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CENTERS FOR MEDICARE AND MEDICAID SERVICES

Medicare Evidence Development & Coverage Advisory Committee

Meeting held virtually via Zoom

February 13, 2023

Centers for Medicare and Medicaid Services

7500 Security Boulevard

Baltimore, Maryland

Panelists

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Vice-Chair

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MEDCAC Members

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Carolyn Ford, PharmD

Genevieve Kanter, PhD

Karen Maddox, MD, MPH, FACC, FAHA

Marc Mora, MD

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Sally Stearns, PhD

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Dru Riddle, PhD, DNP, CRNA, FAAN

Ian N. Kremer, JD

Industry Representative

Parashar Patel, MA

Guest Panel Members

Daniel Arthur Canos, PhD, MD

Craig A. Umscheid, MD, MS

Richard J. Hodes, MD

CAG Director

Tamara Syrek Jensen

MEDCAC Coordinator

Tara Hall

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PANEL PROCEEDINGS

(The meeting was called to order at 10:04 a.m. EST, Monday, February 13, 2023.)

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

The committee is here today to discuss the analysis of coverage with evidence development criteria. This meeting will examine the general requirements for clinical studies submitted for CMS coverage requiring coverage with evidence development. The MEDCAC will evaluate the coverage with evidence development criteria to ensure that coverage with evidence development studies are evaluated with consistent, feasible, transparent and methodologically vigorous criteria, and advise CMS of whether the criteria are appropriate to insure that coverage with evidence development approved studies will produce reliable evidence that CMS can rely on to help determine whether a particular item or service is reasonable and

necessary.

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

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 of has another financial interest in any company that is related to this topic, coverage with evidence development, or has received financial support from such company. This includes speaker fees, salaries, grants and other support.

If you require a financial disclosure statement, please email Ruth McKennon so she can send you the form for completion. Her email is Ruth, R-U-T-H, dot McKennon, M-C-K-E-N-N-O-N, at CMS.HHS.gov.

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

During the open public comment, attendees who wish to address the panel will have that opportunity on a first come basis. Please email Ruth McKennon if you want to address the panel by eleven a.m. eastern standard time.

For the record, voting members present for today's meeting are Sanket Dhruva, Michael Fisch, David Flannery, Carolyn Ford, Genevieve Kanter, Karen Maddox, Marc Mora, Olorunseun Ogunwobi, Sally Stearns, John Whitney and Ian Kremer. Nonvoting panel members are Parashar Patel, Daniel Canos, Craig Umscheid and Richard Hodes. A quorum is present and no one has been recused because of conflict of interest.

The entire panel, including nonvoting members, will participate in the voting. The voting results will be available on our website following the meeting.

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

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

In the spirit of the Federal Advisory

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

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

MS. JENSEN: Thank you, Tara. Good morning, everyone. I would also like to wish all you Super Bowl fans, anybody that was a Kansas City fan, congratulations, and thank you to the panel for getting up this early after watching a late night game. And I also wanted to thank everybody who is participating today presenting, and including public comments later this afternoon.

CMS has given the panel a tall task of giving the Agency guidance and recommendations on coverage with evidence criteria. We've asked the panel to review the recommended updated coverage with evidence development criteria and to give us some recommendations for guidance on what we may want to update or keep.

Just as a bit of background, coverage with evidence development is a result of a national coverage determination. Any time the Agency decides as a result of an NCD to implement coverage with evidence development about a particular item or service, it is this criteria that we use to measure whether the various protocols for studies meet that minimum criteria in order for CMS to approve that study before that particular service or item under the national coverage determination would be covered.

We look forward to the proceedings for the next two days and we also look forward to the panel's recommendations and guidance on what we can update in the CED criteria. So again, thank you all for participating over the

next two days. I know you have very busy schedules. This is important for us and we are very grateful for your time. Thank you.

Dr. Ross, I think we'll hand the agenda to you now.

DR. ROSS: Thanks, Tamara. So, my name is Joe Ross, I am the chair for this MEDCAC, and I'm looking forward to what I anticipate will be a really phenomenal two days of both information gathering and learning, opportunity for questions and discussion as we later get to our voting around the individual criteria for tomorrow.

I see on the participant list there are around 350 people on, which is amazing. I think when we hold these meetings in Baltimore, I don't know if the auditorium can hold that many people, so it's fabulous to be able to have so many people engaged and be able to hear the conversations and discussions.

You will hear that for the most part my role is as taskmaster. I am charged with keeping the trains moving on time so that we can give everybody a fair opportunity to present information to the panel, for the panel

to ask questions, and for us to move through and make sure that we complete the meeting as scheduled.

We do have a very busy agenda that's going to start with Dr. Jodi Segal, who's going to present for half an hour on the AHRQ report that has made some recommendations to CMS on changes to the criteria. Then after her half-hour presentation we will have a half an hour of opportunity for questions from committee members to her. We'll then take a break, and then we have a great opportunity to hear from a number of scheduled speakers.

There's 15 people currently signed up, with and without presentations, for the committee for us to hear from. I will be very strict on time given the number of speakers who are scheduled to present. Our goal will be to hear everybody sequentially. If there's time before our scheduled lunch, we may take a couple of questions then, but for the most part questions will be held until the questions to presenter period, which is currently scheduled for 1:40 to three o'clock.

I'll just note that before that,

there's a 20-minute opportunity for spontaneous public comment. Tara did mention that if you do want to sign up to present, you will be given a one-minute opportunity to speak, starting at 1:20, we can have up to 20 speakers through 1:40. Then those people can also be asked questions in the 1:40 to three o'clock period before our adjourning for the day at three o'clock.

I'll note, there is no requirement for speakers to join the meeting tomorrow during the course of our day tomorrow as we're talking amongst ourselves and asking questions to one another, and then eventually taking votes. There may be additional questions that come up to speakers, so if you are able to join tomorrow, you may be asked, that may be helpful, but it's certainly not required.

I'll note, again, this meeting has been convened not for us to guide and offer recommendations to CMS on when to issue a CED decision, but when a CED decision is offered, what criteria should they be using to evaluate the studies that are proposed. That is our goal here, the latter, so we're here to talk

about what criteria should be used as CMS evaluates a proposed CED study protocol.

And again, everyone on the committee, please remember to keep yourself muted, keep your video on, and I think we can get started with the day. I will turn it over to Dr. Segal go. Thanks for making time to be with us this morning.

DR. SEGAL: I would like to share my own screen if possible.

I'm delighted to be presenting on behalf of the Johns Hopkins University Evidence-Based Practice Center. This is our analysis of requirements for coverage with evidence development. Thank you, Dr. Ross.

This is our team. The evidence-based practice center team included me, an internist and pharmaco-epidemiologist, as well as Dr. Levy and Dr. DiStefano, who are economists, Dr. Bass who is an experienced internist and codirector of the evidence-based practice center, and our colleagues Ritu Sharma, Allen Zhang and Nihal Kodavarti.

We had excellent advisors for this project. They were Peter Neumann, Sean Tunis

and Emily Zeitler, all of whom have been deeply involved in CED. Our involved federal partners were Kim Wittenberg and Craig Umscheid.

I'll begin briefly with CED background and then I will talk about our AHRQ report, including its scope, the literature search, the key informant stakeholder input, the public comments, the resulting final proposed requirements, and then our suggestions for future evaluation of the CED requirements.

CMS may issue a coverage with evidence development if insufficient evidence exists to conclude definitively that an item or service is reasonable and necessary. A CED is a national coverage determination that allows patients to access these select medical items and services with coverage on the condition that there is prospective collection of agreed upon clinical data.

The CED process was designed in 2005. In 2012 there was new CMS guidance that clarified CEDs should be carried out via prospective studies, and a CED cycle is completed when CMS has sufficient evidence to reconsider the coverage decision. In 2014

there was new CMS guidance; it reiterated the CED goal, that is to expedite beneficiary access to innovative items and services while assuring that the technology is provided to clinically appropriate patients. In 2014 were included 13 criteria or requirements that should be met when data collection is underway.

I'm going to read the original 13 requirements so we're on the same starting, at the same starting point. Then there are two interim versions that I'm not going to read verbatim, and then again at the end I will read the final requirements which have grown into 19 requirements. Okay.

The initial 13 requirements:

The principal purpose of the study is to test whether the item or service meaningfully improves health outcomes of affected beneficiaries who are represented by the enrolled subjects.

The rationale for the study is well supported by available scientific and medical evidence.

The study results are not anticipated to unjustifiably duplicate existing knowledge.

The study design is methodologically appropriate and the anticipated number of enrolled subjects is sufficient to answer the research question being asked in the NCD.

The study is sponsored by an organization or individual capable of completing it successfully.

The research study is in compliance with the noted federal regulations.

All aspects of the study are conducted according to appropriate standards of scientific integrity.

The study has a written protocol that clearly demonstrates adherence to the standards listed here as Medicare requirements.

The study is not designed to exclusively test toxicity or disease pathophysiology in healthy individuals. Such studies may meet this requirement only if the disease or condition being studied is life threatening and the patient has no other viable options.

The clinical research studies and registries are registered on clinicaltrials.gov prior to enrollment of the first subject.

Registries are also registered in the AHRQ Registry of Patient Registries.

The research study protocol specifies the method and timing of public release of all prespecified outcomes to be measured including release of outcomes if the outcomes are negative or the stud is terminated early. The results must be made public within 12 months of the study's primary completion date, even if the study doesn't achieve its primary aim. The results must include the number started/completed, summary results for primary and secondary outcomes, the statistical analyses and adverse events. The final results must be reported in a publicly accessible manner such as a peer-reviewed scientific journal, an online publicly accessible registry such as clinicaltrials.gov, or in journals willing to publish in abbreviated format.

The study protocol must explicitly discuss beneficiary subpopulations affected by the item or service, particularly underrepresented groups in clinical studies, how the inclusion and exclusion criteria affect enrollment of these populations, and a plan for

the retention and reporting of said populations in the trial. If the inclusion and exclusion criteria are expected to have a negative effect on recruitment or retention, the protocol must discuss why these criteria are necessary.

And finally, the study protocol explicitly discusses how the results are or are not expected to be generalizable to affected beneficiary subpopulations. Separate discussions may be necessary for populations eligible for Medicare due to age disability or Medicaid eligibility.

The AHRQ process began in May 2022. The scope of the report was meant to be question one, what revisions to the CED criteria or requirements may best address the limitations while preserving the strengths, and how might the revised criteria be evaluated in the future. We note the CED process or other aspects of CED not included in the questions above were not included in the scope.

AHRQ awarded the report to our evidence-based practice center.

We framed the objective as follows: We aimed to refine the studly design

requirements so that investigators are efficient in completing studies that contribute to an evidence base, with the goal of ending the CED process when there is sufficient evidence for a coverage NCD; sufficient evidence for a non-coverage NCD; or a decision to defer the coverage decision to a Medicare Administrative Contractor, such as for a local decision.

We began with a very targeted literature search of PubMed. We looked for studies describing coverage with evidence development, access with evidence development, managed entry schemes, conditional licensing, approval with research. We then expanded the search looking for guidance documents about the production of real-world evidence in the literature. The search strategy is included in your Appendix 1.

We also extended this to a Grey literature search where we searched for CED policies of other countries. We identified candidate countries from three international articles about CED schemes. These included Australia, Belgium, Canada, England, France,

Germany, the Netherlands, Spain, Sweden and Switzerland. So we searched English-language government websites for health technology assessment bodies located in these countries to identify any documentation of their CED policies. We also had some contacts with international experts in the HTA field in Canada, England, the Netherlands, Sweden and Switzerland and discussed with them about the existence and documentation of CED policies.

This process led to the development of the first draft, and in the first draft we reviewed those 13 requirements in the existing CED guidance and for each we assigned one or more labels, and you can see the labels in Table 2 of the report, like events, communication, governance, methods. Then we reviewed our literature and extracted recommendations that are intended to lead to the production of a strong body of evidence. There were 27 articles that were most relevant to this purpose and it included 172 recommendations that we thought to be relevant to this update. So we labeled the extracted recommendations with the labels that belonged

to the initial 13 and added new thematic labels as needed. We aggregated the recommendations sorted by labels and then where appropriate or needed, drafted one or more requirements to correspond to each of the labels based on the language of the initial recommendation, and the perceived intent of the source documents.

So then this was the revised set. There are 22 requirements here and again, I'm not going to read each of them, but I do (break in audio) some of these additions or changes we made based on our literature review.

So for example in E, we perceived the need for a written plan for our milestones to increase the likelihood of timely completion of the process. We saw a need for including explicit data governance and protection since those are considered best practices. We wanted to clarify that there should be an evidentiary threshold set so that the meaningful difference that is the target of the study is known up front at the time of design. We thought that the outcomes should be patient relevant and if a surrogate is used, it should be explicitly recognized.

AHRQ no longer maintains the patient registry so we removed any reference to that.

We added a requirement that the population reflects the Medicare beneficiaries who will use the product or the service. We concluded that the beneficiaries should be studied in their usual sites of care and in this version we used the words real-world practice of medicine; that changes later.

We perceived a need for a data validity requirement. We perceived a need to clarify about the study design's direction and here we list a lot of specific study designs. We included a section stating the investigators must minimize the impact of confounding and biases on inferences by using rigorous design and statistical techniques. We included best practices for understanding heterogeneity and treatment effect. We believed the investigators must demonstrate reproducibility of their results. And we removed the date requirements; we initially said 12 months, we thought that would be folded into the statement of the milestones.

We appreciate the need for a

requirement about sharing analytics-driven results with CMS to allow for replication and verification of results. We need to attend to federal regulations.

Okay. So that was the set of requirements that went to the key informants for input. The expertise among the key informants included those with expertise in patient and consumer advocacy, real-world data generation and evidence production, people from medical specialty societies, from the fields of health technology, from commercial health plans, and experts in health policy.

These were our key informants, Naomi Aronson, Peter Bach, Helen Burstin, Daniel Canos, John Concato, Eric Gascho, Richard Hodes, Ashley Jaksa, Kathryn Phillips, Nancy Dreyer, Michael Drummond and Eliseo Perez-Stable.

Key informants were asked to do pre-meeting activities. They reviewed the first draft and provided comments, and they were asked to assess each of the 22 requirements as being not needed, important or essential, and their ratings are included as

Appendix 4 in your report. They were also asked whether textual revisions were required by two or more KIs for most of the requirements.

There were two KI meetings, each with them split in half, and they received a summary of their grading before their discussion. I focused the discussion on the areas requiring resolution and we altered the requirements slightly between the two meetings. We revised the criteria then based on their input and shared the revised criteria with the KIs for a second assessment, and the second opportunity for input.

The set of requirements after the KI input, and this is the set of requirements that was then posted for public comment. Again, I'm not going to read them, I'll just show you some of the changes that we made based on the KI input. Most of it was textual revision.

Here are the KI suggestions to prioritize precision, which we did. Some other changes for clarity. They suggested that we specify that the data must have attention, the chosen data must have attention to

completeness, accuracy, duration and sample size, and this is described in the protocol.

There was discussion that the evaluation of devices differs from the evaluation of drugs, and that evaluation may be optimal in diverse settings. However, the usual site of care delivery may be a specialized clinical facility like a center of excellence, especially when the product is newly in use, and we certainly agree with that and have changed the term to usual sites of care for delivery of the product, which often may be in a specialized center.

The KI panel agreed on the importance of patient-relevant outcomes. We added a phrase about these as secondary data, that's expected to be common. By that we mean data from electronic health records or claims, or other sources of existing data.

The KIs thought that the detailed list of possible study designs was unnecessary and restrictive, so we removed it. And they encouraged our revision to not prioritize efficiency over validity, so we think the revision accurately captures that now.

They encouraged us to frame this as appropriate statistics in addition to rigorous design.

And they let us know that there is a set of fundamental factors that should always be measured in a standardized way and considered as affecting outcomes until proven otherwise, and those would be the relevance of this.

The fact that reproducibility is a narrow concept and robustness might be the preferred word.

And the KI panel thought there could be a requirement for public posting. We favored the old peer review, although both may be appropriate.

There was a lot of discussion too about sharing the results and the data with CMS. The concern was that patients would be less likely to participate in a study if they know that their data is shared with the government. So we inserted the phrase or trusted third party, to remind investigators to share this data elsewhere if they learn that CMS actually does impact enrollment.

We will continue to adhere to federal regulations.

So AHRQ then posted this revised report and requirements for public comment for three weeks in September. We then received the comments and summarized them. Comments outside of the scope of this project were summarized in an appendix that's Appendix 2 in your report, and comments about the requirements were closely reviewed and informed our final set of revisions.

We received 27 sets of public comments, so 17 of the sets of comments included specific recommendations about the requirements. The other comments, as you can imagine, were overarching comments about the set of requirements, comments about the report methodology, recommendations for revisions to the CED program which of course were out of scope, or comments about costs, cost effectiveness, value and evaluation, which are also outside of the scope.

So these are the final proposed requirements. There are 19, and to the right you can see what changes we made based upon

public comments. And again, if you're interested in tracking the evolution of each requirement, that's included in the report as Table 2. I am going to read now these 19 requirements.

The study is conducted by sponsors or investigators with the resources and skills to complete it successfully.

A written plan describes the schedule for completion of key study milestones to ensure timely completion of the CED process.

The rationale for the study is supported by scientific evidence and study results are expected to fill the specified knowledge gap and provide evidence of net benefit.

Sponsors establish an evidentiary threshold for the primary outcomes so as to demonstrate clinically meaningful differences with sufficient precision.

The CED study is registered with clinicaltrials.gov and a complete protocol is delivered to CMS.

The protocol describes the information governance and data security provisions that

have been established.

The data are generated or selected with attention to completeness, accuracy, sufficiency of duration of observation to demonstrate durability of results, and sufficiency of sample size as required by the question.

When feasible and appropriate for answering the CED question, data for the study should come from beneficiaries in their usual sites of care, although randomization to receive the product may be in place.

The primary outcomes for the study are those that are important to patients. A surrogate outcome that reliably predicts these outcomes may be appropriate for some questions.

The study population reflects the demographic and clinical diversity among the Medicare beneficiaries who are the intended users of the intervention. This includes attention to the intended users' racial and ethnic backgrounds, gender, and socioeconomic status, at a minimum.

Sponsors provide information about the validity of the primary exposure and outcome

measures, including when using primary data that is collected for the study and when using existing or secondary data.

The study design is selected to safely and efficiently generate valid evidence for decision making by CMS. If a contemporaneous comparison group is not included, this choice must be justified.

The sponsors minimize the impact of confounding and biases on inferences with rigorous design and appropriate statistical techniques.

In the protocol, the sponsors describe the plans for analyzing demographic subpopulations, defined by gender and age, as well as clinically-relevant subgroups as motivated by existing evidence. Description of plans for exploratory analyses, as relevant subgroups emerge, is also appropriate to include but is not required.

Sponsors using secondary data will demonstrate robustness of results by conducting alternative analyses and/or using supplementary data.

The study is submitted for peer review

with the goal of publication using a reporting guideline appropriate for the study design structured to enable replication.

