise, because study designs do matter when determining an MCID.

DR. ROSS: No, I think that's actually quite a good point, right, the idea that if there is a known minimally clinically important difference, you would want any comparative

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research between technologies to use that MCID as the non authority margin, saying that it's no worse than this. And I will just say, I think the biggest challenge for all of us and for CMS largely, is the comments that were made at the very end that just the general paucity of studies in older adults and in older adults specifically with Type 2 diabetes requiring insulin, and how to sort of make heads or tails of that. Dr. Dhruva?

DR. DHRUVA: Thanks, Dr. Dhruva, San Francisco. That was actually, Joe, that's the point that I was going to make, just as we sort of get to the voting. As I was reflecting on the clinical endpoints review that I read again last night, that we have a single clinical practice guideline for the treatment of diabetes in older adults, and despite that comprehensive lit search, few studies include older adults, include subgroup analyses by older adults, and so it just helped me to recenter in thinking about the fact that we may be looking at these outcomes in an older adult population that often has multimorbidity and other conditions.

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DR. ROSS: So with that, I would like us to move towards the voting portion of the meeting, and I'm going to remind us exactly what we will be voting on, because we will need essentially 15 minutes or so for each of the domains in order to allow everyone to have ample time to make their comments as part of the voting process.

But just, you know, the clinical endpoints review was a literature review to identify endpoints that have been tested or were found to have been used in research studies for technologies that are delivered in a part of care for Type 1 diabetes and Type 2 diabetes requiring insulin. Our role is to provide advice and recommendations on the body, you know, the body of evidence regarding these devices for self management in older adults, what type of endpoints would you want to see and how you would prioritize them, or should CMS want to see them and how you would prioritize.

And we're going to go through kind of one by one surrogate markers of domain, health outcomes as a domain, quality of life as a

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domain, and device-related safety as a domain. I'm going to ask each of you when you vote on that domain on a scale of one to five, from not at all important to extremely important. And then at our hands in the appendix, there are specific endpoint measures that have been identified, some of which have been studied very well, some of which not. Others were named or you know, or raised in the public comment period. So there's a series of surrogate markers, health outcomes, quality of life measures and device-related safety measures that have been named. You can talk about those which you think to be more suitable versus less suitable when you cast your vote, or you can say your vote is based on this specific measure but you don't have a strong opinion on these other measures.

And then I'm going to ask each of you to talk about the ideal duration of followup that should be required when using those measures, and whether you're aware or would want to see a specific minimally clinically important difference in the evidence, or that you would say is a valid threshold. Any

questions about that?

Can everybody go to the voting site? I just want to remind everyone that I am a nonvoting member, although I'm sure I will be making comments as part of this process. Dr. Carlson is also a nonvoting member, although my understanding is I ask you how you would have voted, right? Is that right? Yes, okay.

Tara, is everyone set up on the voting as far as you can tell? You're on mute.

MS. HALL: Is everyone able to log on?

DR. YOUNG: Working on it.

MS. HALL: Hold on, I can't hear you.

DR. ROSS: As this is getting figured out, I'm going to -- after everybody votes, I'm going to ask you how you voted and your explanations and rationale, and I'm going to go in the order on the roster, so I'll start with the committee vice chair, go member by member, then the industry representative and then the patient advocate.

MS. HALL: I'm sorry, I had a glitch with my sound. What did you say, Heather?

DR. YOUNG: I'm working on it, Tara.

DR. ROSS: So as this is being worked on, our first vote is about the endpoint domain ratings of surrogate markers. Just to remind everyone, these are indirect assessments using biomarkers, physiologic measures or imaging intended to predict or act as a proxy for a target outcome of interest. Examples include percentage of time in hypoglycemia, hemoglobin A1C. We heard other things around time in range or time below range, and coefficients of variability.

And so how, I'm asking you to vote, how important are endpoints in this domain as part of the body of evidence, with a one being not at all important and a five being extremely important? Everyone can cast their votes.

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

MS. HALL: Everyone has voted.

DR. ROSS: Great. Dr. Dhruva, I'm going to ask for you to start, to explain your vote and to address the points in the discussion around which endpoint measures you were thinking of the duration of followup in the MCID.

DR. DHRUVA: Thanks. I voted a three, that these surrogate markers I think are somewhat important. I think I was in between a little bit. I think these are important because they can be easily measured, these are data that are more easily available and so therefore can be assessed. But at the same time, I think they are less important than clinical outcomes to patients.

I would prioritize Level 2 and Level 3 hypoglycemia. I think a lot of what we heard, particularly for older adults, we know from the 2019 guideline on diabetes in older adults that A1c, despite it being the easiest measure it is not prioritized, but that the metrics around hypoglycemia, I think are particularly important.

Given that these are relatively rare, the hypoglycemic episodes hopefully, I think that probably three months is too short, and probably something like six months is more helpful.

DR. ROSS: Dr. Fanaroff?

DR. FANAROFF: So I said five for this one. And I think that, you know, the rationale

for that is that this is really, to borrow Dr. Young's terminology, this is the most proximal outcomes to what the device purports to do. So you know, I think this is important because essentially what you're asking is does the device do what it says it's trying to do. If not, it's not doing that, what else is it doing?

I think the important markers here are A1c, time in range and time below range. I think that those are important, I think that probably the minimal clinically important difference for hemoglobin A1c, I would favor 0.3 percent, based on the fact that that's how, you know, the criterion that the FDA and the AMA used to approve diabetes drugs.

