THE ADVISORY COMMITTEE ON HERITABLE DISORDERS IN NEWBORNS AND CHILDREN

IN-PERSON/WEBINAR

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Table of Contents

COMMITTEE MEMBERS

Kyle Brothers, MD, PhD
Endowed Chair of Pediatric Clinical and
Translational Research
Associate Professor of Pediatrics
University of Louisville School of Medicine

Ned Calonge, MD, MPH (Chairperson)
Associate Dean for Public Health Practice
Colorado School of Public Health

Michele Caggana, ScD
Deputy Director, Division of Genetics
New York Department of Health

Jannine D. Cody, PhD
Professor, Department of Pediatrics
Director, Chromosome 18 Clinical Research Center
Founder and President
The Chromosome 18 Registry & Research Society

COMMITTEE MEMBERS

(continued)

Jane M. DeLuca, PhD, RN
Associate Professor
Clemson University School of Nursing
Metabolic Nurse Practitioner
The Greenwood Genetic Center

M. Christine Dorley, PhD, MS
Assistant Director, Laboratory Services
Tennessee Department of Health

Jennifer M. Kwon, MD, MPH, FAAN
Director, Pediatric Neuromuscular Program
American Family Children's Hospital
Professor of Child Neurology
University of Wisconsin School of Medicine

Ashutosh Lal, MD
Professor of Clinical Pediatrics
University of California San Francisco
UCSF) School of Medicine
UCSF Benioff Children's Hospital

COMMITTEE MEMBERS

(continued)

Shawn E. McCandless, MD
Professor, Department of Pediatrics
Head, Section of Genetics and Metabolism
University of Colorado Anschutz Medical Campus
Children's Hospital Colorado

Chanika Phornphutkul, MD, FACMG
Professor of Pediatrics and Pathology and
Laboratory Medicine and Genetics
Director, Division of Human Genetics
Department of Pediatrics
Brown University
Hasbro Children's Hospital / Rhode Island Hospital

EX – OFFICIO MEMBERS

Agency for Health care Research & Quality
Kamila B. Mistry, PhD, MPH
Senior Advisor
Child Health and Quality Improvement

EX - OFFICIO MEMBERS

(continued)

Centers for Disease Control & Prevention

Carla Cuthbert, PhD

Chief, Newborn Screening and Molecular Biology Branch

Division of Laboratory Sciences

National Center for Environmental Health

Food & Drug Administration

Kellie B. Kelm, PhD

Director, Division of Chemistry and Toxicology Devices,

Office of In Vitro Diagnostics and Radiological Health

Health Resources & Services Administration

Michael Warren, MD, MPH, FAAP

Associate Administrator

Maternal and Child Health Bureau

National Institutes of Health

Diana W. Bianchi, MD

Director, Eunice Kennedy Shriver National Institute of Child Health and Human Development

ACTING DESIGNATED FEDERAL OFFICIAL

LCDR Leticia Manning, MPH
Health Resources and Services Administration
Genetic Services Branch
Maternal and Child Health Bureau

ORGANIZATIONAL REPRESENTATIVES

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Valley View Family Practice

American Academy of Pediatrics
Debra Freedenberg, MD, PhD
Medical Director, Newborn Screening and Genetics, Community Health Improvement Texas Department of State Health Services

American College of Medical Genetics & Genomics
Robert Best, PhD, FACMG
Interim Chief Executive Officer

ORGANIZATIONAL REPRESENTATIVES

(continued)

American College of Obstetricians & Gynecologists

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Chair, OB/GYN Pennsylvania Hospital

Association of Maternal & Child Health Programs

Karin Downs, RN, MPH

Maternal and Child Health Director (retired) Massachusetts Department of Public Health

Association of Public Health Laboratories

Susan M. Tanksley, PhD

Manager, Laboratory Operations Unit

Texas Department of State Health Services

Association of State & Territorial Health Officials

Scott M. Shone, Ph.D., HCLD(ABB)

Director

North Carolina State Laboratory of Public Health

ORGANIZATIONAL REPRESENTATIVES

(continued)

Association of Women's Health, Obstetric and Neonatal Nurses

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Health Board Director

Vice President, Research Officer

University of North Carolina Health

Child Neurology Society

Margie Ream, MD, PhD

Associate Professor

Director, Leukodystrophy Care Clinic

Director, Child Neurology Residency Program

Nationwide Children's Hospital, Division of Neurology

Department of Defense

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Lieutenant Colonel, Medical Corps, US Army

Chief, Genetics, Madigan Army Medical Center

Genetic Alliance

Natasha F. Bonhomme

Vice President of Strategic Development

ORGANIZATIONAL REPRESENTATIVES

(continued)

March of Dimes

Siobhan Dolan, MD, MPH, MBA

Professor and Vice-Chair, Genetics and Geonomics Department of Obstetrics, Gynecology, and Reproductive Science

Icahn School of Medicine at Mount Sinai

National Society of Genetic Counselors

Cate Walsh Vockley, MS, LCGC

Senior Genetic Counselor

Division of Medical Genetics

UPMC Children's Hospital of Pittsburgh

Society for Inherited Metabolic Disorders

Susan A. Berry, M.D.