The sponsors commit to sharing analytical output, methods and analytic code with CMS or with a trusted third party in accordance with the rules of additional funders, institutional review boards and data vendors as applicable. The schedule for sharing is included among the study milestones. The study should comply with all applicable laws regarding subject privacy, including Section 165.514 of HIPAA.

The study is not designed to exclusively test toxicity, although it is acceptable for a study to test a reduction in toxicity of a product relative to standard of care or an appropriate comparator. For studies that involve researching the safety and effectiveness of new drugs and biological products aimed at treating life-threatening or severely-debilitating diseases, refer to these additional requirements.

And the research study complies with all applicable federal regulations.

The proposed requirements, we think, have more explicit expectations for the studies that are designed to generate the needed evidence for CMS, and we really think that they should be easier to act upon by sponsors because they are granular and explicit. An explanatory guide may need to accompany these requirements, but we think they're pretty clear as they stand. We've encouraged use of real-world data when feasible, which describes the inclusion of patients in their usual clinical settings.

There will continue to be the need for more traditional, more explanatory trials. The therapies recommended for CED are often devices or diagnostics, rather than drugs or biologics, or are therapies being used for novel indications. Thus, there may not be the extensive clinical trial record that is generated during regulatory approval of pharmaceuticals.

Here are our suggestions for future evaluation of these requirements. The amended requirements might be evaluated with attention to both process and outcome metrics. If the

protocols are described with sufficient detail on clinicaltrials.gov, this will also facilitate external evaluation of the requirements. The impact of the requirements on outcomes can be evaluated by an assessment of the value of the evidence that is produced, does the evidence generated in a study or a series of studies allow CMS to efficiently end a CED with a coverage or a non-coverage decision, or with deferral to a MAC. The quality and strength of the evidence generated is the ultimate test of the effectiveness of this set of requirements, as this will allow for a timely decision by CMS.

Thank you. I'm very interested in hearing your comments.

DR. ROSS: Thank you, Jodi, that was terrific, and very clear.

So we now have an opportunity to ask questions of Dr. Segal and I see some hands are already going up. As a reminder, only members of the committee are able to ask questions, so please raise your hands, and let's start, the first question that I see will come from Mr. Kremer.

MR. KREMER: Thank you, Dr. Segal, really interesting and valuable presentation and report.

Joe, I have a series of questions. Should I just ask one and let you move to the next questioner and then move back around, or can I ask a series?

DR. ROSS: Let's go with one and then we'll go back around just to make sure everyone has an opportunity.

MR. KREMER: Dr. Segal, first question. Should CMS apply the same CED criteria to drugs, biologics, devices and services, or would it be valuable and productive for the system to have these criteria at least have some variation among those four types of decisions?

DR. SEGAL: We thought of them all together, we did not craft them separately. We think there's enough flexibility in these requirements that they should serve all of the different types of products.

MR. KREMER: Great.

DR. ROSS: Dr. Canos.

DR. CANOS: Thank you. Dr. Segal, I

commend you and the team for, you know, the goal as far as guiding investigators to collect and use data generated in the health care of patients to produce strong evidence for those outcomes for Medicare beneficiaries, a commendable effort. As I look at the individual elements on generalizability and where that carries through, and thinking about how, the emphasis on evidentiary controls and thinking about how data can be collected through these patient encounters, it certainly speaks to the importance of pragmatic clinical trials and leveraging both prospective outcomes that are secondary as well as primary data collection efforts.

When I look at the reproducibility aspects it speaks, secondary data, you know, if you use any secondary data whatsoever, then you have to then do a secondary kind of reproducibility recognizing that, you know, clinical, you know, research itself and evidence with clinical experience in DHR, it's not a binary that you know, within the pragmatic clinical trial construct, you actually have bits of secondary data especially

collected from DHR, as well as primary data.

Is the intent of reproducibility in any part of secondary data, realizing that you have to then reproduce those results, even within a randomized pragmatic clinical trial, or is it if you only use secondary data that you have to do a reproducibility?

DR. SEGAL: We were thinking more about the use of secondary data and it may be just as simple as analyzing it differently, right? If you're doing, you know, a propensity for matching them, trying an interval variable analysis is something to demonstrate that there is the robustness of your results. If you can use another source of data too, another health system or other data, that would be preferred, but we don't really expect that series of pragmatic trials necessarily.

DR. CANOS: Okay. So it you have a randomized pragmatic clinical trial, would there be application of reproducibility to that as well?

DR. SEGAL: Not necessarily. We were thinking more about the secondary data analyses in that requirement.

DR. CANOS: Okay, secondary and exclusive then.

DR. SEGAL: Right, using it, correct.

DR. CANOS: Thank you.

DR. ROSS: Dr. Fisch?

DR. FISCH: Yes. I'm interested in the final requirement where you make reference to both sponsors and investigators on slide 44, and it shows, you know, that phrase, sponsors and investigators shows up on other comments as well.

DR. SEGAL: Right.

DR. FISCH: And of course both play a really important role in generating reliable evidence, but I tend to think about the sponsor's role and investigative role as not being exactly the same. I think about sponsors as providing resources and assisting in the planning of the study, and investigator's role in planning and conducting the study. And they're both involved in interpreting the data and disseminating the results, but I wondered whether you had thought about distinguishing the role of sponsors and investigators in this exercise.

DR. SEGAL: Right. I think the phrase is written that way because in many situations the sponsor will be the investigator. We didn't put a lot of thought into that phrase. I actually think that was a preferred phrase by CMS actually, so this was not something we spent a lot of time on.

DR. FISCH: Thank you.

DR. ROSS: Okay. Just a reminder to all the committee members. When it comes time to vote tomorrow about these criteria, if we have suggestions, that's the time where we can introduce them and provide additional thoughts.

Dr. Ogunwobi? There's a lot of questions and I'm trying to track them in order.

DR. OGUNWOBI: Thank you for that presentation. I particularly appreciate your inclusion in the final requirements, the one that's lettered J, in which you stipulate diversity in the patient population that the device or diagnostic is tested and evaluated on.

I do have a question, though, as to, you know, how you intend to monitor that

because you know, it's possible that people could just include one or two, you know, participants from underrepresented groups. Would that be sufficient? Is there a threshold for, you know, the number that's included in the overall sample size? Is there guidance or do you have any current intentions of how that's supposed to work out?

DR. SEGAL: No, and I imagine that that would be described in the protocol, and I think our focus too is to identify the subpopulations where there might be originated treatment effect and if that's defined by gender, then that's the population; if that's defined by race, then that's the population. It has to be explicitly described in the protocol so that there's sufficient enrolled participants to really understand the effect in that subpopulation. And I would hope that CMS would enforce that when they review their protocol, but I think it would be beyond the scope of the requirement to be so explicit perhaps.

DR. OGUNWOBI: So it's really up to CMS, then, to enforce that particular

requirement?

DR. SEGAL: I would think it has to be. Perhaps you will have creative suggestions about how that can be more explicit in the requirements, but you're right, it isn't right now.

DR. OGUNWOBI: Thank you for your work.

DR. ROSS: Dr. Kanter?

DR. KANTER: Hi. Thanks, Dr. Segal, for that great presentation. I have a general question and then individual questions, which I, on the elements which I'll ask later. I guess the first general question is, do you have, and you may not be able to answer this based on the methodology that you used, but do you have specific examples where certain criteria were not as effective or were more effective, specific examples related to US cases? And if not, I wonder through your literature review of the international work, whether there were specific examples of concrete instances that we could think through, and what the strengths and limitations of the CMS criteria were.

DR. SEGAL: Well, we looked at of course, Emily Zifer's (phonetic) report that she published just a year or so ago that reviewed the existing CEDs. She didn't assess each individual requirement, she just described like you, CEDs. I have a master's student now working on looking more specifically, it's a big task, she has just finished two of the CEDs with that goal. No, that was not something we did in preparation for this report.

And the question about the international experience, I can't address.

DR. KANTER: Thank you.

DR. ROSS: Dr. Stearns?

DR. STEARNS: Yes. Thanks for the direction and my question pertains to milestones. Are you able to give a little more information on what's envisioned in terms of the process of establishing initial milestones? And then also as the investigation proceeds, where there might be a process for revising those milestones as appropriate?

DR. SEGAL: No, we honestly didn't think that through, we didn't. We would imagine that the milestones would be in the

protocol went through, when you enroll participants, when the analyses are done, but not, we didn't set more concretely, honestly.

DR. ROSS: Mr. Patel?

MR. PATEL: Thank you. Dr. Segal and the JHU team, you guys did a very good job of getting this criteria, it's a robust set of criteria, so thank you. I have a question, a couple question, and the first one is criteria C. I noticed that you used the term net benefits and I'm kind of curious why you used that term rather than what traditionally CMS has done, which is improved health outcomes for Medicare beneficiaries. So, maybe a little bit of your thought process why you recommended net benefits versus what CMS has used traditionally.

DR. SEGAL: Okay. We wanted to be able to capture in one phrase of course benefits and harms, and so with using net benefit that was meant to include both. I agree that that's not a phrase that we have come across too often in the rest of the CMS documentation and maybe that is something that requires additional discussion, but that's the

rationale.

DR. ROSS: Mr. Kremer?

MR. KREMER: Thank you. So before I get to my second question, I just want to say I am troubled by the one size fits all approach. I'll save getting into that for our panel discussions but the idea that the same criteria are applicable and adequate across four classes strikes me as unlikely at best. And that may have been beyond the scope of the charge that the center was given, but I find it troubling.

So for my second question, if we could go to the slide around the list of the key informants, and I wonder if you could identify for us which of those key informants are patients and which are representatives of innovation industries, pharmaceutical device, et cetera. I know that there are insurance representatives on the panel but I didn't see and I would appreciate you pointing out to me the patient representatives and the innovator representatives.

DR. SEGAL: There was no patient representatives on this key informant panel. Innovators --

MR. KREMER: I didn't see any, but I would appreciate you correcting the record if I'm mistaken.

DR. SEGAL: I guess I'm not sure how I would define innovators.

MR. KREMER: Well, it's pretty easy to find the insurance companies that were represented so it shouldn't be that hard to identify the innovators, pharmaceutical and device --

DR. ROSS: Mr. Kremer, is there a question --

MR. KREMER: Just to find out if --

DR. ROSS: -- or is this an interrogation?

MR. KREMER: Well, if they were not included I'd like to know why they were not included.

DR. ROSS: Okay. That's a good question.

DR. SEGAL: All right. We did our best to have a diverse key informant panel but you're right, it was not inclusive of all possible key informants.

MR. KREMER: I'll reserve comment,

I'll just, beyond saying representative is really the heart of this. This is about beneficiaries, it's not about the insurers. I'll leave it there.

DR. SEGAL: Thank you.

DR. ROSS: Dr. Dhruva?

DR. DHRUVA: Thanks, Dr. Segal, for really a lot of hard work that was clear went into your presentation this morning. I have a question about item M. When feasible and appropriate for answering the CED question, data must come from beneficiaries in their usual sites of care, and then the word although is more where my question is, although randomization to receive the product may be in place. I'm wondering about this very specific word although, because in pragmatic trials we do seek to conduct, randomizations can occur in the usual site of care. So I'm wondering if there is some reason that randomization was under emphasized, or is there something to that word although that I just want to understand better. Thank you.

DR. SEGAL: So you're looking at H, that's H, right?

DR. DHRUVA: Sorry, yes. Thank you.

DR. SEGAL: It strikes me as a little awkward as well. Yeah, it strikes me as awkward as well.

DR. DHRUVA: Okay. It seems to me that it might under emphasize the importance of randomization, because I mean, we have another criteria that talks about rigor and minimizing confounding, and we all know that randomization is the best way to do that as appropriate, so yeah.

DR. SEGAL: Yes, I agree, and right, something to consider would be ideally randomization to make sure the product might be in place, because we agree. We agree.

DR. ROSS: Just a note before we continue on with questions for Dr. Segal. For anyone who is interested in signing up for public comment, please do so before 11 a.m., which is five minutes from now, just so that the CAG team can make sure that everything is all set.

The next person I have on the list is Dr. Canos.

DR. CANOS: Thank you. My questions

are specific to C under context, as well as J under population. C has a focus on the evidence that's generated, it's expected to fill the specific knowledge gaps, and provide evidence of net benefits. Certainly, you know, after hearing presentations and seeing documentation about the importance of stakeholders, the evidence, the purpose in design is to hit specific evidence gaps that are necessary for CMS decisions.

As you look at the context, that has a very targeted intent to fill a knowledge gap, and then look across to J for populations. The wording on J individually, it talks about the subpopulations reflecting, you know, the demographics and diversity across Medicare beneficiaries.

Is the intent for CED studies to both be directed and focused with filling evidence gaps at the same time as filling and directing more widely a broad population? It seems to me these are sort of two different aspects, so could you provide any clarification on C for context with respect to J, the broader population?

DR. SEGAL: Well, I think when you, when the investigator frames what is the question that CMS needs to answer, what's the evidentiary threshold to demonstrate that the evidence has been sufficient, we think it should be inclusive of the population that will be exposed and will be using this product, so I don't think there's conflict there, right? The people who are studied should be the people who are going to get this product or diagnostic to the best of your ability.

We recognize that's hard, but that's why they're doing these studies, so I rally don't think there's a conflict.

DR. ROSS: I see several more hands raised and we have about 15 more minutes, so we'll try to keep going. Mr. Patel?

MR. PATEL: Thank you. So I have a question about criteria G. The wording comes from data are generated or selected, and the word selected implies maybe the data is there and you're selecting some subset of the data, so I'm kind of curious what the thought process there is. Presumably when the study is completed, you're not just selecting some

subset of the data. So I'm curious whether there was thought given to separating the data sources which might be selected for the study, versus the actual data that was generated from those sources. Does that question make sense or was there a reason why you just didn't need to separate the sources and the data generated.

DR. SEGAL: I think that's fair, although the data used, I think there is a subset of data within the data source that will be chosen because it's complete, right? It's a good outcome to pick because we have complete data on this outcome, right? If you're measuring something and you don't have the amount right, then it's a poor choice of data for your primary outcome, so I think that's okay. I think data sources are separate from data.

DR. ROSS: Dr. Whitney?

DR. WHITNEY: Thank you. I just wanted to comment that with regard to a variety of potential service classes being reviewed under these criteria, I can't really construct a scenario where these very well written suggested criteria wouldn't apply to any

service class that I can think of, so absent some sort of direct information that said otherwise, I would not want to pars this out based on service class.

DR. ROSS: That's helpful. Dr. Maddox?

DR. MADDOX: Thank you for that very clear presentation. I had a question about requirement I and the language for outcomes that are important to patients. I was wondering if you could talk a little bit about your decision making on that phrasing specifically, and also sort of the inclusion of that word important to patients and what it might mean to you. Does that mean that there's a lot of patient-reported outcomes, does it mean that there has to be justification, and did you give any thought to indicating anything about the duration of outcomes, short term versus long term or any other specificity, why you might have sort of selected both the phrase and then also not put in more detail, that would be helpful to understand.

DR. SEGAL: By that we do mean patient-relevant outcomes, not necessarily

patient reported but patient relevant, which can include death, which can include like hospital length of stay, things that patients really do care about, so that was that rationale.

So the second part of that question --

DR. MADDOX: Just the tradeoff in terms of giving more specificity to what might be required in short or long-term outcomes.

DR. SEGAL: Thank you, right. So that was why we included the phrase in one of the other requirements about durability of results and making sure that you had a sufficient length of followup within your data or within your study design, so that you can see that the results are durable, again, over a period of time that is relevant to a patient, right? And two weeks may not be so important to the patient, but if you can measure outcomes for six months, that would be patient relevant.

DR. ROSS: Mr. Kremer?

MR. KREMER: Thank you. So we've established that the key informants did not include sponsors, it didn't include patients, but a conclusion was reached that the criteria,

the proposed criteria should make this easier for sponsors to act on. So with that in mind, I'm curious about your selection of the comparator countries and how you treated those, given that many of those comparator countries consider price and at the time your report was being developed, consideration of price was explicitly against the law in the United States. So how did you factor out the criteria that those other countries found relevant that might inform a U.S. construct without considering that price element in the formulas, in the systems that the other countries use?

DR. SEGAL: We knew that HTA documentation and analyses would not be fully appropriate or relevant here. Those selected countries were largely a convenient sample because we knew that they would have some documentation based on the review articles we looked at. And even our search strategy including health technology assessment as a search term, we knew wouldn't be fully relevant, but it was a way to try to bring in the relevant literature, knowing that it wouldn't all be relevant.

We were specifically looking if they had really CED policies that were more in line with what we do in the U.S., not their general HTE activities.

MR. KREMER: So even if their CED activity is constructed potentially in a way that is designed to help them get at a direct value assessment, a cost and a benefit to the insurance system, the public insurance system, you had a way to weed out their consideration of that element.

DR. SEGAL: I think because we're experts in evidence generation, we understand this field.

DR. ROSS: Mr. Ogunwobi, or sorry, Dr. Ogunwobi?

DR. OGUNWOBI: That's okay, thank you. So I have a question about data sharing. I noticed that there was a requirement that stipulated sharing the data with CMS, and I think you said something about other third parties, but it wasn't clear to me that overall it would be publicly available. I do appreciate the importance of protecting personal identifiable information on any

platform, but it just appears that there is limited public sharing so that for example, other people can look at the data and independently determine if the studies were done appropriately and that the CMS decision was based on, you know, the right sets of data.

DR. SEGAL: Well, honestly, that never came up, to actually publicly share this. We said we were looking for a way of saying that the data would be shared with CMS for replication. I will be interested in hearing other opinion. I was worried that that would further limit studies if they knew that it would be shared.

DR. OGUNWOBI: Right. You know, I definitely am not talking about personal identifiable data, but just overall such data that would include more identifiable, and the goal of that is to enable experts from around the United States and elsewhere to determine that, you know, CMS, or indeed independent of CMS, that that study is appropriately done.

DR. SEGAL: Yeah. That really didn't come up in the discussions.

DR. ROSS: Dr. Umscheid?

DR. UMSCHEID: Thanks, Dr. Ross. Dr. Segal, I thought you did a really nice job on that presentation as well, it was very clear. I did want to ask about stakeholders because obviously I think that's important to many of us. In my reading of the report there was a patient and family stakeholder group who was included as a key informant, the National Health Council. Can you correct the record on that? It looks like they provide a united voice for people living with chronic diseases and disabilities and their families and caregivers, so I wanted to clarify that.

DR. SEGAL: Yes, unless it's possible that they were invited but didn't participate. I'm not remembering but I agree, I would like to address that.

DR. BASS: Yeah, they did participate, Jodi.

DR. SEGAL: Oh great.

DR. BASS: That's the Health Council, yes, so that was part of the justification for including them.

DR. UMSCHEID: And I also wanted to ask about innovators. I did see a number of

industry representatives and academics, and several research agencies on the list of key informants. So it did appear that innovators were included as well, including Delfi Diagnostics and Aetion and others; does that sound correct?

DR. SEGAL: Yes. They're not manufacturers of devices or pharmaceuticals, but the National Health Council, yes, very good.