To make sure there's nothing else that I wanted to say here, yeah. And I think the other important thing to think about is that I think the other rationale for this is that there's a strong association between these, between many of these surrogate markers and outcomes that are important to patients, including cardiovascular and other microvascular events.

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DR. ROSS: Dr. Garrido?
DR. GARRIDO: I voted a five. My rationale is similar to Dr. Fanaroff's. These are the most proximal measures. We know that they are strongly associated with other meaningful outcomes in the other domains without being subjected to confirming factors because the group of older adults with diabetes is so heterogeneous.
I heard a lot of support for time in range. There was one speaker this morning that mentioned an adjustment related to making sure you're not going below the acceptable range might be warranted. I think that might be something that should be considered.
I don't think I have enough information to make a recommendation to the meaningful follow-up time.
I would think for clinically meaningful differences, examining individual variability rather than trying to have a fixed endpoint I think would be important to consider.
DR. ROSS: Dr. Isetts?
DR. ISETTS: Brian Isetts, University

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of Minnesota College of Pharmacy. When I look at the scales here I need to look at the practical anchoring, and I really enjoyed the application of the Dr. Joy Lewis anchoring measuring scale. So the five is we can't live without it, okay? Four is it's expected and highly desirable. Three would be well, you can live with it or without it.
And so in the first domain, I want to just use the relationship of surrogate measures to in vivo measures. Because it would sure be nice, you know, if we could get measures inside the pancreas and inside the endovascular system and what have you in the kidneys, but we really can't. So my vote is that we can't live without it, it's extremely important, a five.
And specifically the measures, this is really the patients that I serve as a geriatric practitioner, are the hypoglycemic measures. I also want to go on record as I said previously, to make sure that for future research we look at this, begin to look at the high glycation index because that does relate to hypoglycemia.
And I do believe that three to six months is appropriate followup.

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DR. ROSS: Dr. Kobylarz?
DR. KOBYLARZ: Yes, Joe. So I also voted five. I think this is extremely important. I think the focus should be on time in range, percent time that's, you know, in Level 1 and Level 2. I think the other surrogate markers like A1c, which lend themselves to variability, would be lower on the list but should be looked at.
I feel just, you know, given the heterogeneity of this, you know, population, and differences between a let's say 65-year-old and a 90-year-old, you know, I think minimal clinically difference, you know, could be challenging here, so I'm not sure if I can give you a number or percent.
You know, I do think that the duration of these studies, you know, minimum of three, perhaps six months would need to happen.
DR. ROSS: Dr. Lewis?
DR. LEWIS: Thank you. I also voted five. I oscillated between four and five as I was thinking about the utility of some of the measures, but given that we're able to explain what measures we think are most important, I

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went with the five. And I agree with the comments that have been made round time in range and time below range, as well as the ability to recognize Level 1, Level 2 hypoglycemia. And then also quite important to me, the ability to recognize asymptomatic hypoglycemia, which can particularly put elderly patients at risk, so the ability to avoid hypoglycemic unawareness to me, may be surrogate markers of the utmost importance.
I also appreciate the mention of the combination, the importance of the combination between time in range with control of time below range, so a composite endpoint that was mentioned by some of the endocrinologists, I think that's really important. The A1c we've used for quite some time, but I do agree that it's less important for this population than it might be for others, and so I weighted that down.
If we did want to look at minimally clinically important differences, even though I'm weighing in my mind the A1c as less, I think the 0.3 percent difference, and I know the literature says 0.5 percent, but others

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have mentioned 0.3 percent. And what I found quite compelling was one of the comments, I don't believe it was said today but was in the materials that we were given, that said we don't want people to have to have worse control going into a trial just to see a difference in the trial. If they're already well controlled, you don't have as much room. So that's why to me, looking strictly for a difference is less important that looking at the individual changes that might occur.

And then similarly for time in range, the numbers that have been presented are the five percent, or even a three percent. So if you're looking for a difference between groups, or someone that already has good control, I would encourage us to look at the three percent rather than the five percent difference. It was also mentioned, the non inferiority, and I think that's really important that we keep in mind, so that we don't stick with strict minimally clinically important differences in these measures, but instead think about non inferiority, and then the ability to use other measures to show the benefits to the patient of

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these devices, and those might be in different domains such as quality of life.

And then for the duration, I think given what I mentioned before, I would stick with the minimum of the three-month timeframe. Thank you.

DR. ROSS: Dr. Wall?

DR. WALL: Yeah, the advantage of being at the end is that everything has been said. But I also voted a five, for much of the same reasons. I think I'll only comment on some issues that may or may not have been raised. You know, it's interesting to me that the time in range is a pretty high priority surrogate marker. I'm surprised that since hyperglycemia is so rare in this population, you could almost have another measure which is time out of range, and that would be, include below and above, and not have to deal with time below range, but it seems to be a standardized metric in some of the device reporting.

Where I get hung up is not so much in the time measurement, which I can go for three months because that's what clinicians are used to, and I'm not terribly impressed with the A1c

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value, the clinical value in this population, but it clearly has some value.

So far what I've heard with the MCID is I kept thinking about what's the evidence basis, not just someone's opinion about what is minimally clinically important, and the only metric that I saw any suggestion that there was evidence for was the A1c MCID, which was five percent or greater than five percent. The thing that I kept trying to keep in mind is that because this is such a heterogeneous population, many, or some individuals who entered seniorhood will already be on these devices. So to suggest that someone has to jump through a hoop when they've already achieved these differences at an earlier point in their lives makes this kind of problematic and it gets to the whole idea of, you know, looking at what the studies, what the study population, the study goals are in the clinical trial design, makes it very critical to interpret that again, outside of the A1c, which I will throw in there only because it seemed to be a standardized metric. I didn't find, I don't know what to make of an MCID outside of

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that, so those are my comments.