Professor, Division of Genetics and Metabolism

Department of Pediatrics

University of Minnesota

Welcome and Roll Call

DR. CALONGE: Good morning. Welcome everyone back to the second day of the May 2023 Advisory Committee on Heritable Disorders in Newborns and Children Advisory Committee Meeting. Again, I want to thank all the presenters and the public commenters that shared with us yesterday.

I think these will help move us forward as we start to spend the day discussing Committee processes, updates, and improvements that we might be able to bring to bear. Our topics include an update from a workgroup that was commissioned and contracted with last year, the Prioritization and Capacity Workgroup.

Then we're going to talk about the decision matrix, and about potential ways to simplify and clarify our processes around the matrix. And then we're going to talk about ad hoc topic workgroups, potential topics to try to recruit participants for specific areas, one of which is being our conflict of interest processes, but then topics that were identified by the workgroups in the last two, three meetings now, so I appreciate that.

And then we have some items for new business. With that I'd like to turn things over

to Leticia for the roll call.

MS. MANNING: Good morning, everyone. I hope folks had a great evening yesterday after the meeting. And before I start with the roll call, I do want to provide you all reminders of our evacuation procedures. If you're in the building, please exit the way you came in. That direction, and then cross the street into the parking lot, and that will be our rally point.

I also want to remind folks we have bathrooms. There's four sets here in the pavilion, and please stay on the fifth floor level. And now I'll go into roll call, and I'll start with the members. From the Agency for Health care Research and Quality, Kamila Mistry, Kyle Brothers?

DR. BROTHERS: Here.

MS. MANNING: Michele Caggana?

DR. CAGGANA: Here.

MS. MANNING: Ned Calonge?

DR. CALONGE: Here.

MS. MANNING: From the Centers for Disease Control and Prevention, Carla Cuthbert?

DR. CUTHBERT: Here.

MS. MANNING: Jannine Cody?

DR. CODY: Here.

MS. MANNING: Jane DeLuca?

DR. DELUCA: Here.

MS. MANNING: Christine Dorley?

DR. DORLEY: Here.

MS. MANNING: From the Food and Drug Administration, Kellie Kelm?

DR. KELM: Here.

MS. MANNING: From the Health Resources and Services Administration Michael Warren?

DR. WARREN: Here.

MS. MANNING: Jennifer Kwon?

DR. KWON: Here.

MS. MANNING: Ash Lal?

DR. LAL: Here.

MS. MANNING: Shawn McCandless?

DR. MCCANDLESS: Here.

MS. MANNING: From the National Institute of Health Melissa Parisi?

DR. PARISI: Here.

MS. MANNING: And Chanika Phornphutkul? She's not here. All right. Ned, back to you.

DR. CALONGE: Org reps?

MS. MANNING: My apologies, Organizational Representatives. From the American Academy of Family Physicians, Robert Ostrander. Okay. From the American Academy of Pediatrics Debra Freedenberg?

DR. FREEDENBERG: Here.

MS. MANNING: Robert Ostrander? American College of Medical Genetics Marc

Williams?

DR. WILLIAMS: Here.

MS. MANNING: From the American College of Obstetricians and Gynecologists Steven Ralston. From the Association of Maternal and Child Health Programs Karin Downs.

MS. DOWNS: Here.

MS. MANNING: From the Association of Public Health Laboratories Susan Tanksley.

DR. TANKSLEY: Here.

MS. MANNING: From the Association of State and Territorial Health Offices Scott Shone?

DR. SHONE: Here.

MS. MANNING: The Association of Women's Health, Obstetric and Neonatal Nurses Shakira Henderson?

DR. HENDERSON: Here.

MS. MANNING: Child Neurology Society Margie Ream?

DR. REAM: Here.

MS. MANNING: From the Department of Defense Jacob Hogue? From the Genetic Alliance Natasha Bonhomme?

MS. BONHOMME: Here.

MS. MANNING: From the March of Dimes Siobhan Dolan?

DR. DOLAN: Here.

MS. MANNING: From the National Society of Genetic Counselors Cate Walsh Vockley?