DR. UMSCHEID: Great. I also wanted to ask about the public comments. I know you mentioned in your presentation that there were 17 public comments or sets of comments if I'm remembering correctly. Do you have a sense of what types of groups those public comments came from? Thanks.

DR. SEGAL: Right. There were 27 sets of comments, the public comments are in Appendix 2. I'm not sure if Appendix 2 lists them by their choices, but maybe it does.

DR. ROSS: Thanks, Jodi. I want to keep us moving if that's okay.

DR. UMSCHEID: I can look at that appendix. Thanks, Jodi.

DR. SEGAL: Okay.

DR. ROSS: Dr. Canos?

DR. CANOS: Thank you. I have a question specific to design, or I guess section L, I believe. And when originally worded the focus was on sufficient evidence generation and the version, the most recent version, it says addition of the word safely, valid evidence safely and efficiently. Recognizing that requirement S is called out specifically in 45 CFR Part 46 as well as 21 CFR Part 56, is that intent that this is additive in some way, that is that Medicare is to look at safety at some form above that of section S, or is this duplicative of section S?

DR. SEGAL: It may be duplicative. And you're right, that word safely didn't appear until after the public comment period, that wasn't something we initially put in or the key informants were responding to.

DR. CANOS: Thank you.

DR. ROSS: Mr. Patel?

MR. PATEL: Thank you. I have, I think it is important that we clarify the key informants at least on the list that was made

public in the report. It did include device companies, it may not be confirmed but clearly they could have (unintelligible).

I actually had a question for you, maybe you could talk a little bit about criteria K, if you can please. So one question, what is primarily, you talk about the validity of the primary exposure and outcome measures. I know what outcome measures are, so I'm kind of curious what primary exposure measures are, that's one question. And then the second part of that criteria talks about using primary data that is collected for a study and when using existing secondary data.

And I guess, you know, there is at least one CED occurring now for pacemakers that isn't using existing secondary data, they're using claims data that are generated by the procedure, so I'm kind of curious what that thought process was, because not all secondary data may be existing, right, it may be created as a result of a study. Am I reading too much into this or is this something I should clarify later?

DR. SEGAL: So I think you're parsing

the first part a little broadly, so it's primary exposure and it's outcome measures, it's not primary exposure measures.

MR. PATEL: So what is primary exposure, I'm sorry?

DR. SEGAL: Exposure to the drug, device, how is that defined, right? If it's a drug, you have to define the primary exposure, is it six months of exposure, is it two months of exposure, is there some measure of adherence that's necessary. It's what you would do when you're designing a pharmaco efficacy study.

MR. PATEL: Okay, fair enough. Thank you for the clarification.

DR. SEGAL: And then the secondary data that you're describing from -- so claims we would say are existing secondary data, right? It exists because the clinician, the provider had to bill for the service, that's why it's existing. So yes, even though it's going to be used for perhaps a patient who's enrolled in the study, that's still secondary data.

MR. PATEL: It's secondary at the time the study was being developed. Thank you.

DR. SEGAL: No, we understand. Yes.

DR. ROSS: Just recognizing the time and the panel still has a number of questions, Dr. Segal, are you able to stay throughout the day to give us an opportunity to ask you questions later on?

DR. SEGAL: Yes.

DR. ROSS: Okay. So going back to actually Dr. Mora -- oh, did your hand actually go down? I wanted to make sure you had a chance to go.

DR. MORA: Thanks. I took it down just in the interest of time. I can hold the question if you're trying to keep us on time.

DR. ROSS: No, why don't you ask your question, and from there we'll take a break.

DR. MORA: Good morning, Dr. Segal, from Seattle, Washington. I thank you so much for all the work you and your team did. From my perspective it really helped to clarify and simplify the task before us.

One of the questions I have is, and it's sort of tangentially related, is I spend a lot of time with patients both as a treating clinician and then on a system level talking

about shared decision making and the importance of trying to help them understand risk benefits, and one of the ways we've done that is to try and move some qualitative statements to quantitative statements, talking about lessening the risk of treatment. I don't see that degree of specificity around quantitative data from outcomes. I know it's probably inherent, but would you mind talking just a bit about how we think about data being moved in these recommendations? Thanks.

DR. SEGAL: I think that's folded into the evidentiary threshold, right? In the protocol it would describe what does CMS need to make a decision and that's probably needing to demonstrate some absolute risk reduction or an absolute benefit. That also folds into that phrase of net benefit, so that is meant to be quantitative.

DR. ROSS: Thank you, Dr. Segal.

So just by way of housekeeping, I have Doctors Dhruva, Stearns, Fisch, Kanter and Ogunwobi who have their hands up. We'll come back to you guys later on for questions for Dr. Segal.

We do want to give everybody an opportunity to take a 15-minute break. We will be back promptly at 11:30 a.m. east coast time in and we will just start our presentation with our scheduled public speakers. Again, there are 15 who are scheduled to speak, I will be going on the order of the agenda. Please be ready, each has five minutes, and I unfortunately will cut off presentations at five minutes, that way we will have an opportunity for everybody. So, enjoy a 15-minute break and I'll see everybody back.

(Recess.)

DR. ROSS: Welcome back, everybody, just running through making sure everyone is here. It looks like it. We're going to start in one minute.

Just before we get started, one minor note that occurred. Dr. Dru Riddle was inadvertently not named as sitting on the committee members. I just wanted to make sure that everyone is aware in case Dr. Riddle asks questions, that's why, he's actually on the committee and that was just an oversight, so apologies to Dr. Riddle.

We're going to start with our list of speakers in the order that they appear on the agenda. Please do keep your presentation to five minutes so that I'm not required to cut you off, and we will start with Ms. Cybil Roehrenbeck. I'm so sorry if I'm mispronouncing your last name.

MS. ROEHRENBECK: Thank you, good morning. I'm Cybil Roehrenbeck. I serve as the executive director of the AI Healthcare Coalition. I'm also a partner with the law firm Hogan Lovells and an adjunct associate professor in health law and policy at the American University Washington College of Law. On behalf of the AI Healthcare Coalition, I'm pleased to speak before the Medicare Evidence Development and Coverage Advisory Committee, or MEDCAC, on the topic of coverage with evidence development or CED. I do not have any financial interests to disclose.

The AI Healthcare Coalition convenes healthcare AI innovators and stakeholders to advocate for patient access to safe ethically developed healthcare AI services. We really appreciate the ongoing efforts of the Centers

for Medicare and Medicaid Services or CMS to engage with the AI healthcare community. We're glad that CMS is considering issues around coverage and payment methodologies for emerging AI technologies and services, and we look forward to a continued partnership with CMS as the Agency continues to develop pathways for patient access to these innovations.

On the informed issue of coverage, the AI Healthcare Coalition was previously supportive in concept of the Medicare Coverage and Innovative Technologies or MCIT proposal. While we advocated for modifications to CMS's MCIT pathway, we were disappointed when CMS rescinded the MCIT proposal in its entirety in November of 2021.

Today we encourage CMS to move forward with its more recent work on a potential transitional coverage for emerging technologies or TCET as a coverage approval pathway. Even though some advancements have been made in the U.S. Food and Drug Administration or FDA, review of AI technologies, as well as reimbursement for AI services, there remains great unclarity with respect to Medicare

coverage for AI healthcare services.

Our concerns regarding the local coverage determinations or LCDs and national coverage determinations or NCDs have been present across multiple healthcare services and specialties. Stakeholders agree that utilizing the LCD or NCD processes for coverage of AI services raises unique challenges.

As greater AI services become available across many clinical specialty areas, patients and providers need clarity on what is and what is not covered under Medicare. Without such clarity, patients may be harmed by lack of access to these forums, many of which are helpful to address specialty care issues in our growing understood community.

We ask that CMS move forward with the TCET process without delay. This pathway should provide clear, consistent and reliable direction for AI innovators with respect to Medicare coverage.

Key components of the TCET program should be, number one, early as possible dialog between CMS staff and innovators going through the FDA authorization process. Number two, add

a measure for temporary coverage that enables immediate patient access. Number three, special consideration for FDA authorized AI services that have received breakthrough device designation. Number four, flexibility with respect to evidence review and data submission. And number five, reconsideration processes for applicants.

Lastly, we understand that TCET could have an evidence development component and that the MEDCAC meeting today may inform CMS's work around TCET. Nonetheless, we request that CMS not pause the creation of the TCET process for innovative technologies in the interim. We ask that CMS issue a TCET proposal without delay and we encourage CMS to work with stakeholders who represent providers in AI services across the continuum of care.

On behalf of the AI Healthcare Coalition, thank you for the opportunity to address the committee.

DR. ROSS: Thank you for your comments. Just a reminder to everyone scheduled as public speakers; anyone who is not on the actual committee, please keep your

cameras off until I call on you, just for ease of being able to focus on the people who are speaking. The next speaker -- and just a reminder that questions will be held until either the end of this session or after lunch. The next speaker is Diana Zuckerman.

DR. ZUCKERMAN: Thank you. I'm Dr. Diana Zuckerman, president of the National Center for Health Research. Our nonprofit research center scrutinizes the safety and effectiveness of medical products, and we don't accept funding from companies that make those products, so I have no conflicts of interest other than being a Medicare beneficiary myself.

My perspective is based on my current position as well as my postdoctoral training in epidemiology and public health, my previous policy positions at congressional committees with oversight over the U.S. Department of Health and Human Services, my previous position as the director of policy, planning and legislation at an HHS agency, and as a previous faculty member and researcher at Harvard. Perhaps most important, I previously served as a member of MEDCAC for two terms, so I'm very

familiar with your important work.

When I served on MEDCAC I was impressed with the generally high quality of the evidence that was considered but that evidence often had a fatal flaw. The studies frequently focused on patients under age of 65 with few if any patients over 70. As is often the case, the research focused on the youngest, healthiest sick patients in order to reduce the confounding impact of comorbidities but as any Medicare beneficiary can tell you, most of us do have at least some comorbidities. For that reason, evidence needs to be focused on representative patients, and the numbers of those patients needs to be large enough to conduct subgroup analyses to determine if the benefits outweigh the risks for those types of patients.

AHRQ and Hopkins did a great job and I generally support their proposed requirements. There are just a few that I think are especially essential and in some cases the wording could be more precise.

Under context, I thought the important point for the study results was that they

provide evidence of net benefit. It's not enough that the product actually has a benefit, but those benefits must outweigh the risks. Also under context, it's essential that there be clinically meaningful differences in any outcomes measured with sufficient precision, and I thought that was a terrific addition.

Also, the outcome is also closely related to that, that a surrogate outcome that reliably predicts outcomes may be appropriate for some questions, but the emphasis should be on reliably predicts, and that the primary outcomes are clinically meaningful and important to patients, absolutely essential.

Under population, there's a very important new requirement that you've added, the study population reflects the demographic and clinical diversity among the Medicare beneficiaries who are the intended users, and at a minimum that should include racial and ethnic background, gender and socioeconomic status.

Under what's generalizable, there's a new recommendation that I strongly support, that there should be studies in beneficiaries'

usual sites of care, but that statement was weakened with the words when feasible and appropriate for answering the CED question, because to my mind it's always appropriate, and it's essential that it be feasible.

Under data quality, I think that could be worded a little more clearly, that the data should be complete, accurate, of sufficient duration of observation, and of sufficient sample size.

And then under subpopulations, I thought it was terrific that it made it clear that it's not sufficient to have diversity, it's essential to analyze demographic subpopulations defined by gender and age, as well as clinically relevant subgroups, and that's an important addition that you've added.

And of course under data sharing, I think that's very important.

In summary, having statistically significant results is necessary but not sufficient. Studying patients who are diverse in terms of race, ethnicity, gender and age is necessary, but not sufficient. The data generated must be relevant to Medicare

beneficiaries, must be valid and reliable, and the results must be clear. Medicare beneficiaries have gotten older, and so the studies need to include and analyze those older patients, for whom the benefits might be smaller and the risks might be greater. We all --

DR. ROSS: Thank you, Diana, I have to cut you off.

DR. ZUCKERMAN: Okay. I just have one sentence, and that's that surrogate endpoints sometimes can predict, reliably predict clinical outcomes, but not all do. Thank you very much.

DR. ROSS: Thank you for your comments. Donnette Smith, you're next. Ms. Smith, if you can put yourself on the video for public comment. Tara, can you confirm that she's on?

(Colloquy off the record regarding Zoom connection.)

MS. HALL: We can come back.

DR. ROSS: Okay.

MS. HALL: We'll go to Jim Taylor. Ms. Smith, are you able to speak?

MR. PATEL: I don't think she can hear us.

DR. ROSS: We'll try to get it straightened out. Jim Taylor, please make your public comments.

MS. TAYLOR: Good morning, can you hear me all right?

DR. ROSS: Yes, we can, thank you.

MR. TAYLOR: My name is Jim Taylor and I'm the CEO of Voices of Alzheimer's. The mission of VOA is to empower people living with or at risk of Alzheimer's and other cognitive diseases, to drive equitable access and innovative care and treatment. VOA accepts corporate support that allows us to develop high quality educational and advocacy material on topics impacting the Alzheimer's community. I have personally never received funding as an advocate.

This is my wife Geri, who was diagnosed with Alzheimer's over ten years ago, and she participated for seven years in the aducanumab clinical trial.

According to CMS, we are here today to focus on proposed revisions to Medicare's CED

study criteria. This meeting has been advised not to review CMS's track record with CEDs. My question to you is why not? In my professional life I worked for over 30 years in IBM finance. We continually scrutinized what was working for our clients and what was not. We set specific development and financial goals and evaluated actual results against those goals.

Of course a big difference between Medicare and IBM is that IBM is a private corporation with stakeholders, where profit driven motivation drove, profit driven companies drive innovation. Medicare is a public insurance program for older adults and people with disabilities. We the American people are the shareholders, participating in a social contract and we enter the program with the assurance, the assurance that it will be available for us when we need it.

So like at IBM, I took a look at the track record of CED as a key component for today's very important conversations. That record is abysmal. Instead of a timely process to inform decisions, half of today's current CEDs have dragged on for more than a decade.

In many cases fewer than a hundred patients have gotten the treatment, and in some cases where evidence is gathered to evaluate CED termination, the goalposts have moved.

Two CEDs are completely blocking access to essential FDA-approved treatments for Alzheimer's. The first restricts amyloid PET scans essential for validating Alzheimer's diagnosis. But that disease modifying therapy, now that disease modifying therapies are finally available to patients, these scans are even more critically important. But for a decade, CMS has used CED to limit PET scan access and reduce costs for Medicare. The Agency is fully aware that its strict conditions disproportionately restrict access to people of color. Despite this, CMS outrageously exploited a PET scan study's lack of diversity as one of the bogus reasons to require a second study.

A second CED is for the newly approved FDA monoclonal antibiotic medications. This CED now is being used to deny access to the recently approved amyloid disease modifying therapy, LEQEMBI. We in the Alzheimer's

community have waited decades for this drug, giving us longer life in the mild stages of the disease, and now CMS has denied coverage for the vast majority of patients for whom the drug was approved by the FDA.

Alarmingly, this unprecedented decision for the first -- this is the first time CMS has used CED on an FDA-approved drug for its on label use. This opens the door to apply CED to future Part B drugs for cancer, infectious disease, and new gene therapies for rare diseases. Given the track record of CED, every one of us should be alarmed by this dangerous precedent.

The ubiquitous language used for several of the proposed CED study criteria gives CMS even more power to permanently prevent access. For instance, CED clinician studies will have to reflect the demographics of the intended users' racial and ethnic backgrounds, gender and socioeconomic status. However, this level of information on subgroups is required for no other drug or device covered by the Medicare program.

Let's acknowledge that CED renders

medications particularly inaccessible to underserved communities. This is especially egregious for Alzheimer's given that black Americans are twice as likely and Hispanic Americans 1.5 times more likely than non-Hispanic white people.

And in conclusion, despite billions of dollars in research, despite FDA-approved breakthroughs in diagnostic treatments, despite FDA approval of life altering disease modifying therapies, we remain a community of six million Americans living with Alzheimer's, disproportionately people of color -- can I just finish the sentence -- who are patients of Medicare now and are intentionally and being systematically denied access to approved medications that will enhance our quality of life. Thank you very much.

DR. ROSS: Thank you for your comments. The next speaker is Jay Reinstein.

MR. REINSTEIN: Yes, good afternoon, or morning. Thank you for this opportunity to provide comment on CMS coverage under CED. My name is Jay Reinstein and I am here as a board member of Voices of Alzheimer's, and I'm also a

person living with the disease, excuse me, and someone whose life and health is directly impacted by the decisions made by this group.

First I want to thank the experts who helped prepare this testimony for me. On behalf of the Alzheimer's community I respectfully submit that the advisory committee has asked the wrong questions and will be asked to vote on the wrong issues. While you spend two days debating the nuances of the proposed criteria to conduct CED studies, the more important question that the advisory committee should be considering is whether the CED process works, whether it is legal, and whether it is meeting its goals.

The Agency for Research and Healthcare Quality has deemed these questions out of scope, but they are very much in scope as it makes no difference whether a trial is or is not listed on clinicaltrials.gov if the CED process is fundamentally broken, and I submit that the CED process is broken, at least for the more important people in the Medicare program, its beneficiaries like me.

Experts tell us that dozens of CEDs to

date teach us that CED clinical studies are applied unevenly, subverting the health needs of some to support those of others. I'm sorry.

For years, the Medicare program has gotten away with paying only a fraction of the costs for Alzheimer's disease. And by finalizing the strict CED coverage policy for monoclonal antibiotic therapies last year, federal officials made it clear that they intend to keep it that way. Medicare currently pays just 60 percent of lifetime costs for a person living with Alzheimer's. The price tag for Medicare is so low because without treatments, expenses primarily for nonmedical services such as at home help with bathing, eating and using the bathroom, those are the expenses that the Medicare program doesn't cover. Families must pay a staggering 70 percent of overall costs, that Medicare picks up the remaining 14 percent of costs primarily for nursing home stays and related long-term services.

The discrimination in our meetings last year with CMS, HHS and officials at the White House was palpable. Under no

circumstances should someone like me be told, who is otherwise healthy, other than having Alzheimer's, which is a progressive and deadly disease, in light of FDA-approved therapeutics that show promise in slowing disease progression but that beneficiaries are currently unable to receive, it feels like a way to keep millions of people from accessing therapeutics because of the cost to Medicare.

I'm here to tell you that the cost of Alzheimer's, the human costs are crushing the Medicare population, and for the most part we're being forced to take care of ourselves. That's why I'm here today to speak on behalf of the community and tell you three things that experts in Alzheimer's disease believe.

First, CMS doesn't have the statutory authority to use the CED process, and now it's being used with a wink and a nudge as a cost control mechanism.

Second, instead of providing medically necessary care, the CED process is denying access to treatments that particularly affect people who are already facing other systemic disadvantages.

And third, the CED process allows the restrictions on access to continue in perpetuity, even in the face of clear evidence and value, because evidence was never the point.