DR. ROSS: Dr. Young?

DR. YOUNG: Thank you. I gave this, rated this a five as well, because I like the proximal nature of these indicators and I in general am in favor of the time in acceptable range and the hypoglycemic indicators of Level 1 and Level 2 hypoglycemia, because I think that they're probably the most sensitive in this particular population, and also the most appropriate given the heterogeneity of the population. I'm less excited about A1c for a variety of reasons, the heterogeneity.

Also because I think these monitors provide some data for patients, for people to start making decisions around their lifestyle, it's insulin management but it's more than that, it's their nutritional intake and their physical activity, and it take a while to use actionable data, there's a lag between getting that data and making some changes and doing the little experiments that will result in ultimate changes in glycemic control. And so I think that, coupled with the confounding by other conditions, makes me less excited about A1c as

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a surrogate marker for this purpose, so I definitely will go more with the percentage of time in range and the hypoglycemic indicators.

As far as time goes, I think the duration of three months is adequate to demonstrate the issues that we need to see, and I also share the perspective of Dr. Wall around it depends on where you start with what's a meaningful difference, a clinical difference. And if someone has been in control for a long period of time, the goal might be to maintain that control, not necessarily to improve it. And so I think that the within patient comparisons are really important in that indication, and if people are already achieving high levels of control, it's a tool to enable them to keep that high level of control, whereas those who are less in control, a meaningful difference would be five percent, say. Thank you.

DR. ROSS: I'm going to call on Mr. Frankel next so that we go through all the voting members first, and then Dr. Carlson, I'll come to you. So, Mr. Frankel?

MR. FRANKEL: Naftali Frankel. I

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voted four because I think that there were certain caveats mentioned here today that would limit it from a five, but of course four as stated on our voting is very important. Of course there is the challenge that we talked about before, really differentiating that from extremely important, but you know, the fact that there were certain limitations led me in that direction rather than a five.

In terms of the specifics, I'll just quickly echo what mostly has already been mentioned. Number of hypoglycemic events, percentage of time in range seems to be more important in terms of prioritization than A1c, let's important.

I agree also that it seems that 0.5, the lean would be towards 0.3 based on consensus with the limitations that were discussed and identified in the materials as well as today, particularly in this population where the metrics may not be as accurate in the first place.

In terms of followup, it seems that the broad consensus is three months, and I'm in agreement with that.

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DR. ROSS: Dr. Carlson? Are you speaking? Sorry, I don't hear you.

DR. CARLSON: I had to get off mute, sorry.

DR. ROSS: How would you have voted, and your rationale?

DR. CARLSON: Okay. My rankings are focused on what evidence should be appropriate and adequate for CMS to consider in making decisions, in other words, what should be important to make a coverage decision. I agree with ranking these surrogate endpoints as five. They predict and correlate with health outcomes. In my view they are the most important of the domains listed to make coverage decisions. Time in range and some measure of hypoglycemia duration or episodes are important.

I agree with the consensus that three months is an appropriate duration for studies using surrogate endpoints.

DR. ROSS: Great. So that, we finished that domain and I think we took longer, which is not surprising since we have the most endpoints to review as part of the

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surrogate marker domain.

As we move to the second domain of health outcomes, I do just want to remind that this is regarding devices for self management of Type 1 or incident dependent Type 2 diabetes in older adults, so we're not talking about all diabetes. You know, in therapies, broadly we're talking about these devices for self management. The health outcomes domain is around direct assessments, the target outcome of interest, for instance complications of diabetes or diabetes-related emergency department visits or hospitalizations, which could include both hypo and hyperglycemic reasons for admission.

And I'll ask you to go to the voting system, and talk about whether this domain and endpoints, how they rate to you from a scale of one, not at all important, to five, extremely important, and everyone should cast their vote.

Tara, I am still seeing domain number one on the screen.

MS. HALL: Yes. Next screen please, John.

DR. ROSS: There we go, thank you. So

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people should cast their vote.

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

MS. HALL: Everyone has voted.

DR. ROSS: Great. And the scores have a little more of a spread. So we will start with, talk about please, explain what you voted, which endpoint measures you were considering, the ideal duration of followup and the MCID. Dr. Dhruva?

DR. DHRUVA: Sanket Dhruva, San Francisco. I voted a four, very important. I think that what matters to patients and what patients care about is the sequelae of diabetes that could be improved through the use of these devices that we're discussing today. I think these are more important in my view than surrogate markers, and I think those, although they certainly take more time to accumulate endpoints, I think it's the most important. And I think that all of the health outcomes, cognitive function changes, emergency department visits and hospitalizations from hypo and hyperglycemia, as well as all their complications, are relevant, again, fully

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acknowledging it adds length to the duration of studies that are needed, but for patients for whom I care, I think that this is what matters most to them.

DR. ROSS: Dr. Fanaroff?

DR. FANAROFF: So I put a three for this one, somewhat important. I agree with what Dr. Dhruva said, these are important outcomes to patients, they matter to patients. But thinking about each of the endpoints individually, I think some of them are more important than others, and I think that most of them are sort of infeasible in this population, in this device, or have other challenges. We have the recitation of hypoglycemic awareness in there. I'm not, I think there are some questions to how that's measured.

We talked about cognitive function changes. I think there's a question there about whether we expect this intervention to improve cognitive function. I think the diabetes-related emergency department visits are important and if I had to, I would give that one a four. But the diabetes-related hospitalizations, I think there are questions

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about definitions and how you define a diabetes-related hospitalization. Is a hospitalization for an amputation considered a diabetes-related hospitalization? Should that be affected by this technology, I think that's the asking question.

And then last is the question about complications of diabetes. I'm a cardiologist. As nice as it would be to actually know whether these devices and interventions improve cardiovascular outcomes, yeah, it's probably in practice but you'd need trials with, you know, 7,000-plus patients like we have in our cardiovascular trials, and that's probably impractical with the pace of technological change. I will say, I think it's an important scientific question whether in an era with, especially for patients with Type 2 diabetes, whether that's GLP-2 inhibitors or GLP-1 antagonists, that if the relationship that we found in the UKPDS study, you know, a long time ago still holds today, but that's sort of outside the realm of what maybe these device numbers should be ideal.

DR. ROSS: Dr. Garrido?

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DR. GARRIDO: I also voted a three, somewhat important, and that relates to the use of these measures for making coverage decisions. I think these are highly important clinical outcomes, especially for patients and family members. I am concerned about the amount of time it would take to measure these, and I think the surrogate outcomes are kind of necessary conditions for these outcomes to be realized. So I'm not seeing the added benefit of requiring the health outcomes to be produced or provided to CMS for a coverage decision.

If these were to be measured, I would think we would need probably a 12-month followup to get adequate power to be able to actually observe it. And again, I would be concerned that, about whether we could attribute changes in emergency department visits and hospitalizations to use of the device itself.

DR. ROSS: Dr. Isetts?

DR. ISETTS: Brian Isetts from Minnesota. I rated this as very important, and that's in comparison to extremely important, and really relates to what Dr. Fanaroff said.

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I have concerns about the reliability of the measures, all right, the fact that you have patients with diabetes who have multiple comorbidities and how is it, how can we say that fall may be from a high blood pressure medication, hypertension, it's splitting hairs. It's an important measure because it is important to patients, and so that's why I rate it as a four.

And of course in the duration, the complications of diabetes such as major cardiovascular events and death, these are taking, we're talking years now, and so a one-year followup really may not be enough, it may have to be longer.

DR. ROSS: Dr. Kobylarz?

DR. KOBYLARZ: Thank you. I voted a four and I thought that, you know, this is a highly desirable measure, domain, but essentially we need data. I was during the discussion of the presenters earlier today and just our discussion, I was just thinking of how this could be framed, and what was kind of coming to mind was the four Ms, you know, what matters, mentation, mobility and you know,

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medication. You know, what matters to these patients is they don't want to end up in the hospital, they want to avoid hospitalization, they want to avoid amputation, they want to avoid blindness or visual impairment.

Regarding mentation, I think what's important is to just have a baseline screen for detection of a cognitive impairment, I think just having some baseline screening. And then I also think screening for other geriatric syndromes, not only cognitive impairment but depression, falls, pain, you know, all those.

I think you know, regarding mobility, other complications, there's neuropathy, you know, again falls, so I think we just need data on this, and you know, trials would take -- I mean, these would be long studies. I don't know if I can comment on a particular timeframe but again, it's highly desirable information and we just need data in this area.

DR. ROSS: Dr. Lewis?

DR. LEWIS: Thank you, this is Joy Lewis. I voted two for this, slightly important, and I actually oscillated between one and two on this, and I chose two because of

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the inclusion of admissions for hypoglycemia and hyperglycemia in this category.

And I agree with the overall importance of health outcomes as being extremely important, complications of diabetes are extremely important to measure, but not for this task. And for this task we're saying what do we need to measure for CMS to make a coverage decision of already approved devices, and with that in mind I'm fearful that having strict measures that require looking at diabetes complications including kidney disease and major cardiovascular events, for CMS to cover these devices would be prohibitively expensive, long and expensive for the manufacturers, and would then make it so the devices would not be available for the Medicare population. So that was my framework for deemphasizing these outcomes despite how important they are.

I also agree with Dr. Garrido that there is already great evidence that shows that the surrogate markers, shorter term measures, do provide good evidence of correlating with longer term outcomes, and with the use of these

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devices, we are now going to have better evidence going forward of these correlations between things like time in range, lack of time below range, the GMI and clinical endpoints, but I don't think that those studies are necessary for CMS coverage of these devices right now right now.

In my mind, the restoration of hypoglycemic awareness fell under a surrogate marker. I know it's on our list as a health outcome but I was counting it under the surrogate markers, because the surrogate markers are meant to help with recognition of hypoglycemia. And then we also discussed the cognitive function changes that I was putting more in the quality of life, because I think they're harder to change, and we discussed that earlier. So leaving this more to the emergency zoom visits, that's why I felt it was important, but because these visits may be more rare, I don't think we need to prove a decrease in order to approve a device when you have strong evidence in other domains, and that's why I deemphasized this domain as well. Thanks.

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DR. ROSS: Dr. Wall?

DR. WALL: Like Dr. Kobylarz and Dr. Fanaroff, I also rated this a four and I actually did this for a couple reasons. I looked at this in terms of wearing two hats, one was that hat of a researcher and this kind of prevented me from going to a five. I mean, I find to do some of the studies about, to study complications of diabetes, I just don't know how you would do that. It would take forever to do a study that shows that that kind of outcome would be directly attributable to an intervention over, I mean over a long period of time, and you'd have to do an immense amount of controlling.

Cognitive function changes, some of these metrics are worth tracking, but I'm not sure I would require them as kind of a ticket of entry.