I want to add one more very important comment about the specifics that the committee is considering. First, the Alzheimer's community is very troubled that one of the proposed CED study criteria specifically references surrogate outcomes, which are study outcomes that are reasonably likely to produce a clinical benefit for patients. The FDA's congressionally authorized accelerated approval program allows for initial approval of a drug based on surrogate endpoints for life-threatening diseases where patients have no treatment options or have run out of them. Surrogate endpoints were used in the trials for Alzheimer's monoclonal antibody therapies, and is CMS suggesting that their role is to review trials the FDA has already reviewed? Is CMS a biomedical agency like the FDA? And why is this even here?

In addition, and finally, the proposed

report requirements are over the top and unrealistic for people with Alzheimer's, who do not have the time for peer reviewed publication requirements as the disease progresses, people will literally be dieing waiting for the peer review process.

DR. ROSS: Please conclude.

MR. REINSTEIN: The cost to me personally of not being able to access treatments currently under CED will be less time with my family, less independence, and such profound sadness and frustration of the pain I will cause to my loved ones as my symptoms progress.

Thank you very much for your time.

DR. ROSS: Thank you for your comments. The next speaker is Kay Scanlan.

MS. SCANLAN: Good morning, can you hear me?

DR. ROSS: Yes, we can, thank you very much. You have five minutes.

MS. SCANLAN: Hi, I'm Kay Scanlan, speaking to you on behalf of Haystack Project. Haystack is a nonprofit membership organization with members representing approximately 130

ultra-rare disease patient advocacy organizations. I am not receiving funding from commercial entities with an existing interest in CED.

The CED and the study criteria discussed in this meeting are particularly important for our patient community. 95 percent of the 7,000-plus rare diseases identified to date have no FDA-approved treatment option. Most of our patient communities rely on off-label treatment regimens while waiting and hoping that a treatment is discovered and makes it through clinical trials to FDA approval. That almost always involves accelerated approval, surrogate endpoints, and single-arm studies given the small disease populations.

If CED were used broadly to address evidentiary uncertainties on direct clinical benefit, ultra-rare disease treatments would be routinely subjected to national coverage scrutiny and CED. Even more daunting, though, is the impact of off-label use. NCDs with CED could foreclose development of and access to emerging off-label regimens that patients need

to reduce disease burden or even slow disease progression.

This is why we believe that context is important and patient protections should be paramount as the MEDCAC discusses CED and study criteria. Each NCD with CED does two things. Yes, it sets up national coverage for patients able to qualify for and enroll in CMS-approved studies. It also immediately cuts off coverage until those studies are started and creates national non-coverage for all uses outside of those studies.

Unless CED mechanisms and study criteria expressly provide for or exempt off-label uses supported by evidence in very rare conditions, any NCD requiring CED would completely foreclose access to treatment in these patients unless they are somehow able to sustain a direct appeal against the NCD itself. So that is our first request, that you consider the downstream impact of CED study criteria on our patient populations.

With respect to patient protections, we urge you once again to keep context at the forefront of your discussions and

deliberations. Study criteria crafted to ensure scientific integrity and data validity can appear inappropriate when the investigational item is not actually investigational and the studies are required for meaningful access to treatment. They can move toward and beyond the lines of ethics when that care is subject to randomization and providers otherwise managing the patients' care are blinded to the treatment received.

So first, we ask that a study criteria be added to ensure that each CED study complies with an overarching set of requirements established for and applicable to the specific CED NCD and the study questions CMS poses to resolve the reasonable and necessary question.

Although including a requirement that each CED study be reviewed by an IRB is important, it does not sufficiently protect the Medicare beneficiary population. The existing review requirement does not address the ethical considerations associated with conditioning coverage on clinical trial participation that may vary based on the disease state, availability of alternative treatment options,

assessed safety and efficacy of the intervention, and other factors.

The Federal Policy for the Protection of Human Subjects, the Common Rule, has been codified at subpart A of 45 CFR 46. Haystack urges MEDCAC to consider that each CED NCD and its study questions, priority outcomes, data thresholds and other structures constitute research on human subjects not clearly falling under any exemptions from human subject protections under the Common Rule. Medicare is primarily a lifeline for our nation's aged and disabled, not a research entity, and the program should submit each NCD CED structure to review and approval by a central IRB.

Second, we strongly urge MEDCAC to recommend informed consent requirements that protect beneficiaries as patients, including that any FDA-approved or cleared treatment is not experimental or investigational; whether research subjects will be able to access treatment outside the clinical trial and any longitudinal studies if emerging evidence demonstrates improved patient outcomes; whether research subjects or their treating providers

will be informed on whether they are in the active treatment or control arm of the trial; availability of the FDA-approved treatment for individuals unwilling to accept the risk of randomization to the control arm or otherwise unwilling to participate in research who are able to find alternative funding.

Third, we ask that a study criteria be created to require a monitoring function over all studies within a particular CED NCD to ensure that randomization of research subjects ceases when likely clinical benefit is shown through a CMS-initiated CED study or other evidence in a manner generally sufficient for claim-specific payment by the MAC.

Fourth, there should be an alternative coverage pathway within the CED design for Medicare beneficiaries who are unable to participate in a CMS-approved clinical trial but seek coverage for use within the FDA-approved labeled indication of a medically accepted off-label use. This is also important for beneficiaries who have received a clinical benefit from the product or service from use outside of Medicare, since those individuals

would not generally be accepted into clinical trials.

Finally, we believe that our recommendations are essential in addressing health inequities associated with lack of diversity in clinical studies. Patients with adequate financial resources have always been able to access treatments that individuals who relay on insurance coverage are unable to afford. Rare disease patients and their families are often forced to decide whether they can afford a non-covered but potentially promising on- or off-label treatment regimen, and too often face the crushing reality that evolving standards of care are financially out of reach.

DR. ROSS: If you could conclude quickly?

MS. SCANLAN: Sorry?

DR. ROSS: A quick conclusion?

MS. SCANLAN: Okay. Any government initiated paradigm conditioning coverage for safe and effective treatments on participation in research, including randomization, controlled studies is likely to further, rather

than reduce, medical mistrust. It also negates the critical element of informed consent that researchers have historically denied to black communities and other underserved populations.

Thank you for your considering our comments and recommendations, and I'm happy to answer any questions you may have.

DR. ROSS: Thank you for your comments. The next speaker is Tara Burke.

MS. HALL: Sorry, no, the next speaker is Susan Peschin.

DR. ROSS: Oh, my apologies. Susan Peschin.

MS. PESCHIN: Thank you. Hi, everybody.

DR. ROSS: You have five minutes.

MS. PESCHIN: Sure. I'm Sue Peschin and I serve as president and CEO of the Alliance for Aging Research. The alliance receives funding from VMA, Ava, Biogen Relief for non-branded patient advocacy on coverage related issues. I have comments from the proposed clinical study criteria but I want to start by providing some context.

Many of you know the experience of

going to the doctor for yourself or with a loved one and being told the office must call the insurance carrier to obtain coverage approval for a particular treatment, or the doctor might break the news that you have to first try and fail with a standard treatment before insurance will cover a new or better one. This is called utilization management and it's regularly used by insurance companies to save money. Coverage with evidence development or CED has become utilization management for CMS and the Medicare Part B program.

Under CED, Medicare denies coverage for an FDA approved item or service except through a very limited clinical study, either a CED clinical trial or a data registry. Both CED clinical trials and data registries are subject to the criteria that you all are voting on.

Today the alliance is releasing a report called Facade of Evidence, How Medicare's Coverage with Evidence Development Rations Care and Exacerbates Inequities. Our report includes examples where only a fraction of estimated eligible beneficiaries are treated

in very small CED studies, sometimes as little as in the dozens, as in the case of cochlear implants, and that's been going on for 17 years.

Once CMS places a treatment in CED, it's extraordinarily difficult for it to end. An August 2022 systematic review of CED in the American Journal of Managed Care identified that CMS issued a total of 27 NCDs requiring coverage for evidence development between 2005 and 2022. Only four of the CEDs have been retired from the Agency, and several have been ongoing for more than 15 years.

Our report finds that Medicare beneficiaries in rural communities and communities of color are more likely to be denied access under CEDs because the conditions of coverage primarily direct care to urban medical centers in wealthier areas. Worse, CMS has exploited inequitable participation in existing CED clinical studies as justification to keep CEDs going, and this happened with the amyloid PET and TAVR CEDs.

The vague CED study criteria people voted on will afford CMS unchecked power to not

only lock up many more pressing treatments and services in future CEDs, but to throw away the keys, and here are just a few examples. In CMS's use of the term sponsor/investigator, the Agency doesn't distinguish between the parties that will carry out the CED study and the parties that are responsible for the overall conduct, funding and oversight of the study, and the context recommendation sets up a pass-fail construct, by requiring that, quote, sponsor/investigators establish an evidentiary threshold for the primary outcomes so as to demonstrate clinically meaningful differences with sufficient precision. It's totally inappropriate for CMS to require this in postmarket evidence development to demonstrate the use of quote-unquote reasonable and necessary for Medicare beneficiaries.

While these recommendations remove the explicit inclusion of the randomized clinical trial, they fail to clearly state that the use of an RCT, especially an RCT that's placebo controlled, should be rare and relied on only in unusual circumstances. We are concerned that these criteria are veiled attempts for CMS

to require RCT participation for novel drugs that are authorized by the FDA under accelerated approval. CMS may not agree with Congress on the FDA's accelerated approval pathway, but that doesn't give them the right to take it out on Medicare beneficiaries with Alzheimer's or other life-threatening conditions.

In addition to reviewing the CED process, my request is for the CMS Office of Inspector General to examine whether the MEDCAC chair and vice chair, Doctors Ross and Dhruva should be permitted to vote on these recommendations or whether another chair and vice chair should be appointed for this meeting. On October 27th right after the public comment on the AHRQ report while the process was still open, Doctors Ross and Dhruva aired their views publicly in an opinion piece in the New England Journal of Medicine before CMS asked them to do so, which goes against the MEDCAC charter.

The Federal Advisory Committee Act instructs against biasing activities, and Doctors Ross and Dhruva's op-ed seem counter to

that. CMS is not a payer, it's not a biomedical agency or anybody's family doctor. There are strong signs that CMS intends to apply CED to upcoming FDA approved gene and immunotherapy drugs, and I encourage Congress to codify its CED authority. These are worrisome issues that should concern all of us. Thank you for the opportunity to present them.

DR. ROSS: Thank you for your comments. Tara Burke, five minutes.

MR. BURKE: Hi, good morning, give me one second. Good afternoon. My name is Tara Burke, vice president of payment and cost share delivery policy at the Advanced Medical Technology Association, or AdvaMed. AdvaMed is a national trade association representing manufacturers of medical devices and diagnostic products. Our members range from the largest to smallest medical technology innovators and companies, and we appreciate the opportunity to comment today.

CMS held a MEDCAC meeting on evidentiary characteristics for CED in 2012 before updating its existing CED guidance. We said then that the medical device industry has

long supported the use of sound evidence to inform medical practice. We also said we'd become concerned with a CMS decision that requires CED in order to allow certain Medicare beneficiaries access to medical technology as significant requirements for manufacturers and providers. These statements hold true today.

Today's MEDCAC meeting centers around a recent AHRQ report updating these criteria. We submitted specific comments on the draft AHRQ report last year, and we also provided those comments to CMS in advance of this MEDCAC. Our comments today reflect more overarching concerns regarding the potential implications for future CMS coverage decision making.

For example, in the context of the forthcoming transitional coverage for emerging technologies (break in audio) proposed regulation. AdvaMed supports policy and policy improvements that will result in a predictable pathway to Medicare coverage for new medical devices and diagnostics. Advancing access to technologies that improve health outcomes for a wide array of Medicare beneficiaries is also

critical to insuring CMS's goal of advancing health equity. We have often said that CEDs should be used to expand, not restrict coverage.

AdvaMed has advocated for a coverage pathway for emerging technologies that is separate and distinct from the existing NCD with CED process. Therefore, any evidence generation required under TCET should insure a least burdensome approach distinct from the NCD with CED process that insures timely access to new and innovative technologies.

With respect to CED, when an additional data collection is deemed necessary, the process must involve cooperation between CMS and its stakeholders such as medical device companies, to identify data collection objectives, appropriate study endpoints, and the duration of data collection. Whenever possible, such policies must minimize administrative burden.

We reiterate previous comments to CMS that when Medicare coverage is contingent on collection of additional clinical or scientific evidence beyond FDA requirements, CMS should,

one, collaborate with stakeholders to clearly identify the data collection objectives; two, consider the minimum data necessary to achieve those objectives; three, clearly identify with input from interested stakeholders, scientifically supported study endpoints and the duration of data collection in advance, including clear stopping rules for data collection under CED; and four, identify an appropriate mechanism to insure continuous coverage of an item or service after the CED ends to support the structure and coverage to continue to allow Medicare beneficiaries to benefit from important FDA-approved technologies and services until a new or revised coverage determination is issued.

Additionally, if a CED provides evidence supporting a new innovation or service as reasonable and necessary, Medicare's coverage policy should be updated in a timely manner to reflect those outcomes, at the same time minimizing additional administrative burden and simplifying program requirements where possible.

Again, AdvaMed submitted more detailed

comments to AHRQ on its draft CED report, and appreciates that the final report reflects several of those comments. We believe that CMS's decision about coverage criteria and the CED process should be clear and should not result in delayed access to promising medical technologies. We appreciate the opportunity to discuss this important issue and we welcome further discussion. Thank you.

DR. ROSS: Thank you for your comments. The next speaker is William Padula.

DR. PADULA: Hi, Dr. Ross, can you hear me okay?

DR. ROSS: Yes, I can, thank you. Five minutes.

DR. PADULA: Thank you. My name is William Padula, I'm a professor of health economics at University of Southern California and the Schaeffer Center for Health Policy and Economics. I am speaking on behalf of myself and colleagues Dan Goldman, Joe Grogan and Barry Widen, and our views expressed in this panel don't necessarily reflect the views of USC or the Schaffer Center.

I want to explain that. We're

experienced clinical and economic researchers with policy insights that we believe through our recommendations and comments today could incentivize technological innovation that will ultimately improve health outcomes for patients, but concern us that study design requirements of CED in some ways run counter to the goals of providing coverage, collecting clinical evidence, incentivizing innovation and incorporating a patient perspective. It concerns me that increased requirements would compound the barriers that innovative technologies face to access healthcare markets.

What we want to start off with that I believe is most important as well, is the fact that the patient perspective could be better recognized and highlighted through the CED program. So we recommend that AHRQ and CMS consider prioritizing requirements in order of importance and allowing sponsors of CED studies the ability to remain flexible to the less important criteria. In alignment with the CMS's mission, put patients first. CMS should prioritize study design elements that are focused on a patient population that the

technology or therapy is designed to treat, including over sampling for underrepresented populations.

Therefore, there are two study requirements under consideration that deserve special priority. First is the prioritization of measurement of outcomes that are reported to patients. And second is establishment of an evidentiary threshold that is consistent with patient values.

Now I want to move on to some specific amendments for the requirements, and the first being in outcome measures. Outcomes -- this is part I if you're curious -- outcomes should be limited to those that are of high importance to the target patient population. And we actually agree with Dr. Jodi Segal's earlier suggestion of thinking of these as net benefits, not just the positive, but the negative consequences that matter to patients as well to be reduced in burden, so based on quantitative evidence of patient preferences with risk and benefits.

The second issue regarding study design, or part D among the amendments, our comment here is evidentiary thresholds for

outcomes should be set by the target patient populations themselves based on quantitative evident of patient preference, elicitation, and tolerance for uncertainty.

The third matter is regarding transparency. We believe that high priority final amendment requirements are related to E, P and Q. Our comments here are that a description of the study should be registered at clinicaltrials.gov, I believe that was mentioned earlier. The results should be published, submission to peer review is not sufficient, the peer review process should be completed and lead to a publication of these results. And thirdly, that taxpayer funded data collection mandates should require that the identified data be made publicly available as soon as ethically and reasonably possible.

My last point for comment is that we reflect on reducing budgets and these recommended requirements should be optional, that is with regard to K, L, M, M and L. We want to comment that studies should be least burdensome, I believe Ms. Burke mentioned that in her previous comments right before me, and

evidentiary requirements should be limited to unanswered questions related to CMS jurisdiction that is reasonable and necessary, as opposed to simply looking at endpoints of safety and efficacy.

So in conclusion, my colleagues and I believe that the importance of CED effort by CMS and AHRQ is important and noteworthy. CMS coverage of health technology impacts payer trends globally, not just in the United States, so if CED doesn't work as intended, manufacturers do not have a clear roadmap for translating research into market assets, ultimately patients lose, as you've heard some patients comments so far today, that when they don't have access, they can't get treated to get better.

CED study design requirement should be least burdensome for the manufacturer adjusting for the safety of patients. What we want to know from other researchers at Johns Hopkins, Caleb Alexander and colleagues, that clinical trials cost upwards of $20 million per trial. Alternative methods for clinical research that include real-world evidence as Dr. Segal

mentioned earlier, makes clinical research more affordable, especially for smaller manufacturers that seek to enter these markets.

The final comment here is that in our field like what the Schaeffer Center represents in health policy and economic research, is prepared to conduct innovative affordable comparative effectiveness research and adjacent economic research to help innovative manufacturers achieve market access through CED under these amendments. I'd like to thank the panel for their time, and turn it back over.

DR. ROSS: Thank you for your comments. One more speaker in the open phase before the presentations, that is Yajuan Lu.

MS. LU: Yeah, thank you, Dr. Ross, Yajuan Lu. Good afternoon, everyone, it's a great pleasure to be here. I am the director of corporate research and health policy at Boston Scientific, and it's one of the world's largest companies dedicated to developing, manufacturing and marketing innovative therapies. Boston Scientific supplies many devices and technologies to provide Medicare beneficiaries high quality care in many areas,

so we have had experience, really extensive experience with the CED program since its creation, and we're really pleased to have the opportunity to provide input based on that really direct experience.

We believe that CED provides a valuable appropriate pathway for Medicare coverage for certain technologies and we agree with many of AHRQ's recommended modifications. In considering AHRQ's recommended modifications to the CED criteria, Boston Scientific believes first and foremost that that evidence generation should be designed to insure that an appropriate level of rigor is used to address the specific questions and support Medicare beneficiaries' access to innovative technology to improve health outcomes.

Specifically, we support the final report requirement C, the rationale for the study is supported by scientific evidence and the study results are expected to fill the specific knowledge gaps and provide evidence of net benefit, as well as amended at the final report, the final proposed requirement D, sponsors/investigators establish an evidentiary

threshold for the primary outcomes so as to demonstrate clinically meaningful differences with sufficient precision, with the following additions to the CED.

We further recommend that manufacturers and CMS should look at existing evidence and collaboratively give out a specific evidence gathering strategy to address the specific gaps CMS and the manufacturer identify within the existing evidence base. The subsequent plan should be designed to evaluate and provide evidence regarding the effectiveness of the technology in the Medicare population. While the evidence plan would not require a specific type of study, for example a randomized control trial, it would include a research method rigorous enough to evaluate the technology's effectiveness in the Medicare population. We believe criteria C and D should explicitly reflect these principles.