But I think what got my attention as kind of a coverage decision person is, I mean, I do think there has to be something in here about healthcare utilization, and a reduction in healthcare utilization in some way that is a direct result of this technology. Otherwise,

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I'm not sure if we're paying for it, you know, we haven't really talked about cost effectiveness on this because it's kind of a dirty word, but I actually do think that somehow you've got to be able to show that as a metric, that at least it's not increased and potentially it's decreased.

And I do think there are probably ways of teasing out diabetes-related hospitalizations, although I put a question mark after that, saying it's not easy to measure that, but I'm certain someone has. For these reasons I gave this a four.

DR. ROSS: Dr. Young?

DR. YOUNG: Yes, thank you, Heather Young. I rated this a two. I do think that these health outcomes are vitally important for patients and also have broader implications, but there is a well-established evidence base for connection between glycemic control and health outcomes. And for the purposes that we're charged to think about, which is about evaluating the CGM, insulin pumps and AID, I think these outcomes are too far out and problematic. It takes much more time to show

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the effects, there are other confounders that are involved, and it also involved the physician and the disease trajectory. So if someone has had undiagnosed or untreated diabetes for a long period of time, the complications may be there, but it may not be attributable to the device and using the device, and it could be a longstanding condition.

I'm also a little concerned about the healthcare utilization indicators because hypoglycemia may be undetected, and it's something that someone has been unaware of, and once they get the CGM they find they are having hypoglycemic episodes, which leads to a visit for healthcare utilization. And so it's actually a benefit that they get treated for something that's occurring that they were previously unaware about. So I think there's just too many complications in using this as an indicator for the purpose of granting access to these technologies. Thank you.

DR. ROSS: Mr. Frankel?

MR. FRANKEL: Yes. Naftali Frankel. I voted four, but I would like to say that

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juxtaposed to that with a very strong caveat, which is that, you know, theory versus practicality. And in theory this sounds great, and I think that it was pointed out before, this is what patient want to know. As a practical matter, it was also mentioned by those that were more detractors towards the utility of this measure, of whether or not it's confounded. And I think it's essential, first of all, for there to be direct adjudication, if that's possible, towards the device when we're looking at this. And if it's not possible, then I would say that this is not useful at all, you know, I would say that was a one, not a four.

So going with the assumption, with the premise that we're going to be able to apply specific health outcomes that are directly attributed towards the device and it can actually be measured in that way, and that it won't cause additional burden towards access towards the device, then that's my four. So I just want to, I think it's an important footnote for that four and again, if those premises are incorrect, then obviously that's

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what that four is grounded in.

DR. ROSS: Dr. Carlson?

DR. CARLSON: Sorry. I ranked this a two and I yield my time to Drs. Lewis and Young, who could have written my comments.

DR. ROSS: Okay, great. So we're going to move to the third domain if that voting question can be opened up. Here we're gong to rate the importance of quality of life as an endpoint domain. These are patient-reported assessments of burden or function, including measures we've heard, like the Audit of Diabetes Quality of Life questionnaire, the distress scale, impacting better scale. Some people have talked about patient preference and using these devices, I'm sure there's scales that get at that.

I'm going to ask you to rate from one to five, with five being not at all important, to five being extremely important, how important is it that this domain of evidence be developed as part that CMS should be looking at for use in older adults.

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

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MS. HALL: So, waiting for one more vote. Everyone has voted. The voting is closed.

DR. ROSS: Great. You guys voted faster than I could get that mouthful out, and again, we have a wide range of scores. Dr. Dhruva?

DR. DHRUVA: Thanks. Sanket Dhruva, San Francisco. I voted a four, very important. I'll make a couple of points. I think that quality of life is incredibly important to patients, so I voted very important.

I just wanted to make a couple of points. A very rich discussion over the past half hour or 35 minutes as we've been going through the voting. I think it would be nice to know if the -- I am not as convinced. It would be nice to know if the metrics that we're able to measure from these devices around time in range for example, was definitively correlated with, for example, patient-reported outcomes or other clinical outcomes. And if that's not the case, then in this case I have voted a four, and I think that these need to be evaluated.

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And I think just another point, I think a lot of people made great points around the clinical trials, and just the need to continue these clinical trials. I'd just say that these trials are often being conducted to receive FDA authorization, and so it's, I don't think it necessarily has to be a new trial to look at the clinical outcomes, but I think the trial needs to include older adults, have sufficient followup and incorporate quality of life metrics as well.

DR. ROSS: Dr. Fanaroff?

DR. FANAROFF: So I said two, slightly important, mostly because I'm not sure that any of these scales necessarily measure the concept that, as a lot of these scales measure the patient-reported outcomes in a way that necessarily reflects the value that patients get from it. I think that the idea of quality of life is important, I just don't know how important it is to see that evidence prior to approval for payment.

I also think that, again, this is one where it depends, it depends on what the goal of the study is and what it's being compared

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to. You know, if it's a device that is intended to achieve equivalent outcomes by seeing a control that gives patients some benefit in terms of usability, then it's more important than a device that's intended to -- basically, I think it's just a big it depends for this one.

DR. ROSS: Dr. Garrido?

DR. GARRIDO: I gave this one a one, and not to say that quality of life isn't important, I think the quality of life measures are important, should continue to be studied, but I don't think they should factor in to a CMS coverage decision.

I'm thinking of a scenario where maybe fear of hypoglycemia goes down with use of a device but we don't see any meaningful movement in the measures of glycemic control. I'm not sure, then, that that warrants coverage of a specific device. I'll stop there.

DR. ROSS: Dr. Isetts?

DR. ISETTS: Yeah, Brian Isetts from Minnesota. This is the one domain I wavered and struggled with from this time that we've been together. I started out at first that it

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was somewhat important, because I had concerns about the practical application to the scales in practice, but I really have now migrated to it's very important, and I'll tell you why.

And Dr. Kobylarz hit the nail on the head in the last discussion when he addressed the four Ms, okay? So I might have mentioned to you folks that this is one of the things I've done in life is to, I spent an extended sabbatical at CMS for two-and-a-half years right after the Affordable Care Act was passed, and who was the administrator, we talk about the 4 Ms at The Institute for Healthcare Improvement, it was Don Brewick. And the first thing he did when he walked in was say wait, let's stop this. The patients are always in the room, they're always first, we hear their stories that start and stop, and all contacts include a person and family engagement component.

And all of the measures listed here, I don't have a lot of confidence in the context of what we're doing here. We need to do more to hear from those patients. If we're talking about self management, self efficacy, maybe we

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have to use more qualitative studies in terms of focus group sessions to hear what's happening, and I think that will also play into the discussion we're going to have about device discontinuation here in a minute.

So for those reasons, that's why I voted very important.

DR. ROSS: Dr. Kobylarz?

DR. KOBYLARZ: Thank you for that segue because I gave this, I voted this a five, and I think it's extremely important. I think these need to be included. They focus on, you know, symptom burden, you know, focus on function. They should not be exploratory. I feel that, you know, any validated instrument that could be used in, you know, diverse populations that you know, that pertain to diabetes can be utilized. It is a challenge because we need to think about, you know, these are self reported, you know, measures, so that does present a challenge.

And you know, I think in terms of the time duration, I would say no less than three months, you know, and we could expect to maybe see a change. So I see this as very important.

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DR. ROSS: Dr. Lewis?

DR. LEWIS: Thank you. Joy Lewis. I too deliberated over this number. I considered a five but then given the limitations of the existing measures, I didn't want it to stand in the way of a device that could benefit Medicare patients being approved. I ended up settling on a four because I do feel these are very important. And I actually feel that if a device can be measured as non inferior in terms of the ability with the surrogate markers, if it then can show benefit in the quality of life domain, then I think that's worth covering. And whether that's non, whether that's an improvement in psychological safety and hypoglycemic awareness, or even just someone more able to eat what they choose to eat and to exercise without fear, to sleep safely, maybe there's a device that has a better way of waking you up if you're hypoglycemic and it's less stressful, then that's a benefit from the alarm going off. Or for the integrated devices that you don't even get an alarm, you just get some glucose, so that there could be a benefit to the overall wellbeing. I think that's of

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utmost importance, and I'm hoping that we can get improvement in measures and really emphasize the importance of studying health-related quality of life in Medicare patients, so that even early in the FDA process these measures can be included as a norm and not an abstract. But maintaining my approach of what's needed for this population, I feel the four, it is a very important step.

DR. ROSS: Dr. Wall?

DR. WALL: I struggled between a three and a four on this and I settled on three but I could go, easily be talked into a four. Like the previous panel members, I feel this is an incredibly important measure. You know, empowerment, self control, self empowerment of patients and assessing that is enormously important. And we certainly do need more quality of life metrics when we work on approving any technology as part of the approval process.

That being said, again, I kind of focused on -- I'm not all that familiar with most of these questionnaires or surveys, so I couldn't speak to which was preferable. It

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seems like the ADQOL was cited in a number of studies. But again from a coverage standpoint I kept thinking, you know, many, a substantial population of Medicare eligibles and Medicare age individuals are entering this kind of decision making with many years of, with the use of this device, and I don't know how you control for, you know, that in kind of a study. And I just felt like it relative to the other domains, this was not as high for me, and I feel a little guilty as a family doctor saying that, but it is really important that we address this, but from a coverage standpoint I had do drop it to a three.

DR. ROSS: Dr. Young?

DR. YOUNG: Thank you, Heather Young. I'm in the same camp as Dr. Wall around, I think that these measures are incredibly important and vital for understanding the effects of different treatment for people in their lives. I'm troubled by them being used as a coverage decision, and I voted a three for that reason. I think that these measures include broader considerations that can affect their score. When you look at the item level

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issues, they're not all really proximal to the device itself. And other considerations like being in pain or having a relationship that's not so positive with a provider, or financial pressures, can change someone's rating on these scales when it's really not related to the specific indication that we're thinking about.

Also, older adults commonly have multiple comorbidities, and people don't separate their perspectives and say I feel this way about my diabetes, I feel this way about something else, and quality of life in many of these indicators are really a more global assessment of one's subjective wellbeing. And so I think it's difficult to get highly valid, we can have reliable measures but they may not be valid for a specific purpose and so they may not be salient, these measures may not be actually salient for what we're trying to address here in particular.

I think it is really important for us to have indicators of quality of life. If I were to pick one, I would pick the Diabetes Dependent Quality of Life Index, because I feel looking at the item level that they're the most

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connected to what we're trying to assess, but in general I would urge that we look at these issues in broader studies because they're relevant and important, but not for the purposes of the coverage.

DR. ROSS: Mr. Frankel?