One of the key challenges we have here with the program is the lack of a definitive timeline or process to decide when sufficient data has been collected to reach a coverage or a non-coverage decision. The lack of,

uncertainty on the duration of the studies adds to unpredictability for manufacturers, creating delays in access for patients and providers.

We completely agree with one of Dr. Segal's suggestions earlier today for continued evaluation of the CED final proposed requirements, for the quality and strength of the evidence generated is the ultimate test of the effectiveness of these requirements in order for CMS to reach a timely decision. In order to facilitate to achieve this objective, we encourage CMS to develop a process through which the clinical team, manufacturers and CMS, could collaboratively identify and decide on the endpoint of the studies once sufficient evidence has been collected.

For example, Boston Scientific's Watchman atrial appendage closure system has been covered under NCD 20.34 since February of 2016. Watchman LAAC has been extensively researched with ten clinical trials completed and more than 200,000 devices implanted in patients, the vast majority of whom are Medicare age. The clinical trials have consistently demonstrated the product's safety,

effectiveness, and low adverse events. Despite the significant clinical evidence available, the NCD for LAAC has been in place for over six years and it remains unclear when the CED will end. We believe a process that establishes a clear endpoint for sufficient evidence and data collection under CED would benefit all stakeholders.

In conclusion, Boston Scientific appreciates the opportunity to offer our input to the CED evidence generation criteria and the overall preventive line. We look forward to a continued partnership with CMS and the other interested stakeholders to improve the program. Thank you very much for all your time.

DR. ROSS: Thank you for your comments. Now before we move to the presentations portion, I just want to check again whether Donnette Smith is now able to make public comment.

MS. SMITH: I'm here, yes.

DR. ROSS: Great. You have five minutes.

MS. SMITH: I apologize for that.

DR. ROSS: Oh, don't worry.

MS. SMITH: Hello, everyone. My name is Donnette Smith and I serve as the current chair of the board of directors at Heart Valve Voice US. Heart Valve Voice US is a patient-led organization that exclusively focuses on improving the diagnosis, treatment and management of heart valve disease by advocating for early detection, meaningful support and timely access to appropriate treatment for all people affected. Heart Valve US receives funding from industry, Abbott, Medtronic and Edwards Life Sciences for non-branded health education and advocacy on heart valve disease.

Professionally, I had a 30-year career in civil service as a technical writer, editor with the U.S. Army Research, Development and Engineering Command at Redstone Arsenal, Alabama at the George C. Marshall Space Flight Center. I have been a patient advocate on the local, state and national level, and the reason I do all I can to help educate others about heart disease is because I have been a member of the heart community my entire life.

My journey with heart valve disease

began with a bicuspid value, aortic stenosis and an enlarged heart. I had valve replacement surgery in June 1988, again in May 1993 and again in March 2010, and I received a TAVR, or transcatheter aortic valve replacement in December of 2020. When TAVR was approved by the FDA in 2011, it was reported that for older adults who were too frail to withstand traditional open heart surgery found improved outcomes with shorter hospital stays and recovery times, and better quality of life measures.

I was able to access TAVR because I was privileged to have exceptional access to the best health care and the financial resources to pursue it. Most Medicare beneficiaries are not as lucky. Medicare only covers TAVR for Medicare beneficiaries with severe systematic aortic stenosis who consent to participate in the TVT registry.

The TVT registry is a clinical study and it must adhere to the study criteria you are reviewing today. In general, the TVT scales, which can take a year or more to set up, and coverage for the new treatment is

unlikely during that time. With TAVR, the studies compare the group to patients who receive open heart surgery. Even when patients can have a less invasive TAVR procedure, a current number, a certain number must be placed in the open heart group, and the TVT registry requires informed consent, which can be a deterrent for folks who don't like the idea of being required to enroll in a clinical study to receive access to it, especially people of color who may have a strong mistrust in clinical research like the one for TAVR, which goes far beyond what the FDA requires on the device label. In the case of TAVR, residual volume requirements for TAVR, SAVR and PCI shut out smaller less resource settings, providers and communities from participation up and around $10,000 yearly acknowledge, and if asked how you know, that's what they told us when we called them and asked them.

In November 2020 an article published in the Journal of the American College of Cardiology on TAVR TVT registry reported that significant disparities in access persist. In 2019, 92 percent of patients that received TAVR

were white, only four percent were black, 1.4 percent were Asian, and five percent were of Hispanic or Latino ethnicity. The same report acknowledges that it took eight years before TAVR became available to Medicare beneficiaries in all 50 states.

The TVT registry reports that 72,991 patients received TAVR in 2019, which sounds like a high level of success, but a 2017 article in the American Heart Association Journal, Circulation, Cardiovascular Cause and Outcomes estimates that number of U.S. patients with severe systematic aortic stenosis eligible for TAVR is 235,932 per year, and of that high risk is 111,205, intermediate is 34,991, and low risk is 89,736. So only an estimated 31 percent of those eligible for TAVR in the U.S. receive it, continuing the theme that seven in ten patients are not getting the help they should.

This is a life or death issue. Without aortic valve replacement, patients with symptomatic severe aortic stenosis have a 50 percent mortality risk at two years. The fact that there is still a CED in place for TAVR

raises urgent questions. If we as patients don't speak up, we will never see the changes in health care that we want and need. I am a voice for those who won't or can't speak for themselves. Thank you.

DR. ROSS: Thank you for your comments. The next speaker, who has a presentation, is Beena Bhuiyan Khan. You have five minutes.

MR. KHAN: Thank you. Good afternoon. My name is Beena Bhuiyan Khan, I'm assistant research director at the Duke Margolis Center for Health Policy, I thank you for the opportunity to present. Next slide.

I have no disclosures. Next slide.

The Margolis Center for Health Policy is part of Duke University and as such it honors the tradition of academic independence. Next slide.

The center's mission is to improve health, health equity, and the value of health care through practical, innovative, and evidence-based policy solutions. Next slide.

Coverage with evidence development or CED was implemented to facilitate access to

therapies with outstanding evidentiary questions. The current evidence requirements reflect an opportunity to build on previous steps to clarify the scope, requirements and evidentiary expectations of CED studies, as well as improving the overall process to be more transparent, predictable and timely. Next slide.

This panel's convened during ongoing discussions about modernizing Medicare coverage processes for the growing number of novel technologies which may not have sufficient evidence for Medicare coverage at the time of FDA approval. Continued evidence development can inform the value of such technologies, which underscores the importance of CED and the discussions today. Next slide.

Concurrent with the growing pace of medical innovation are the growing number, the growing importance of real-world evidence for evaluating health outcomes for Medicare beneficiaries. Novel real-world evidence generation methods may be an efficient way to substantiate this concept of appropriate for use in Medicare beneficiaries in Medicare's

longstanding definition of reasonable and necessary. The proposed requirements will support innovation in real-world evidence generation strategies that support fit-for-purpose studies, allowing CMS to reevaluate appropriate coverage in a predictable, transparent and timely manner. Next slide.

As cited by the AHRQ report, the Duke Margolis springboard for the rigorous treatment of evidence states that real-world evidence must be reliable, relevant and of high quality to be inclusive. CED studies that meet these criteria will allow CMS to determine if a product is performing as expected in real-world settings and in the intended Medicare subpopulations. The proposed requirements on data generalizability, robustness, completeness and accuracy are important additions to ensure data relevancy and quality, and will help investigators design rigorous studies that will allow CMS to confidently interpret results.

Finally, the proposed requirements targeting data validity, relevancy and accuracy will contribute to the degree of confidence

that CMS can derive from study results. A key element of data relevance is collecting data that is representative and generalizable, and will support CMS's goals of ensuring generalizability to the Medicare population. Next slide.

Oh, next slide, sorry. Oh, sorry, go back one slide. Understanding how a technology performs in usual sites of care is important for CMS to determine the appropriateness of a technology. The proposed requirements allow CMS to set provider, site or patient criteria when patient safeguards are needed. Additionally, the requirements will allow for data collection to reflect changes in sites of care and intended populations over time, wider variability and experience with the technology, and differential data collection capabilities across sites of care. Ultimately, the proposed requirements allow CMS to establish standards for use of novel real-world data sources. Next slide.

In order to reduce patient, provider and sponsor burden, postmarket studies could be designed to meet both FDA and CMS data

collection requirements, which could be achieved through early engagement across sponsors and both agencies. Investigators may need additional guidance from CMS on outcomes of interest and study duration to plan an effective study that would generate the types of evidence that CMS would need to ultimately end a CED. The proposed requirements will support early engagement between CMS, sponsors, FDA and other stakeholders, ultimately allowing CMS to efficiently identify evidence gaps, provide guidance on study design, and complete the whole process in a timely predictable manner. Next slide.

Finally, the proposed requirements on protocol communication will benefit from adequate resources to ensure that CMS has the capacity to engage with stakeholders and provide guidance on the CED studies. Next slide.

Thank you very much for your time and attention.

DR. ROSS: Thank you for your comments. The next speaker is Brian Carey.

MR. CAREY: Good afternoon and thank

you. Brian Carey speaking on behalf of the Medical Imaging and Technology Alliance. Next slide.

I'm an attorney at Foley Hoag and represent MITA which, many of the members manufacture medical devices or imaging devices and will be financially impacted by the discussions today. Next slide.

We want to thank CMS and the MEDCAC for the opportunity to present at this meeting today, and to share our thoughts on the analysis of the requirements for CED, and I'll discuss in this presentation, MITA has been involved with CED programs since the beginning of the policy, and we think we have some experience this year as the Agency looks at refining the evidentiary requirements.

Additionally, our main view is that CED should really only be used when it's going to expand Medicare access to new technologies for its beneficiaries, and we have several specific points that we will go through, and echo many of the points we've heard from other speakers when they were focusing on the process of moving from a CED study to full coverage,

looking at outcome measures that are appropriately diagnostic, and limiting CEDs to a certain duration. Next slide.

As noted, CMS has had PET imaging agents in CED studies going back to the beginning of the program in 2005, and MITA and its members have been sponsors and contributors to those programs starting first with the National Oncologic PET Registry and constantly now with the IDEAS imaging study for Alzheimer's. Next slide.

One of our key focuses is really on looking at expanding access through the CED and a specific point we wanted to raise is that the current policy is limiting coverage to only beneficiaries enrolled in those clinical trials, which really does restrict access, and so one of the ideas that MITA supports with other stakeholders is really allowing coverage, both for study participants in the CED, but also outside the CED. Next slide.

We're also very focused based on our experience of streamlining the process of moving from a national coverage determination requiring CEDs, to getting the CED studies

approved and up and running, and then ultimately having the data reviewed through a reconsideration process, and moving towards full coverage. If we could move to the next slide?

We have, this is a case study, the current CED for beta amyloid for the detection of Alzheimer's disease that MITA members and others have been working on with CMS for the past ten years, and we're just contending NCD reconsideration and the process has taken a long time, there's been a lot of data reviewed, it's produced and been published, and really having some set timelines and guidance on how items would move from CED to full coverage is helpful. Next slide.

In terms of specific study elements that AHRQ and Hopkins had looked at, I think the three main points we wanted to really raise are when looking at outcome requirements for diagnostic technologies it should really focus on impact on patient management. I also wanted to raise the issue of when randomized control trials would be necessary, versus prospective registries, and incorporate real-world

evidence, realizing that randomized control trials can raise ethical issues and also ethical treatment of coverage among beneficiaries.

And then the final point really builds on the last presentation, it's really moving towards more opportunities to incorporate real-world evidence through claims data from electronic health records and other systems to streamline the CED process that will also allow a broader benefit for populations to be covered in CED studies and outside of the CED studies.

So we thank the panel for your consideration of this and your work during this MEDCAC hearing. Thanks very much.

DR. ROSS: Thank you for your comments. The next presenter is Cathy Cutler.

DR. CUTLER: Good morning, or good afternoon depending on where you are. I --

DR. ROSS: I'm sorry to interrupt. Can you go on video? Oh, there you are.

DR. CUTLER: All right, I think we got it now, thank you.

DR. ROSS: Yes, five minutes, thank you.

DR. CUTLER: Yes. So I am actually speaking on behalf of the Society of Nuclear Medicine and Molecular Imaging. Next slide please.

So I'm actually a researcher that works at Brookhaven National Laboratory, I'm the head of their isotope program there. I'm also the vice president-elect of the Society of Nuclear Medicine and Molecular Imaging. This is an international professional society that represents over 15,000 members that are made up of physicians, technologists and scientists who set the practice guidelines for nuclear medicine, and I have no conflicts. Next slide please.

So SNMMI appreciates CMS's commitment to transparency in decision making related to coverage with evidence and national coverage determinations. We strongly urge the MEDCAC to recommend that CMS allow targeted and real-world evidence collection to satisfy CED requirements. Most importantly, we urge the MEDCAC to recommend that CMS include terminating any CED requirements that at the time that a CED NCD is created, and evaluate

each NCD with CED every five years to determine whether the CED should remain in place or should be retired. Next slide please.

As pointed out by many others during these talks, there have been 27 therapies that have been subject to CED since 2005. Six have achieved coverage or the coverage has been covered discretionary. CMS has not set guidelines for duration of CED or timelines for reconsideration which, we were disappointed to see that that did not occur here.

CED can inappropriately restrict access to new and emerging technologies. For some therapies, CMS has combined CED for specific indications with very broad non-coverage indications. Use of technology can evolve rapidly in ways that are difficult for physicians or CMS to see at the time. Broad CED NCDs can limit coverage for new uses that were not conceived of at the initial time CED was considered. CED criteria may not be appropriate to other uses and therefore, use of CED can stifle innovation in emerging technologies as well as patient access.

CMS has established a process to

remove NCDs that no longer reflect current practice, and we commend CMS for earlier removing the NCD for non-oncological PET. Removal typically allows for coverage of technology at the discretion of Medicare contractors. It's unclear whether or how this standard could be applied to CED NCDs. Next slide please.

Nuclear medicine studies account for almost 15 percent of current CED NCDs. As pointed out, there's one for beta amyloid positron emission tomography in dementia and neurodegenerative diseases, FDG PET and other neuroimaging devices for dementia, and sodium fluoride PET for bone metastasis. As you can see, the effective dates for these range anywhere from 2004 to most recently in 2013, showing a long timeframe that these have been in effect. Although multiple requests have been made to CMS to retire these, there's been little response to allow these to coverage with MAC discretion. Next slide please.

So sodium fluoride PET was originally for the imaging of bone to define areas of altered osteogenic activity. NCD 20.6.19

limits coverage of PET to identify bone metastasis to try to answer the following questions: Whether there will be a change to a more appropriate palliative care; a change in patient management to more appropriate curative care, improved quality of life or improved survival. All other uses in clinical indications for sodium fluoride PET are nationally noncovered. Recent studies have been detecting activity related in tears in the outer wall of the aorta and managing patients with acute aortic syndrome. No ongoing studies are practical and the result is permanent non-coverage for an important imaging modality. Next slide please.

SNMMI asks that MEDCAC recommend that CMS not apply blanket non-coverage for an item that is not subject for NCD indications other than those that are subject for the NCD; establish specific criteria as to when CED will end; ensure that NCDs and criteria are designed to allow outstanding questions to be addressed with minimal burden on providers and manufacturers; review CEDs every five years and reach out to stakeholders for comments on the

continuing need for CED, to analyze are these ongoing trials or will there be future trials to ensure that the CED will be retired with coverage of the item being left to the MAC.

And on that, I thank you for the time to speak today.

DR. ROSS: Thank you for your comments. The next speaker is Lindsay Bockstedt. Lindsay, are you --

MS. BOCKSTEDT: I am here, I'm just having -- my computer is very slow so just one moment please.

DR. ROSS: No problem. Please do come up on video.

MS. BOCKSTEDT: That's what I'm trying to do. One moment. I am getting an error message about not being able to start video. Is it okay if I proceed without that, or should I go --

DR. ROSS: Actually, we're going to end this meeting to move one speaker to the next session anyway, so maybe you can fix this and then be the first speaker at 1:20, if you're available.

MS. BOCKSTEDT: That's fine.

DR. ROSS: Ralph Brindis, if you're available?

DR. BRINDIS: I'm here but I need my presentation.

DR. ROSS: Great. We'll bring it up please, and you have five minutes.

DR. BRINDIS: Hello. I'm Ralph Brindis, I'm a cardiologist and clinical professor of medicine at UCSF, a former MEDCAC member, and here presenting for the American College of Cardiology and the National Cardiovascular Data Registry. Next slide please.

Here are my disclosures. Next slide please.

CED is an extremely powerful mechanism offering tremendous value to payers, clinicians, but most importantly our patients. CED has been demonstrated to be an ingenious technique, allowing the diffusion of diverse innovative cardiovascular technology and services into the marketplace, while simultaneously promoting timely clinical safety and effectiveness evaluations. ACC supports the use of CED to provide Medicare

beneficiaries with prompt access to new technologies and services when early evidence suggests but does not yet convincingly demonstrate the net benefits for beneficiaries. Next slide.

Registries such as ACC's NCDR provide a valuable cost effective mechanism to help provide, meet the needs for CED evaluation, while also fostering improvements in the quality of care. CED-mandated registry participation, when appropriate, promotes a powerful national research and data collection infrastructure for large patient populations, allowing assessment of treatment in relatively modest-sized patient subgroups not well suited for RCTs, but certainly present in Medicare beneficiaries. Next slide.

The National Cardiovascular Data Registry is the largest most comprehensive outcomes-based cardiovascular registry in the world. We have eight registries, two collaborations, 95 million patient records and 25 years of experience. Next slide.

Here's a graphic of our current state of registry operations, started with our

Cath PCI registry in 1998. Next slide please.

When you look at our registry scope, one appreciates that we have three registries that are either prior or currently meeting CED evaluation criteria, including our EP device implant registry, our STS/ACC TVT transcatheter valve registry and our LAAO left atrial appendage occlusion procedure registry. Next slide please.

The NCDR data serves many purposes for many stakeholders, helping with quality and performance improvement, evidence-based medicine, reimbursement, research, surveillance, performance monitoring, state and federal QI, and public reporting. Next slide please.

From our longitudinal ICD registry, these are three studies showing CED examples helping CMS assess what is necessary and reasonable subgroups not well evaluated in any randomized clinical trials for ICD implantation. Next slide please.

In our STS/ACC TVT registry looking at TAVR, Mitral and TEER, we've assessed for CMS valve in valve therapy, bicuspid valve therapy,

the use of anticoagulants in patients with atrial fibrillation, the use of TAVR in patients with renal insufficiency, and evaluations of frailty indices and geographic access. Next slide.

In terms of our LAAO registry we've been looking at clinical outcomes, patient level analysis and procedural safety, sex differences in procedural outcomes, clinical impact of residual leaks, and the use of antithrombotic therapy post procedure in patients with atrial fibrillation. Next slide please.

In terms of our analysis of the proposals, we've had the opportunity to review the proposed requirements for CED from the AHRQ draft report. We're supportive of many of the proposed updates and we support modernizing the criteria to promote increased transparency and replicability. However, while the proposed criteria tends to do this, some of the proposed measures also add undue burden and cost that would create barriers to access novel therapeutics and hinder the collection of real-world evidence.