MR. FRANKEL: I also have some reservations about this metric. I voted three and my concerns have already been voiced by multiple different members of this panel, but predominantly that in theory this is of course a very important thing to understand and to receive input from patients in terms of quality of life. But when we're discussing coverage, there are questions in terms of the specifics of that individual patient. I'm always very hesitant when we're talking about policy for a patient population, quote-unquote, when we're talking about quality of life, because the measure of quality of life varies depending on the individual patient, and I feel that sometimes there's somewhat of a sense of paternalism even, where we're deciding for the patient in effect by determining that something should not be covered rather than for them to

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determine that as an individual with their specific physician. And you know, in terms of practicality, in terms of application of these measurements, the accuracy of them, the potential confounders, for example when we're talking about something under the category of patient-reported outcomes, PROs, there's sometimes the question of, you know, you're asking the patient what their quality of life, how they're measuring it based on the current treatment or the specific medical device, you don't really have a picture of how they'd answer that same question in a control group where they were not actually receiving that therapy or treatment.

So you know, these are different scenarios where I've seen in the past where sometimes we're saying yes, of course, this is extremely important because we care about the patient, but sometimes they can actually get in the way between the patient and the treatment that they may actually benefit and actually appreciate having.

DR. ROSS: Dr. Carlson?

DR. CARLSON: I would have ranked this

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a three also, for the reasons that have been stated. I think that quality of life is most important to physicians and patients who are making decisions about an individual patient's therapy. I think it's less important, if important at all, for making coverage decisions, for the reasons that others have stated.

DR. ROSS: Okay. We have one last domain to discuss, we might end up going a little bit over, I apologize, let's try to move the last domain as quickly as possible to meet the two o'clock meeting end.

But this relates to device-related safety as a body of evidence, for example hypoglycemia related emergency department visits or other harms, perhaps illustrated by device discontinuation rates. Please vote on a scale of one to five, one being not at all important, five being extremely important.

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

MS. HALL: Everyone has voted, voting is closed.

DR. ROSS: Great. Dr. Dhruva?

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DR. DHRUVA: Sanket Dhruva, San Francisco. I voted for very important, I'll be brief. I think that ensuring the safety of these devices when used in an older adult patient population that has multimorbidity oftentimes, usually has greater risk that a younger patient population without other co-occurring condition, I think is very important to assess.

DR. ROSS: Dr. Fanaroff?

DR. FANAROFF: I said five. I'll echo what Dr. Dhruva said, that safety is important to an older population, and I think device, I don't know if this really falls under safety, but I think that ensuring that an older adult population is capable of using this device and continuing to use the device over, I would say a six-month followup, is probably necessary to make sure they get the benefits related to glycemic control.

DR. DHRUVA: I think --

DR. ROSS: Sorry, my Zoom froze and I got kicked out. Did Dr. Fanaroff finish his explanation?

DR. FANAROFF: I did.

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DR. ROSS: Okay. Dr. Garrido, I apologize.

DR. GARRIDO: I gave it a three. I was waffling between a three and a four. I think demonstrating safety in the older adult population is extremely important. I'm concerned about some of the metrics that were listed in this domain, being able to disentangle discontinuation of a device from safety reasons versus patient reasons, so that was the reason I gave it a three rather than a four.

DR. ISETTS: Dr. Ross, you look frozen again. You're on mute.

DR. DHRUVA: Joe, I think you're on mute.

DR. ROSS: Ah, thank you. Dr. Isetts, my apologies.

DR. ISETTS: No problem, thank you. Brian Isetts from Minnesota. On the rating I have written down on my notes here is 4.5. In light of the fact that we have to use whole integers, I registered a vote of four, very important, and here's the context of why I was leaning towards that half integer.

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It is okay, we're going to include device accuracy, correct? Of course. If I'm a patient, I want to make sure it's accurate. We kind of talked about device discontinuation, and I also want to address equitable use because when the devices are being used, there's a lot of things, stuff happens to patients, okay, in the real world, so I'll address this equitable use.

So you're living in a section of town, in south Chicago for instance, and the only time that you can get help is after hours, and you don't have transportation. How do you get to the pharmacy or the clinic to get the support you need or the supplies that you may need?

Also device discontinuation, we need to study this further in terms of, I saw rates as high as 20 percent. Let's sit down with those that have discontinued the device and find out what those reasons are, because maybe it's that they don't have the cognitive ability, or maybe it was really related to safety. I think that's going to be critical as we move forward in terms of as we keep talking

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about these coverage decisions, why were these devices discontinued? I think that's important because it's such a qualitative measure.

DR. ROSS: Dr. Kobylarz?

DR. KOBYLARZ: I gave this a four and I thought this was very important, you know, highly desirable information, and so the data should be, you know, expected. I kind of focused on the discontinuation rates just to echo my colleague, and I think focus on capability, adherence, this is all very important, and I think this could be studied in a relatively short time, I don't think this would, you know, be a long trial, but I'll stop there.

DR. ROSS: Dr. Lewis?

DR. LEWIS: Thank you. I also gave this a four, many of the same reasons that have been mentioned, and in our initial review the endocrinologist who reviewed the clinical evidence review mentioned the accuracy of devices at lower levels of glucose reading in the older population and I just wanted to highlight that. I know that the accuracy would have been evaluated by the FDA, but looking for

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coverage for Medicare, I think we would also want to insure that there were older patients included and that the question she raised regarding accuracy at the lower levels of the glucose measurement is addressed by each of the devices that are included for safety reasons for the Medicare population.

And I had similar questions regarding, and thoughts regarding the importance of the patient's perspectives and device discontinuation, and I want to echo the importance of studying the reasons why patients would, as Dr. Isetts brought up, would discontinue the devices. I think that's very important, so that we can continue to do better to meet the needs of all patients. Thanks.

DR. ROSS: Dr. Wall?

DR. WALL: I vacillated between a four and a five, and settled on a four for the following reasons. Device-related safety is pretty key and I would have given it a five just by its name. The measures that are listed here I was troubled with, only because when I looked at the hypoglycemia related ED visits, you know, we already kind of addressed that as

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a health outcome I think, so it's already subsumed in another domain and we already heard that tissue damage was pretty miniscule.

So then I got to the device discontinuation rate and I think it's been already mentioned, I think there's multiple reasons why people might discontinue a device or the use of a CGM or a pump, and that's not necessarily inherent in the device itself. Clearly we need to know more about that. I thought one of the speakers spoke to an MCID of looking at less than a 20 percent discontinuation rate as an MCID. I don't know where that came from, sounds nice to me, but again, I don't think there's any evidence supporting any kind of MCID.

And then patient preferences, you know, again, I think it's really patient adherence is to me, and again it's, relating that to the domain is a bit problematic for me. Patient adherence, is that really a device-related safety issue, is it a quality of life issue, is it a health outcome issue? But I don't -- so I was troubled with the measures that were listed here and I was trying to come

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up with something other than that which are kind of the obvious stuff which is we are assuming that these are a hundred percent accurate, so what other safety issues would be talking about? So again, it's kind of more, the semantics here troubled me a little bit, which had me drop from a five to a four.

DR. ROSS: Dr. Young?

DR. YOUNG: So I voted as a four on this because I believe safety is an important consideration. I was troubled, like Dr. Wall, with the actual elements in this category and these particular measures as not being necessarily indicative of safety, particularly the discontinuation and patient preferences elements. And there are many different reasons that people might discontinue use.

I think the hypoglycemia related emergency department visits is a good safety indicator as long as it's positive and not, and the benefits of being monitored, that someone ends up at the ER and is checked out for a hypoglycemic episode. So that's why I voted for a four. Thank you.

DR. ROSS: Mr. Frankel?

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MR. FRANKEL: I thought this was extremely important. So you may be wondering then, why I voted one, and the answer to that really is that first of all, what was just mentioned by Dr. Young and Dr. Wall, the subsets that we have under device-related safety, it's a little bit unclear to me how those are directly defined as device-related safety using a strict measure.

But the overarching thought process that I had was that this is literally FDA's job, to ensure safety. For those that know the history of FDA, before they were tasked with safety and effectiveness it was just safety. So it's foundational to FDA to get this right. And if we do trust the FDA, it is very questionable to me why we would be looking at this as a precondition for coverage, set aside from the FDA already deciding that it is indeed safety from looking at a device-related safety perspective, and that's why I voted one.

DR. ROSS: Dr. Carlson?

DR. CARLSON: I would have ranked this as a four for all the reasons that have been discussed, including the questionable relevance

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of some of the specific measurements to safety.

However, having heard Mr. Frankel, I think he make the overall arching important point that this has already been done and why should we have to reinvent the wheel. So I have the option of changing my vote from a four to one, and will do so.

DR. ROSS: Okay. I want to thank all of our panel members, both voting and nonvoting for just their thoughtfulness, the way they approached these issues, their consideration and their ability to sort of explain broadly, you know, what was driving their votes and what was most important to them.

I know we're over time, not by much, which is pretty impressive given the amount of ground we had to cover. I don't know, Dr. Farmer, from CMS, if you want to make any closing remarks? This is the first of the clinical endpoints reviews as part of this guidance program to CMS and hopefully this is what you were looking for, as I asked all along.

DR. FARMER: Yes. CMS thanks you for your participation in today's meeting. I

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wanted to take this opportunity just to reiterate the meeting's intent, which was to identify the endpoints that are most relevant to the Medicare beneficiary population, the changes in those outcomes that are clinically meaningful, and the duration of followup that we should be looking for.

CMS does not consider cost when reviewing technologies for coverage.

As a next step, CMS will carefully review the public comments, panel notes and dialogue from today's MEDCAC. This input will assist Medicare in developing a clinical endpoints, guidance document on this topic. Guidance documents do not review specific technologies and are not national coverage analyses or NCDs. Instead, they identify health outcomes of interest to CMS from reviewing technologies and considering reasonable and necessary NCDs.

CMS does recognize that some endpoints discussed in today's meeting may not be commonly used. Nonetheless, we hope that guidance from this meeting will be helpful to manufacturers as they conceive future studies

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such that they can offer greater clarity on the benefits and harms of these technologies for the Medicare beneficiary population. So again, thank you so much for your participation today.

DR. ISETTS: Brian Isetts, I have a quick questions procedurally. So will we receive a copy of the draft of this, or it just goes final and you'll send us a link that I can share with my dean and my department chair?

DR. FARMER: You mean the guidance document?

DR. ISETTS: Yeah. So whatever the product of this, or these meetings, will be published somewhere. Will we see a copy of that and how will that work? What are the procedures there?

DR. FARMER: A copy of today's transcript of the meeting will be made public, along with all the other related meeting materials and the voting scores from the panel vote.

As to the guidance document, a guidance document will be proposed, and also will be subject to public comment, so the public will have ample opportunity to

contribute to this review.

DR. ISETTS: Great, and you'll share all that with us?

DR. FARMER: Yes.

DR. ISETTS: Thank you.

DR. DHRUVA: Joe, I think you're on mute.

DR. ROSS: Thank you again everyone for making the time today, I appreciate it, and have a good rest of your day.

(Whereupon, the meeting adjourned at 11:10 a.m. EDT.)

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 5th day of June 2024.

Transcriptionist

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