The NCDR is well positioned to play an active role in any future CED mandate. Moving forward, it's essential that CED programs continue to be designed collaboratively with input from all relevant stakeholders, including clinical experts, professional societies and patient groups that are most likely to provide and receive the services in question. Next slide please.

DR. ROSS: Please wrap up your comments.

DR. BRINDIS: And we would encourage both the panelists and CMS to review our in-depth letter and our in-depth comments related to the 17 voting questions. Thank you very much.

DR. ROSS: Thank you for your comments.

So we are right at 12:50, which is our opportunity to break for lunch which will got for 30 minutes until 1:20 eastern. At that time we'll come back, Lindsay Bockstedt will have her opportunity to make public comments for five minutes, and then we have three individuals who have identified themselves to

speak during the open public comment period, and each will have one minute.

After that, just a reminder to every committee member, we will then have the opportunity to ask questions to any and all presenters. I want to thank all the presenters who offered to speak today on behalf of themselves and their organizations, it's very valuable to have their input.

So enjoy your lunch and I'll see everybody at 1:20 eastern.

(Lunch recess.)

DR. ROSS: Welcome back, everybody. So just as a reminder, we're going to continue with one last presentation from our scheduled public speakers, Lindsay Bockstedt will have five minutes, and then we will turn to our open public comments where each individual who had signed up today to make public comments will be given one minute.

So Lindsay Bockstedt, the floor is yours. Five minutes please.

MS. BOCKSTEDT: Thank you, good afternoon. My name is Lindsay Bockstedt and I am vice president of health economics and

outcomes research at Medtronic. Thank you for the opportunity to present today on the criteria for coverage with evidence development, and also the flexibility given the technical issues earlier. My disclosures are included in the next slide. In summary, I am an employee and shareholder of Medtronic. Next slide please.

First, Medtronic has a long history of working with CMS to generate meaningful evidence under CED for a variety of therapies including implantable cardiac defibrillators, transcatheter valves and leadless pacemakers. Each of these CED programs, two of which are still ongoing, have had different approaches to evidence generation, different study designs, data collection mechanisms and study sponsors. These CED programs ranged from registries to traditional clinical data collection, to observational studies using Medicare claims data to enroll patients and observe clinical outcomes.

It is with this experience that Medtronic commends CMS on the flexibility, engagement and recent innovative approaches to

CED, with the goal of balancing access to these new technologies and the need for additional evidence generation. As exemplified in the leadless pacemaker NCD and its associated CMS-approved CED studies, CMS has embraced this innovative approach to CED with the need for other data, in this case Medicare claims data linked to manufacturer data is used to guide real-world evidence and clinical outcomes associated with leadless pacemakers in the Medicare population, including a comparative analysis to transvenous pacemakers.

Not only are these studies relying on real-world data, specifically existing secondary data and generating high quality evidence, but they are also minimizing provider burden associated with data collection while enabling patient access to new technology. All of these study elements are aligned with the proposed CED criteria for sufficient clinically meaningful and transparent evidence generation for CMS decision making. Next slide please.

I'd like to emphasize three principles for CMS to consider while evaluating the CED criteria.

First, continue to ensure flexibility in study designs, data sources, methods and outcomes for CMS-approved CED studies. Flexibility allows the studies to be tailored to meet the specific evidence gaps identified in the NCD with the most efficiency. CMS should continue an open engagement with manufacturers and other stakeholders to ensure input and provide input on premarket evidence development, evaluation of existing evidence, as well as proposed study design.

Second, CMS should have the ability to extend coverage for a technology to beneficiaries beyond the enrolled CED study population in instances where the study is designed to enroll a population that is considered generalizable to the eligible Medicare population. Currently under CED, Medicare beneficiaries are covered for the specific technology only if they are enrolled in a CED study. Expansion in access requires enrolling the entirety of the eligible Medicare population. In other words, CED studies have the potential to become overly burdensome for multiple stakeholders or limited access to

Medicare beneficiaries. With innovative study designs, growing sources for real-world data and advanced analytic methodologies, there are scientifically valid approaches to developing evidence that is generalizable to Medicare populations without necessarily enrolling every eligible beneficiary into the CED study. CMS should evaluate proposed CED study designs to ensure the enrolled population will be representative of the demographic and clinical complexities of the Medicare population, and consider extending coverage beyond the study population if so. Results of an appropriately designed study using a sample population can be generalizable, therefore balancing the needs for evidence as well as minimizing burden.

Third and lastly, an effort to improve predictability and efficiency. CMS should establish predetermined stopping rules for data collection under CED. This can be achieved through engaging manufacturers and other stakeholders during the NCD process and CED study protocol review to determine the appropriate duration and sample necessary to meet the specific evidence gaps identified by

the NCD.

Again, thank you for the opportunity to provide comments during today's MEDCAC. We appreciate the revisions made in response to comments from industry as well as other stakeholders thus far, and we look forward to continuing to engage and shape the CED process going forward. Thank you.

DR. ROSS: Thank you, thanks for your comments.

So we have three people who signed up for public comments and I was informed by CMS that we can give everybody two minutes, not one minute to speak, which is reassuring since one minute is very hard to start and stop on. So the first speaker will be Candace DiMatteis, and you will be given two minutes to speak, if you can come up on camera.

MS. DIMATTEIS: Thank you. Can you hear me?

DR. ROSS: Yes, I can.

MS. DIMATTEIS: Good afternoon, Candace DiMatteis, I'm the policy director for the Partnership to Fight Chronic Disease and we receive funding for non-branded educational and

advocacy work from our partner organizations, which include trade associations, pharmaceutical companies, insurers, patient and provider organizations. I am also a care taker for my mother-in-law, who is living in the moderate stage of dementia.

The AHRQ report emphasizes the importance of real-world evidence on decision making, yet excludes consideration of the real-world evidence of CMS's record on CED, and most importantly its impact on beneficiaries. As other speakers have noted, particularly those speakers on the receiving end of those policies, the real-world evidence and real-world impacts of CED on these patient populations is abysmal. CMS's recent CED that singled out FDA-approved medications utilizing the accelerated approval pathway for differential treatments under CED undermines both congressional intent to expedite access for patients and FDA's expertise on the safety and benefits of these treatments.

More importantly, it has a devastating impact on people living with serious often life-threatening illnesses without available

treatment options. The patient community is gravely concerned about this new development and if you are truly interested in real-world evidence as this report would indicate, then we urge you to examine the real-world impacts these harmful CED policies are having on the beneficiaries.

Thank you so much.

DR. ROSS: Thank you. The next speaker is Pamela Price.

MS. PRICE: Hi and good afternoon, everyone. My name is Pamela Price, I am the deputy director of The Balm in Gilead. I also serve as the director for our Brain Health Center for African Americans. I'm here representing the leadership of the Balm in Gilead, as well as our stakeholders of our denominational health leadership initiative, which encompasses the three large historically black denominations that serve and advocate on behalf of African Americans both here in the U.S., as well as internationally.

I won't belabor because I think a lot has already been brought up, but I do want to just again emphasize the lack of the, again,

real-world evidence as how these types of decisions that this group and this body will be considering over the next two days, and how that actually plays itself out in the community that we serve, particularly in those communities who are most impacted not just by, you know, very specific disease states, but really as we think about both, from whether it's biologicals that are coming out or just a new therapeutic and technology that are being made available, I do want to challenge this group to make sure both from a legislative and you know, authoritative kind of lens, but also looking at how we can do better about getting patient voices to the table and how we can do better about streamlining this process.

A lot of these recommendations seem duplicative of what the FDA is trying to do around increasing diversity and how they're trying to shift and have more transparency with our trials and with the evidence that is being collected. So I really challenge this group to say, are you duplicating effort that is actually creating an additional barrier to these communities who are already being

marginalized by the things that we have in place, like the CED as it currently stands to date.

Thank you.

DR. ROSS: Thank you for your comment. The last speaker is Rita Redberg.

DR. REDBERG: Thanks very much. I have no conflicts of interest. I'm a cardiologist and a professor of medicine at University of California San Francisco, and a past chairperson of this Medicare coverage committee, as well as the past Medicare Payment Advisory Commission, but I'm talking today because I think coverage with evidence development is a really important mechanism to try to improve quality and care for Medicare beneficiaries.

My position is based on my strong belief that all Americans deserve the highest quality of health care, and during my medical training it became very clear to me that for many reasons, although we spend more than twice as much per person in this country on health care, our outcomes are not better, in many cases are much worse, and certainly our access

is much worse, and a lot of that is because we are providing health care of not only no benefit, but often with multiple harms.

And the reasons are that we don't have, we haven't held to the Medicare criteria that treatments are reasonable and necessary, particularly for a Medicare population. In this case in particular, you know, we cannot make the assumption that an FDA-approved treatment is reasonable and necessary for a Medicare population. And I think with all due respect to the FDA for example, with the recent Alzheimer's decision, we all know that the committee, the expert panel, that there were no benefits of the trial. There was a congressional investigation which found a lot of irregularities between the FDA and the company, and that there were a lot of concerns with harms with a 40 percent risk for bleeding, it was based on a surrogate endpoint, and it was an amyloid which had not been shown to be meaningful clinically, and even the clinical endpoints were not shown to be meaningful clinically because it was a .2 change in a 19-point scale.

And so I think it's really important to thing of coverage with evidence development not based on whether it was FDA approval or not, not based on the kind of pathway, but based on is there evidence of benefit in the Medicare population. If there's a randomized control trial showing that the treatment or therapy is better than the alternative, then certainly that is something Medicare wants to cover, because that's reasonable and necessary. But if it is available but there is not evidence of benefit, then I think coverage with evidence development offers the ability to make the treatment available, but to also gather that really necessary evidence.

DR. ROSS: Thank you for your comments. I'm sorry to cut you off.

DR. REDBERG: No problem.

DR. ROSS: So that concludes our public comment period. We now have 90 minutes where we can ask questions to all presenters, including to Dr. Jodi Segal, she's remained on.

I do want to just note, I see both Mr. Kremer and Mr. Patel already have hands up. Given that I had to conclude our last session

where other individuals had hands up, I'm going to give these people in the order from before and I'll call on them and then we'll come around.

So the first person from the prior session that I had not called on was Dr. Dhruva.

DR. DHRUVA: Thanks so much, first off, to all the public commenters and again to Dr. Segal. We learned so much from all the experiences and all the thoughtful comments all across the board.

I wanted to, my question initially was for Dr. Segal, and I think I still want to address it to Dr. Segal, but I heard so much during the public comment period about the sunsetting of CED requirements, and Dr. Segal, in the report that you led, one of the criteria of the plan was describe a schedule for completion of key study milestones to insure timely completion of CED process, which I think gets to that.

My specific question is, what do we do in situations where we have new evidence of safety and effectiveness of benefits and harms

for Medicare beneficiaries that arise during the evidence generation process? It seems to me that we can't just start a CED and then have specific milestones, but evidence may evolve, we may learn new things. For example, one of the commenters in my field of cardiology mentioned left atrial appendage occlusion as a part of the coverage with evidence development, data generated through the national cardiovascular data registry that Dr. Brindis mentioned, showed that for example, women with an average age of about 75 years have a much higher rate of adverse events associated with placement of left atrial appendage occlusion devices compared to men.

So I'm wondering, Dr. Segal, what do we do when we have new evidence that's generated, and there's new evidence of benefits and harms? Are we supposed, based on your report, supposed to stick with those same milestones, can they be amended?

DR. SEGAL: That's an interesting question and it's easier to envision that there could be new evidence of safety or harm in the comparators, right, because every patient

treated with a product under consideration will be in the CED process because that's the way it's covered, but I could see with the comparators that happening.

I would think that yes, there has to be a mechanism for updating the milestones as you gather new information and evidence. I guess that may be a little bit outside the scope of these specific requirements, but totally important.

DR. ROSS: Dr. Stearns?

DR. STEARNS: Thank you very much. I appreciate all the presentations we've heard. My question, which is a little topic that was raised earlier by Mr. Kremer, and it had to do with the fact that the key informants for the report came to a great extent from countries that do use a price or cost effectiveness type criteria for decisions, and I wondered if I could ask Dr. Segal, is the -- my familiarity with those systems, and I have more familiarity with some rather than others, but I believe that they all use processes, or I know some of them use processes where they do separate out key issues in their determination of coverage.

I believe there's a great focus on effectiveness separately from issues of what were ultimately important in their decision process, which includes cost effectiveness and overall budgetary feasibility. And I'm just wondering if in the discussion, Dr. Segal, if there was any indication of specific prioritization of effectiveness in the review or assessment process used by other countries that might help us understand what insights those informants are bringing to the table.

DR. SEGAL: Again, among the key informants, only one was international, Michael Drummond. Everybody else was really U.S. based, so it was the Grey literature review that led us to the online CED policies, so I would not say we had a lot of input internationally.

DR. STEARNS: Okay, thank you. You're right about the importance, I guess. I thought there was more about specific countries' systems but there wasn't.

DR. SEGAL: No, there really wasn't. But you know, it would be a good time for me to say we did have a lot of input from drug and

device manufacturers in the public comment period, but they were not included among the key informants as that was CMS's preference. They certainly gave input at the public comment period and you can see the list of who they were in Appendix 2. Column A has the list of all the public commenters, and you can see the nice rich input from there.

DR. STEARNS: Okay. Thanks for that clarification.

DR. ROSS: Dr. Fisch, I had your hand up earlier in the day; do you want to --

DR. FISCH: Yes, thank you. My question is for Dr. Segal and it relates to criteria E that was in slide 45 of your deck. Criteria E was about the CED study is registered with clinicaltrials.gov and a complete protocol delivered to CMS. In the comments about the revisions, it was noted that industry representatives strongly urged against publicly posting complete protocols, and that makes sense to me because protocols often have proprietary information that companies wouldn't want to have publicly presented.

But I wonder if there was any

consideration of something in between, which is a redacted version of the protocol, which in academic journals frequently in the supplementary appendix we see the full protocols with redactions of appropriate proprietary information. So was that in between option discussed to your knowledge?

DR. SEGAL: No, we didn't discuss that option.

DR. FISCH: Thank you.

DR. ROSS: Dr. Kanter, I also had you as having a question from the prior session.

DR. KANTER: Yes, thanks. I actually had questions on three of the items and we can go through them pretty quickly.

On L, related to contemporaneous control comparison group, I wonder if you all -- so the standard is just that the choices be justified if the contemporaneous comparison group is not included. I wonder if you discussed at all the need to include measures that would be taken to compensate for a lack of contemporaneous comparison groups.

DR. SEGAL: No, we didn't. I think many of us would be strong advocates for having

comparison groups, but we do recognize that that may not always be the case, particularly I suspect with diagnostics. No, we did not discuss --

DR. KANTER: Actions that could be taken to demonstrate, yes.

The second question relates to B as in boy, the justification for the timeline, which I think everyone is sort of on the same page on, is that it would first help firms meet milestones, but the true question is the publication or the submission of a timeline doesn't really have an enforcement mechanism, like what happens if you don't hit the timelines and are, did you discuss any wording activity related to that, so I was wondering what your thoughts were.

DR. SEGAL: No, and I think that's partly why we thought maybe there needs to be a document that accompanies this that has more details, but no.

DR. KANTER: And then finally, letter E relates to the registries, so we sort of abandoned sort of the registry requirement because they don't have the AHRQ registry.

What about, have you considered other kinds of registries such as ACC or STS and so on, or were you thinking it would go into, you know, be considered at a different level?

DR. SEGAL: No, we're certainly supportive of registries and the use of registries in which evidence can be studied. I think a registry by itself is insufficient, it's just a registry. I don't know if CMS has another idea of where these might be, the registries might be registered.

DR. KANTER: Thank you.

DR. ROSS: Dr. --

DR. SEGAL: I suppose they could be registered in clinicaltrials.gov, but I don't really know.

DR. ROSS: Dr. Ogunwobi, you're the last of the holdover questions from this morning.

DR. OGUNWOBI: Thank you very much. I want to thank everybody for the very active discussion so far. There's a couple points I just wanted to maybe get thoughts from the first speaker this morning, because it was kind of highlighted by the public comments related

to not really new barriers, but you know, for end users, and one of them relates to for example the recommendation to replace reproducibility with robustness. I'd like a comment on whether or not she feels that reproducibility is actually easier to define and would create less bias than the use of this, I think potentially nebulous expression of robustness.

And then a related point into the issue of the (break in audio) you know, the comments of how does it impact whether there is approval or not. So for example, will the patients meeting one particular requirement be sufficient to deny coverage, or is there guidance on, you know, other requirements are required, do all requirements need to be satisfied, and so forth?

DR. SEGAL: Thank you. I rather agree with you that I think that reproducibility is more easily defined than robustness, although I think robustness can be defined, it just isn't in this document, but I don't disagree with that.

I think if we keep in mind our goal is

generating evidence to make a decision, that's the goal of this, right? So I think if the sponsor or investigator is able to generate the necessary evidence and not every requirement is met, that's okay, because the goal is met, the requirement is met to make it more likely that the sponsor/investigator will actually meet the goal.

DR. OGUNWOBI: Thank you very much, and just one brief comment. I think the very first public commenter spoke about artifical intelligent technologies, and I was just wondering if that person is still here if they could comment on, or anybody, knowledge that suggests that in some instances with this new AI technology, there is actually potential of creating a whole litany of disparities in health outcomes.

DR. ROSS: Your question is to Cybil Roehrenbeck. I'm not sure if she's still participating in the meeting.

DR. OGUNWOBI: Okay. No problem, thank you.

DR. ROSS: Okay. Mr. Kremer, you're next.

MR. KREMER: Thank you. So with gratitude to all the presenters, incredibly valuable and I hope we all take to heart the messages we were hearing even if they were sometimes discordant, but I have three questions for Sue Peschin.

First, can you speak to the burdens or benefits of registry participation and any implications to representatives?

MS. PESCHIN: Am I on?

DR. ROSS: Yes.

MS. PESCHIN: So the burdens of registry participation?

MR. KREMER: Right.

MS. PESCHIN: Sure. I think that there's, I think some folks see data registries as something that's completely different, CED data registries as something completely different from CED clinical trials. But they're both subject to, you know, the guidelines that you all are going to be voting on, they have conditions of coverage around them, things like the type of facilities that can offer the treatment, the care teams who have to be on those, the types of doctors

people have to go see in order to be evaluated, there may be procedural volume requirements. And all of those types of things combined really restrict where the types of treatments are available and as a result, they tend not to be in smaller rural areas or in areas with lower income folks, and that, you know, that's one of the things that we found.

There's also like very low participation in some of the registries. There are stem cell transplants that are part of CEDs that are incredibly low, sickle cell is an example of that. And you know, there's also, I think there's been actually a request for myeloplastic syndrome to be reopened, I don't know if that's been responded to yet. So these just, and cochlear implants, super low in terms of who's been able to get them.

So it's really random, that's one of the things the Zeitler study found that Jodi, Dr. Segal referred to, and so I encourage folks to take a look at Dr. Zeitler's study as well as the study that we just put out today.

MR. KREMER: Thank you. And second question, and understanding that your view is

that CED perhaps just as a matter of law is not legitimate or real, but let's just compartmentalize that for a moment. Just looking at this set of voting questions, are there any of these voting questions that you think if there were a legal basis for it, would support assisting patients, beneficiaries, Medicare beneficiaries having access to needed devices and therapies and services, are there any proposed revisions notwithstanding your concerns about the legal basis?

MS. PESCHIN: I mean, we -- you know, when we were involved in TAVR a couple of years ago, we learned through that process that CMS really has no kind of control over how these registries are run or what the organizations that run the registries decide to do in terms of studies, if they answer the evidence questions on time or at all. So I think that allowing CMS to at least have more access to more things is a good thing, and that's a good thing to see, certainly, I mean if the studies are listed.

But you know, to go back to Jay's point, it really doesn't matter if they're

listed or not if the whole thing is kind of broken. So I think that there are, you know, the point that I just raised, but aside from that, it's not a good tool and what it's turned into is what has become so disturbing. I think it had good intentions in the beginning around medical devices, having those products be available a little bit sooner than they might have been otherwise, but it's just turned into a utilization management tool for Part B. And this, all these study requirements are really meant to kind of lock in that process even further.

MR. KREMER: So I won't editorialize, but it sounds like there are at least a couple here that you think would make a, what you view as a bad system slightly less bad, and it's helpful to have those identified, so I appreciate that.

The last one, and I apologize because this is invoking another one of the public comments, but given that I've spent a quarter of a century working on Alzheimer's, this one is near and dear to me in particular.

There was a reference to the FDA

approval of one of the monoclonal antibodies to treat Alzheimer's and the need for further CMS examination given some of what I think everyone would agree were unfortunate and complicated fact patterns in that one. So I wonder if you could sort of zoom out and speak to, this goes to your earlier public comment, to sort of the fact pattern with how CED gets used. I wonder if you could just speak for a moment to us to give us context if that national coverage determination with CED, the application of one product's fact pattern to an entire class and what the implications may be, not just in Alzheimer's but across diseases when CED applies to an entire class based on evidence, good or bad evidence, but evidence for one product in the class, what you think the implications there would be for health, but specifically for health of often overburdened and underrepresented communities.

MS. PESCHIN: Yeah. I mean, the CED is applied to a whole class of products so when it is a medical device that also applies, so it is across the board, I think it's used for, another part of disease groups rely on you

know, medications, and to see something like that is a bit jarring and it is unfortunate because, you know, the latest research was published in the New England Journal of Medicine and it did rely on old information. So the ability for that to reopen again, they have the purview, and there was a request put in, I know, by the Alzheimer's Association, because it will be 60 days at the end of this week or early next week. I hope CMS responds to that in that period of time to reopen the MAC given the new information that was presented at a CTAG and other places on the new therapy. But it remains to be seen and things just get dragged out just for, at their discretion.

DR. ROSS: Thank you for those comments. I do want to remind everybody, we are not discussing CMS's NCD around Alzheimer's disease drugs. I know that the agenda ahead of us that is our task is a little bit of threading the needle. We are being asked to judge the criteria by which NCDs are being evaluated by CMS to satisfy a requirement and there is a lot of interest around the decision,

specifically around monoclonal antibodies. I do want people to try to avoid talking about specific CEDs outside of the context of the criteria CMS has imposed on it, and what we can learn from those decisions.

Mr. Patel, you're next.

MR. PATEL: Thank you. I just have two quick questions for Dr. Segal and one for Dr. Brindis. But thank you to all the presenters, I think they raised some interesting viewpoints, one of which I'm going to get to for Dr. Brindis, but Dr. Segal, how should criteria E, it talks about the study registered with clinicaltrials.gov and a complete protocol being delivered to CMS.

Sometimes protocols can change, right, either after it's been finalized or it might be modified once the study starts. Was there a discussion around envisioning that possibility happening and then further communication to CMS, or were you envisioning a protocol that is set and then not subject to further change in the CED process?

DR. SEGAL: We didn't specifically discuss it, but I would imagine the protocols

do change.

MR. PATEL: And would they communicate that to CMS presumably?

DR. SEGAL: I would think so.

MR. PATEL: Okay. And then on criteria O, again something similar but I want to make sure I'm not reading into something, but just reading the words, right? You have sponsors/investigators using secondary data to demonstrate benefit, et cetera, and then it talks about conducting alternative analyses and/or reviewing supplementary data. Are you envisioning the alternative analyses to be part of the initial publication that comes out, or are you envisioning that to be separate? Because throughout most of it you talk about within the study and you didn't use those phrases here, so I just wanted to understand what the thought process there was.

DR. SEGAL: No, we meant as part of the initial package, the initial study demonstrating evidence, that this would be an important part of it.

MR. PATEL: Great, thank you, and just one quick question. I don't know if

Dr. Brindis is still with us, but you heard a lot from many of the presenters talk about the need for a CED to end at some point, right, the data collection. I'm wondering, can you give us sort of a perspective on that in terms of, do you support criteria that would actually explicitly say that at some point further data collection, once you move away from CED, would not be required for healthcare coverage, or is something you would not want to see built into that criteria?

DR. BRINDIS: So, thank you, Dr. Patel. The answer to that question kind of, has multi components. From the NCDR perspective in terms of improving health and quality at local hospitals, the ability to have data collections with some, if you will, carrots and sticks, is an advantage to our Medicare population, but that doesn't necessarily meet the need or definition of what CED is.

So I do understand the appropriateness for having a sunsetting feature within CED; in fact, our ICD registry was affected and sunsetted that CED requirement which, when

those key questions that I raised earlier were answered. Now the loss was at a patient level in terms of making sure we assure quality.

One of the things talked about earlier just in this session is an important one related to the sunsetting. That is, different CED criteria related to devices, the device iterations change constantly and some of the changes are quite significant, and the ability for CMS to assess whether it's reasonable and necessary related to new iterations of this device will depend, I think, on continued analysis of these new devices as they are put into the marketplace.

MR. PATEL: So it sounds like you would support a criteria that would explicitly say that there ought to be explicit discussion of when the data collection would stop, or did I or did I not characterize it accurately?

DR. BRINDIS: I think you did it quite well, to have a discussion within the relevant stakeholders related to an individual CED and how that particular drug or device is being affected in the marketplace, and new iterations and so forth may lead to an informed discussion

for CMS.

DR. ROSS: Thank you. Dr. Canos?

DR. CANOS: Thank you. My question is for Dr. Segal, and we heard from public, the open public comment period here today about the importance of patient preference, patient preference information, and within the topic refinements document as it pertains to outcomes, or the exception to I as you have it, there was noted that there was some comments that suggested that the first report was advocating for patient-reported outcomes but this is not the case, important outcomes may or may not be patient reported.

As I look at outcomes, it does say, I think it differs a little bit in your slide versus the voting question. The voting question says primary outcomes for the study are clinically meaningful and important to patients. So my question to you is kind of inherently an epidemiologist question which is, is and the union or the intersection of events, is a primary outcomes something that is either clinically meaningful or something important to patients like a patient-reported outcome, or

does it have to be, is it the intersection of those events and not the union of the events?

DR. SEGAL: I think it's the intersection, although it would be hard to argue that something is clinically meaningful if patients don't care about it. So I think yeah, right, if it's clinically meaningful, then it's important to the patients.

DR. CANOS: So just to be clear, so would patient-reported outcomes be in or out of the clinically meaningful and important to patients in a primary outcome?

DR. SEGAL: So, I think the fact that it's patient reported is irrelevant here. Patients reported is a subset of patient-relevant outcomes, things that patients can talk about, their headache, their pain, right? There's lots and lots of patient-relevant outcomes that patients can't report, so we are thinking about the bigger category of patient-relevant outcomes.

DR. CANOS: Okay. So those would be all the primary outcomes as you would see it for that question.

DR. SEGAL: Yeah.

DR. CANOS: Thank you.

DR. ROSS: Dr. Whitney?

DR. WHITNEY: Thank you. Such interesting discussion, we really appreciate that, and I'm not sure if it's for you, Dr. Ross or Dr. Segal, but the whole notion of stoppage criteria was an interesting suggestion in large by the commenters, and it seems largely within the control actually of the sponsors of the study to document the benefits of their intervention to produce the stopping point, and it seems to me that criteria B addresses this already with the notion of milestones and time to completion, but I guess the question is, you know, is it worthy to provide a modification of an explicit requirement for your own review, maybe it's outside of this criteria or maybe they're inside, I'm not sure, but it was stated new information comes in many forms, and it could be new beneficial information that plays in stopping CED because otherwise there's data that comes in, and it could be new information that suggests something is no longer worthy of study and the CED should be discontinued. And

so I don't know whether, you know, the stoppage criteria construct should be more explicit in the criteria.

The other is more of a comment than a question, you know, this notion of sort of different statutory authorities of the FDA and CMS in terms of safe and effective versus reasonable and necessary, and the importance of those distinctions, and just noting for the record my support of those distinctions and what CMS does with NCDs and the CED criteria is really important. The FDA approval process is different from it, it's not the same, it's not going to be the same. And if you look at the well-documented record of accelerated approval under the FDA and the requirement in some cases to do a follow-up study in any kind of timely manner when the follow-up studies aren't actually negative, you know, or to withdraw approvals, just again, supports the strong and important need for independent CMS conclusions on these documents.

DR. ROSS: Jodi, do you want to address the milestone question? I know it's an issue when CMS engages and makes a decision,

but the criteria around it should be part of this.

DR. SEGAL: You're correct, we did not specify what the milestones would be, but I suspect yes, provisions for internal analysis, that would be appropriate, I certainly don't disagree with that. I agree with everything you said really.

DR. ROSS: Thanks. Dr. Dhruva?

DR. DHRUVA: Thanks. I have a question for Dr. Brindis. Dr. Brindis, we heard a little bit of discussion about registries and restricting access, as well as not enrolling diverse patients. I was wondering if from your vantage point at NCDR, if you could talk to point J. The point is the study populations request information reflecting diversity levels of Medicare beneficiaries who are intended to be users of the intervention, specifically focused on racial and ethnic backgrounds and gender and socioeconomic status at a minimum.

Are these variables that have been included, and can you talk a little bit about if you've seen access has been restricted, or

if we've generated this type of evidence using the registry framework, and what indications it's had for some of the CEDs that you mentioned in your presentation? Thank you.

DR. BRINDIS: Thank you, Dr. Dhruva. In terms of being fully representative of Medicare beneficiaries, one of the advantages of course of CED for coverage and payment, all patients who are having that device or therapy are included. With that, for example in the TVT registry we have about 880 centers. I would say that the number of centers in the United States for population, age adjusted, is markedly greater than any country in the world. We have excellent access in terms of centers and availability.

In terms of actually the demographics, socioeconomic graphics and all those issues, one of the earlier public speakers is correct, we under utilize. For example in TAVR, it is (break in audio) groups. However, within our registry we're able to assess reasonable, necessary and reasonableness, and also efficacy in such a large patient population with which to study.

The other comment is rural, and like I say, hospitals. Again, with CED coverage, we're able to have a greater representation of rural hospitals and safety net hospitals. Without CED, rural hospitals and safety net hospitals oftentimes are a little underrepresented in the registry portfolio.

DR. ROSS: Thank you. Dr. Kanter?

DR. KANTER: I just had a couple of questions for Dr. Brindis, and then one question for Ms. Peschin.

Dr. Brindis, you mentioned, and this is mainly coming from the information that was submitted, so just a couple questions. If you could talk a little bit about your data sharing for revocability, there seemed to be some negative sentiments, I think, that I was reading from the public comments.

Secondly, if you could elaborate on what you mean by undue compliance burden, something you had spoken about earlier, you know, examples of what might be too much of a burden.

And third relatedly is this idea of when data collection ended, you know, there

were comments as well and I'm wondering, first, we're sort of relating the time with the evidentiary standard of time, so I just wonder if you could clarify, you know, if we have a stopping rule, it's not really based on clock time, it's really based on achieving the outcomes as specified, again, with reasonable dates.

So I'll pause there and then wait for your comments.

DR. BRINDIS: Okay, there were a bunch of questions, let's see what I can remember. I think --

DR. KANTER: The data share.

DR. BRINDIS: The data share. Conceptually we're in favor, not against data sharing, but one has to appreciate the increased burden, particularly on sponsors and that sort of thing involved in that. In some instances even the underlying data used in analysis, such as from a clinical registry, may be unique and so these results might not be able to be replicated against other data sets. And so I think, you know, we need to be cognizant of the increased burden as we go

about pursuing any concept of data sharing. It's not that we're totally against that, it's just the appreciation of the extra work involved.

Then what was the, you had two other questions.

DR. KANTER: Yes, the one related to other compliance burden that's separate from the data sharing.

DR. BRINDIS: I don't have any additional comments related to that, and the third was?

DR. KANTER: The stopping rule, and the difference between clock time versus evidentiary standard time.

DR. BRINDIS: I think that's a really good point. I think we shouldn't just use a clock per se. The amount of data collected, or even the signals one gets during a timeframe may actually indicate to CMS increased scrutiny and that we require more time.

And as I mentioned earlier, again, the things are different with drugs versus devices, but the changes in iterations particularly related to devices really oftentimes lead to

increased scrutiny over time, so I think it's a discussion that should be had with the relevant stakeholders and over time in terms of figuring out is this the right time to stop or do we need more data related to something that's going on related to that particular device.

DR. KANTER: Thank you. And then just a quick question for Ms. Peschin. As I understand it, your position is that the requirements for FDA are coincident with the evidentiary standards for CMS. So would you be saying that, you know, we don't really need -- so suppose a clinical trial doesn't really, you know, enroll older populations, those with comorbidities that are representative of Medicare beneficiaries, your position is like you're cool with that, like that's --

MS. PESCHIN: No, no, no, not at all. And we worked on, yes, there were changes around diversity in clinical trials, and legislation for more diversity in clinical trials. But also that's under FDA's purview, and CMS sort of shrouds themselves in caring about that as a way to ration care, and that's really the only thing.

Now with regard to this TAVR registry, I'll tell you, when it was reconsidered in 2019, one of the reasons was it (break in audio).

DR. ROSS: Mr. Kremer?

MR. KREMER: Thanks. I was just coming off mute.

So a couple of questions for Dr. Segal, and Dr. Segal, thank you again for bearing with me. I don't mean my questions to be overly aggressive, I'm learning as we go, and I'm trying to, I'm a staff of one, so I have no one to learn from until we get to these meetings, because I take very seriously the requirements from the CAG that we not engage outside organizations to inform our opinions before we get here. So two questions, and just apologies in advance if they're terribly aggressive.

Does your report or your advice to CMS speak to whether CMS ought to measure clinical meaningfulness based on patient preference or based on clinician evaluation of what patient preference ought to be, or do you not really address that at all?

DR. SEGAL: I don't think we explicitly addressed that.

MR. KREMER: All right, thank you. And the second question is, do your recommendations vary or differ at all in terms of the proposed voting questions that we're going to look at, in terms of whether the item or service is for an on-label versus an off-label use, or is that again beyond the scope of your report?

DR. SEGAL: We certainly did not discuss that. I think in my head I believe these were on-label uses.

MR. KREMER: I think I'm following. Would you have us consider these questions regardless of whether they're for on-label or off-label use, should we think of these questions essentially in two separate buckets as to whether they're going to be applied for an on-label or off-label use?

DR. SEGAL: I think that might be outside the scope of the specific requirements, how CMS chooses to apply the requirements, but we did not really think about that.

MR. KREMER: Thank you.

DR. ROSS: Dr. Brindis, if you're on, if you want to address that, I know that within the NCDR registry it does include information on both on and off-label uses, if you want to try to answer Mr. Kremer's question. Mr. Kremer, do you want to repeat it just to make sure?

MR. KREMER: Since my question was convoluted, I'm not sure I can repeat it but the gist is, I'm just trying to figure out in the real world, how does this work, do the CED standards, do the standards for the CED that are being studied work exactly the same, should we be asking the same questions regardless of whether it's an on-label or off-label intended use that CMS is looking at?

DR. BRINDIS: Well, I get your point, and I thank you, Dr. Ross, for offering me the opportunity to respond. One of the incredible side benefits of having CED for TAVR, I'll use that as the example, in that we had all these hospitals, is that clinicians over time have oftentimes been doing things off label because they realize there was need there, even if there was no randomized clinical trial showing

efficacy. So a side benefit of the TAVR registry is that the FDA and us noticed that a whole bunch of people were doing things that were off label, particularly for this group, the use of TAVR inside somebody who's had a previously placed surgical valve, valve in valve.

Based on the analysis of these, a fairly good substantial size patients who were having this procedure, the FDA was feeling comfortable in terms of safety and efficacy in extending the label, which also implies that CMS at that point could feel comfortable that knowing things are safe and effective, that it might be appropriate for reasonable and necessary for their population. A very important side benefit.

And there are other examples that I could give, but that to me is one of the most significant ones. Industry won't necessarily want to fund these key trials for doing off-label work and yet here is a legacy that's offered us huge benefits in assuring our patient population, in this case Medicare beneficiaries, that things can be done safely,

effectively, and in a manner that we should for all intents provide.

MR. KREMER: Thank you.

DR. ROSS: Sorry to put you on the spot, Dr. Brindis. I just knew you had the answer. Dr. Fisch.

DR. FISCH: Thank you. Dr. Brindis, I'd like to put you on the spot again, and it has to do with the detailed letter that ACC produced from Dr. Frye with some specific comment. And getting back to my remarks about criteria A in reference to the study being conducted by sponsors/investigators, you know, I was trying to distinguish the rule there. The ACC letter also was worried about definitions there, definitions of resources and skills, but also that letter seems to be worried about introduction of investigators at all, because investigators may be later and there's a concern about slowing down the process.

So I'm trying to figure out, maybe you don't recall which point I'm making here. What is says is the introduction of specific investigators as part of the CED application

process may cause delay in CMS achieving its objectives in evidence development since this is a very operational requirement. So I guess, I'm trying to figure out, where does the ACC think that reference to investigators ought to come into play?

DR. BRINDIS: All right, let me see if I can handle that in a manner that might sort of answer your question. First of all, the NCDR has a very robust research and publications committee. In fact in terms of TAVR, we get somewhere between 50 applicants for studies to look at related to TAVR, whether they be issues related to use in minorities or as mentioned in my own presentation, uses in patients with renal failure, whatever. And so we're able to hopefully within our own construct in terms of our funding available be able to take up questions that we think have a lot of face validity with importance. So within our own registry portfolio research and publications, we don't feel particularly limited, if that's sort of what you were getting at.

In terms of outside investigators, I'm

not sure how I can address that question.

DR. FISCH: Thank you.

DR. ROSS: Mr. Patel?

MR. PATEL: Yes. And before I ask my question, maybe I can go back to Dr. Fisch and maybe share with you a perspective from a company that put a technology through CED, so I think the change to sponsor/investigator is a good one, because what typically happens is the company will come to CMS giving them a heads up, saying hey, we have a technology that's in the FDA approval process, we'd like to get coverage, can we get national, do we have to go through CED, you know, there are good conversations that took place, you know, our technology has met with full disclosure, and we have a pretty good sense based on our sense of what the clinical data was, what CMS's expectations were, of what type of outcomes they would want in the study.

Now the challenge was, and I think with registry-based studies, that just because data goes into the registry, as we all know, doesn't necessarily assure a publication out of hand, right? So we were fully going to go

ahead and do publications, but I think it's good to fill in a requirement that publications happen, I think the industry generally is comfortable with that also.

So you end up with a situation where the study sponsor, in this case a company, might be out of the conversations, and then bring in investigators much later in the process. On the other hand, if you've got to line up investigators, get their commitment, I think that was part of the thought process that went into those kinds of comments from industry. Is that helpful?

DR. FISCH: Yes, thank you.

MR. PATEL: And to go back to the stoppage, and I think when we talk about two clocks, there's actually three clocks. Because you know, in the past the CED studies, most of them just had this registry requirement and you keep collecting data, keep collecting data, with no stoppage, and as Dr. Brindis said, it went on for 15 years, and I forget how long it was for ICDs, it just went on and on. And I agree that when we talk about stoppage requirements it shouldn't be one year or two

years certainly, calendar based, it ought to be based on how much time is for the question being asked, do you have enough patients, it's all about the scientific data, so when do you feel the study is complete and ready for publication.

But I think there's a third clock which is, when does CMS then actually decide to go revisit that CED, right? And that's the third clock, and I think we're hoping in the industry frankly that if you have built in stoppage in the criteria, then that may provide the basis for CMS to say you know what, you've got a published decision and we've got a published study, let's go back and revisit the decision and decide whether of not we have to continue it. So I think there's a third clock, and I know the third clock is outside the scope of this conversation, but hopefully with stoppage criteria, I think we can help CMS actually go back and feel confident that they can revisit it, they either continue or stop data collection. So that was just a comment, Dr. Ross, more than a question.

DR. ROSS: No, no, no, and I

appreciate that, and I think, you know, as Ian brought up early on, there's sort of, that there's differences in thinking about these criteria depending on the product being covered and studied, right? And to Dr. Brindis's point, medical device models change substantially, the implications for when to stop collecting data is different than if it's a, you know, a product that goes unchanged and the criteria should reflect that.

Dr. Dhruva, did you have your hand up?

DR. DHRUVA: Yes, thanks. I have a question for Dr. Padula, and I'm not sure if he's -- Dr. Padula, are you there by chance? If not, Dr. Segal, I might direct it to you. It's actually sort of a multiprong question and I'm hoping you might be able to address it.

One of, Dr. Padula mentioned publications, so Dr. Segal, your report criteria P says it's submitted for peer review with the goal of publication using a reporting guideline.

So my first question is, why not publication, because we know that actually seeing something out there is very helpful and

possibly the peer review process really strengthens it.

And then a second question, totally unrelated but just to squeeze it in, in item I the primary outcome is important to patients. How can we measure non-claims-based patient reported outcomes? How can we ensure that we're hearing the patients' voice?

DR. SEGAL: I'm going to the last one first. Remember, they don't have to be patient reported, they just have to be patient relevant, right? So you're right, they won't be patient reported in claims, but they're still things that are important to patients that are measurable in claims.

We felt a little funny saying that we would require publication because we don't have control over the peer review process and the journal publication process, so that seemed like a bar we wouldn't really set. The purpose of the peer review submission, though, is there is the documentation, right, and CMS can say good, give us your manuscript and all of the data that you have submitted for publication so we can review it; it sort of requires that

there be a product.

DR. ROSS: Thanks. Dr. Umscheid?

DR. UMSCHEID: Dr. Segal, I had a similar question. I was looking at that criteria in P around submission for peer review. I know the criteria that was revised, criteria K also noted, results must be made public within 12 months of the study's primary completion date, but it doesn't seem like the new criteria P has something similar. I don't know if you could comment on that, or if you thought that that was included in the broader scheme around milestones.

DR. SEGAL: Yes, and because like Dr. Brindis has been saying, we're thinking more in milestone and evidence generation time rather than calendar time, so we did not want to include calendar time.

DR. UMSCHEID: Thanks.

DR. ROSS: Dr. Segal, can you speak to that publication issue, was there a discussion around whether CMS should be publicly posting those final reports even if the paper described in the study itself is not published? Particularly with registry studies where

multiple publications are derived from a single study, does CMS have a role in disseminating this work or ensuring that this work is publicly available, was that discussed?

DR. SEGAL: I think it was discussed but not included. We thought if it's ultimately posted in clinicaltrials.gov and then submitted for peer review, we did not include CMS in the dissemination steps. As to why, I'm not sure I can recreate that discussion.

DR. ROSS: Okay. Dr. Canos?

DR. CANOS: Thank you. Dr. Segal, just to clarify the importance of some of the criteria, can you help us better understand the intents of when these requirements are going to be kind of assessed by CMS, is it kind of within the plan or protocol in front of them and then the approved CED and make sure that they're meeting the milestones? You know, my question is specific to the publication, right, so the publication is going to be coming at the tail end of this. If we were to add in for this specification that it must be published, is that, you know, is that going to be

enforceable, is it going to come on at the tail end once the studies are done already, you know, is it worth putting further specification around there if CMS is not going to look, you know, and keep on kind of reassessing? I'm just wondering, you know, where we should kind of focus our efforts in providing feedback and how this is going to be used ultimately.

DR. SEGAL: Well, again, we didn't lay out what the milestones are. I could certainly envision that separation of the manuscript, or sharing of the draft with CMS could be a milestone. We really didn't get that granular. I think most of what was done will be in the protocol, and that seems to be the time where CMS would negotiate or lay out the expectations, so I think a lot of the work does happen up front very early on.

DR. CANOS: Thank you.

DR. ROSS: Mr. Patel?

MR. PATEL: I would be cautious about laying out months or days deadlines in terms of publication, and I would also be cautious about requiring CMS to make the data or the report available, because as everybody on this panel

and the participants know, the journals frequently want to make sure that they're the first ones to publish the data. So you could end up with a product less attractive to investigators if they know they're going to be preempted and their manuscript won't be published in a relatively high stake journal. So I think it's something that certainly, put it in the milestones, make it part of the protocol, but then let CMS and the company kind of figure out when that happens. Now I'm not sure to what extent and again, it may be outside the scope of this panel, but to what extent CMS will take steps to make sure things get published, and certainly a requirement that says hey, here's documentation we sent a draft manuscript should be sufficient, rather than developing a requirement that will jeopardize publication.

DR. ROSS: All right, that's a good point, particularly since there are requirements to report the progress, so some results will be available. I think it's in everybody's, if the study's done, people are going to want to report it.

Dr. Dhruva?

DR. DHRUVA: Thanks. I have a question for Dr. Zuckerman and this is about, this is related to item J. Dr. Zuckerman, if you're there. So we heard from some of the public commenters about FDA approval for a given therapy essentially being the equivalent of, for example, suggesting there is not, or there is sufficient evidence for Medicare beneficiaries. I want to talk a little bit about item J, criteria J, about the demographics and diversity among Medicare beneficiaries who will be the intended users of the intervention, including attention to racial and ethnic backgrounds, gender and socioeconomic status at a minimum.

Is that quality of data, it being really important that we have data on Medicare beneficiaries, is that something that you've seen at the time of FDA approval?

DR. ZUCKERMAN: I'm sorry, I missed the very first part of your question, but I got the last part which I believe was, has FDA been making approval decisions that are not, that are on production that are not diverse in terms

of racial and ethnic diversity and age and so on; is that, did I get that correctly?

DR. DHRUVA: Kind of. More so when we see FDA approval decisions for therapies that are use in Medicare beneficiaries, how often are the patient populations representative of Medicare beneficiaries?

DR. ZUCKERMAN: Almost never. I think I can say that with confidence. I have been to, you know, well over a hundred FDA advisory committee meetings where they had that information about, you know, who was studied. I've also read the different studies that have been done, and we've done our own analysis, and what we found were a couple of different things.

First of all, I should state by law, FDA is the only HHS agency that is not required to acquire diversity in clinical trials, they only recommend it, and they are held to a different standard than NIH or CDC or CMS because the sources of the funding are industry rather than the American taxpayer, so that's the justification.

And what we see is that they might

have a few people over the age of 65 but not very many, they might have zero over the age of 70 for example, and often they have very few people of color. So FDA makes these approvals based on mostly the younger, younger relative to 65, younger population, healthier populations. Of course they avoid comorbidities whenever they can, which is understandable, but as a result, their FDA approvals really have little relevance, and I should say both in terms of whether you're talking about devices or drugs.

You know, drugs are different, we metabolize drugs differently as we age, and devices are different, particularly implanted devices, because when we have older people, they may be less healthy and the risks of surgery with certain kinds of implanted devices might be higher for those older patients.

So I hope I've answered your question, but I'm glad to talk more about it if I didn't.

DR. ROSS: Thank you. And not to always be the taskmaster, but I don't want us to start talking about whether, you know, FDA, CMS, you know, rules, requirements, oversight

responsibilities, but keep the conversation as focused as possible on the criteria when CMS makes the decision to issue CED.

So, Dr. Umscheid, you're next.

DR. UMSCHEID: I may go to Dr. Zuckerman myself as well for that same criterion that references attention to racial and ethnic backgrounds, gender and socioeconomic status. I'm wondering, how feasible do you think it is to capture socioeconomic status at an individual patient level, or might this criteria apply more at an aggregate level, maybe you could speak to that?

DR. ZUCKERMAN: Yes, I think that's a good question and I agree that it might, you know, you can't look at everything. I mean, if you really wanted to look at everything, you wouldn't just be looking at, you know, black women for example, you'd be looking at black women over a certain age and black women under that age, higher socioeconomic status or lower. You know, you can't do everything even, you know, as much as with my training in epidemiology I would like to and as much as with large data sets sometimes you can't, so I

agree with you.

And I also wanted to respond to something in the chat or Q&A. To be clear, yes, some medical products are tested primarily on older patients because they're the only ones using it, but that's unusual, and many many of these products are tested on, you know, maybe they're in their 50s or maybe they're in their 60s, but they're not in their 70s and they're not in their 80s, and yet a lot of the patients using them would be older.

DR. UMSCHEID: I want to ask Dr. Segal the same question, if this issue had been considered when drafting the criteria, around the feasibility of collecting individual socioeconomic data?

DR. SEGAL: We did not discuss the feasibility.

DR. ROSS: Thanks. Dr. Stearns, you're next.

DR. STEARNS: I've got a question for Dr. Segal and it pertains to this issue of when studies are done, the results are out, whether it should be submitted for peer review or accepted for publication. There is a process

that some journals are adopting called registered reports, and I actually put a website in the chat and I'll just go through it quickly if you're familiar with it, but it has to do with the best way of registering a study and getting a commitment where you give the method and then the study is carried out, it's published. And I'm just wondering if there was any consideration by the report team or among the key informants about that as one option that might help address this issue.

DR. SEGAL: No, we didn't discuss that, and I wasn't aware of this.

DR. STEARNS: Thank you.

DR. ROSS: Mr. Kremer?

MR. KREMER: Thank you. So trying to be very mindful of Joe continually trying to corral us, I think we all appreciate there is a context in which these questions live, and that's why I think so many of us keep coming back to the broader ecosystem, but I will try to ask a question specific to the voting questions.

Dr. Segal, again, just help educate me. In one of the voting questions there's

reference to durability of results, and I just wonder if you can give us some context for that, but before I give you the floor to answer my attempt at a question, let me just tell you why I'm curious about this. Again, most of my world view outside of my family's experience which is across many diseases, many really terrible life-threatening, life-preventing conditions, most of my experiences within the context of Alzheimer's or related disorders.

And for us in that community, that vast community of six-plus million Americans, durability of result means something very different than it does in cancer, where you might be able to just eliminate a tumor and cure the disease, I don't know any responsible Alzheimer's or related disorders researcher who thinks we're going to cure somebody who already has the damage and the clinical and lived, experienced detriments of dementia.

So what we're trying to do is slow down the progression, the onset if we can, and the progression and intensity of the symptoms with either disease modifying or symptomatic relief agents and other interventions. So in

that context I worry about a phrase like durability of results, because the dementia is not going away, we're just trying to right now in a field that is in some ways in its infancy, per DMTs, we're trying to slow down the rate of decline.

Does your report or -- excuse me -- does the utilization of CED take that into account or is it looking for curative benefit being the durability?

DR. SEGAL: I don't think anything in the requirements speaks to cure. I think the durability of results is going to be very specific to each CED, and what's appropriate for TAVR is going to be different than what's appropriate for a new diabetes drug, so I don't think that that's a problematic phrase, because I think it will be defined as appropriate for each CED.

MR. KREMER: Thank you. Again, just helping me with the historical context, historically has that been the way CED is used, or is that another area where we might look to these voting questions as we perhaps have an opportunity tomorrow to suggest some revisions

to the voting questions, should we be looking at documenting whether there is this sort of very careful tailored use and whether the voting questions could support tailored use to not treat disorders causing dementia the same way we treat disorders causing tumor growth in cancer?

DR. SEGAL: Well, there wasn't anything similar in the initial 13 requirements.

MR. KREMER: Right, so a flaw in the status quo, I'm just asking, is there an opportunity to address that flaw in the path forward?

DR. SEGAL: I think so, and I think by including this we have, and I don't think anything even applies here in any of the requirements, so I don't see this as a problem.

DR. ROSS: That is a really great point, just to say, because the concept of durability, I don't think it has to, the endpoint can be tailored and it can be, you know, sort of a difference in cognitive, in terms of your context, a difference in cognitive decline measured over two years, and

so the durability context can simply be like at the point of endpoint ascertainment, that's how I interpret it, Jodi, but I don't think you meant durability to say forever, but that's why I'm asking this point of clarification.

DR. SEGAL: Right. But you could envision if there's a trial and everybody responds within the first two weeks, but then the comparison group is at the same point, you know, after one month everybody's at the same point, that's not really a durable absolute benefit to the patient if you end up at the same place as the comparator group after just a few weeks or however you define that.

MR. KREMER: Again, as a real layperson, I'm not a clinician, I'm not a scientist, I'm just trying to be a good representative on this panel as a so-called patient representative.

DR. SEGAL: Right.

MR. KREMER: I really worry about that because you know, there are concerns, very substantial concerns across a lot of the patient community that CED has been used inconsistently, to put it generously, and

whether those concerns are legitimate or illegitimate, you know, fact based or imaginary, the concern is tangible and palpable and deep. And there's a real anxiety there for about how much, I don't mean this in a pejorative way about these sort of questions or about your report, but how much vagueness can the patient community stand behind and feel comfortable with in terms of how much gets left to CMS discretion.

And this question of, I guess the long way around of saying, and Joe, I promise I'll stop and give the floor to others, but my real fear here is that whether by intention or accident, if, if CED is not being used in an appropriate, consistent, responsible and equitable way across varied patient communities, various clinical settings, various diseases and conditions, that there's a real risk that a standard like durable benefits, in conversation we might all say of course CMS will be reasonable and apply it with confidence. What if they don't?

What if, God forbid, people with Alzheimer's never get a treatment because the

first treatments weren't going to be curative? And what if that's the standard that CMS writes in subsequent to the votes we will take tomorrow? I couldn't live with myself in that circumstance, had they voted yes on a package putting the trust in CMS, when there are I think, again, pretty substantial, serious, and I at least would say legitimate concerns about how the authority of CED winds up getting exorcised by the Agency. And I love and adore my friends across CMS, but where the rubber meets the road for patients, that's where I get really scared about how this winds up playing out.

DR. ROSS: Thank you, appreciate that. Two more hands up and we have about ten minutes left, so we should make it right on time. Dr. Umscheid?

DR. UMSCHEID: This is for Dr. Segal. This is the requirement theme on data quality, it's requirement, new requirement G. There's a comment about the data are generated or collected with attention to completeness, accuracy. I think we've heard some support for that and I'm also supportive of that as well.

And then there's the piece about sufficiency of duration of observation to demonstrate durability. I think to Mr. Kremer's point, that to me seems more like an outcome question, so perhaps a criteria D question, and you could imagine that wrapped into a clinically meaningful difference aspect of that new criteria D.

I'm curious if that was discussed when developing that data quality standard, about taking the durability of results, and whether that was more around an outcome rather than data quality.

DR. SEGAL: No. I guess you could put it in either place. It really was about picking data, right? If you are using commercial claims, as you know, you're not going to keep people in the data for longer than about 18 months. So if you're looking at an outcome that's, you know, is four years in the future, you better pick a different source of data.

Sure, you could also test durability of results when you're framing what it is in clinically meaningful outcome to patients, that

would also be appropriate.

DR. ROSS: Great. And Dr. Whitney?

DR. WHITNEY: Thank you. I guess this is a question for any of the physicians, Dr. Zuckerman or Dr. Brindis, or Dr. Segal, whether there exists such a source that uniformly defines what, you know, what duration means for any condition at any particular stage of that condition, and it might be rhetorical, I get that, but I think the point is really important, because the whole NCD process involves comments and the whole CED process includes a negotiation between the investigator and CMS in defining those endpoints.

I'm not aware of any data sets that would allow you to sort of use this criteria in this kind of environment that would allow you to define those terms in a very narrow and precise way to take it out of CMS's hands, which are important for both directions. We want to make sure that people have access to drugs or devices that work, but also that they aren't exposed to drugs and devices that don't work.

DR. ZUCKERMAN: If I could answer that

since you mentioned me, I just wanted to say that it is very difficult to figure out how to address this, but the incentives aren't there currently for companies to do better studies, longer term, more diverse populations and so on, because the FDA standards have changed over time, the studies have gotten shorter, even though the use of many of these products is decades long if not the rest of peoples' lives.

So if there was an incentive, you know, this is not CMS's job, but it might be since FDA has lowered their standards, to have products that are studied for a somewhat longer period of time on larger numbers of people with subgroup analyses of major demographic groups. But right now there is no incentive to do that because FDA will approve a drug that hasn't been studied on, you know, any people over 65 or any people of color in some cases, and they will approve it for everybody, and so there is no incentive.

DR. BRINDIS: Nothing to add.

DR. ROSS: So, I do think we've reached the end of the useful discussion period of our day, with just a few minutes to go.

This has been an amazing conversation and I think that tomorrow is going to be even more interesting as we walk through the criteria, think through the criteria, and obviously put to a vote our decisions on how the criteria have been proposed.

I want to take a moment to thank all the members of the committee who are volunteering their time to participate. I also want to thank all of the presenters who have made time in their schedules to join us today and offer their own opinions that we can then best inform ours. I will note as we discuss tomorrow, there might be opportunities to answer questions again if you are available, but it's certainly not required.

I especially want to thank Dr. Segal and her team for moving this work forward in such a clear and concise way and presenting the work today, and essentially having to go through a live key informant phase as we all gave you lots of comments and thoughts and pushed it forward, whatnot. I appreciate you answering all of our questions thoroughly.

Tamara or Tara, before we adjourn, are

there any specific announcements?

MS. JENSEN: I don't have anything except thanking everyone today who did comment, and we start tomorrow at ten a.m. eastern, sharp.

DR. ROSS: Great. Thank you to all, I'll see you in the morning.

(Session for first day adjourned at 2:55 p.m. EST.)