MS. WALSH VOCKLEY: Here.

MS. MANNING: And from the Society for Inherited Metabolic Disorders Sue Berry?

DR. BERRY: Here.

MS. MANNING: Thank you.

DR. CALONGE: I want to officially welcome Sue since she's with us in person today, and it's great to see you and put a face with the name. So, let's see where we are. We're to the point -- you remember that we talked about the minutes yesterday. We've been having a discussion after my first three meetings, the length of the minutes, the level of detail, and the fact that we already print the entire transcript on the website for every meeting, as well as all the slides.

Going from that transcript to detailed minutes, are timely labor intensive, and we'd like to move to a high level minutes, kind of action oriented, which is almost the way every board I'm on, or a committee deals with, and then provide a direct link to the transcript to provide the additional information and level of detail that I think individuals who want to review exactly what's said, what was said, have available to it.

There were some Committee members who provided substantial comments to the original draft of the minutes, and in the spirit of moving towards action-oriented minutes we decided instead to remove the sections for those additions and have – refer people to the posted slides in the transcripts to get the additional detail.

These are the minutes we've emailed to the Committee members. We've also distributed hard copies. I think what I would like to do is propose that we save the vote until the end of the day to give you all opportunities to see what we've distributed, and see what you're voting on, and so that's kind of where I'm at the with minutes.

So, moving on to our agenda for today. In 2022, a prioritization and capacity workgroup comprised of current and former Committee members and subject matter experts was created to look at how the Committee might respond if many conditions are nominated in a short period of time. I'd like to welcome Dr. Kemper to provide a presentation to update us on this.

We all remember Dr. Kemper as the Division Chief of Primary Care of Pediatrics at Nationwide Children's Hospital, and Professor of Pediatrics at the Ohio State University College

of Medicine. His research focuses on the delivery of preventative care services, including newborn screening.

Since 2013, Dr. Kemper has also served as a Deputy Editor of Pediatrics. Dr. Kemper?

DR. KEMPER: Thank you very much, Dr. Calonge, and this will be a 15-minute presentation now, and then discussion, and then we'll follow it with another section. It just suddenly struck me that for me talking for 15 minutes is the shortest period of time I've ever been up here.

So, and before we get going, I want to also make sure to thank Ms. Manning for all the help that she's given us on this project. So, do I use a key to advance? Oh, that will be easier. So, I want to thank the project leads who helped put this work together. I guess I can't use that either. No, now it’s fine. I'm going to take back what I said about 15 minutes if this keeps going this way.

And I really do want to thank the workgroup members who are listed here, who have given us feedback and advice about the work that I'm going to be sharing with you today. I'm not going to read all the names, but I'll leave it up there for a second.

So, the project goals I'm going to talk

about are three-fold. The first is to explore an alternative strategy for soliciting nominations. This is the first time at this meeting that we've discussed this particular goal. The second goal is to develop an approach to prioritization in the event that there's more than one condition at a time that meets the criteria for evidence-based review.

And then the third goal is to provide the input to the Advisory Committee about potential revisions to the nomination form, and ultimately to the decision matrix. I'll be talking more about the decision matrix later, but I think as you'll see, the other aspects of this project will lead into that discussion we'll have a little bit later this morning.

So, first I want to begin by talking about an alternative strategy for a conditioned nomination.

So, as everyone in this room knows, the current nomination process begins with advocates submitting a nomination package. And when I use the word advocate, I'm using it in the broadest sense. So typically, when we think of advocates in this room, we think of family members of affected individuals, but here I'm really talking about anybody who thinks that a particular condition should be added to the

recommended uniform screening panel, or the RUSP.

Now, that nomination package includes a lot of detailed information, including information on the case definition of the condition, what's known about the natural history of the condition, accuracy of screening, so sensitivity, specificity -- that sort of thing. What's known about the benefits and harms of treatment and screening overall, and information about outcomes of perspective newborn screening activities.

So, once this package is put together it goes to the designated federal officer of the Committee, who confirms that all the material is submitted, and then that's when the nomination prioritization workgroup reviews the package, and might ask for additional information if it seems like there's a gap in the package.

And then ultimately the workgroup and the Chair present to the full Committee the nomination package, and then a deliberation ensues about whether the condition should move to full evidence review. So, that's the current state.

So, the challenges with the current nomination process include the fact that it requires significant work to nominate a

condition, and there's been some current concerns that have been raised in this group about whether or not that may disadvantage conditions that are not well resourced.

And then there's also concern that despite revisions that have been made to the nomination package, it can still be difficult to complete, and that there can still be important gaps by the time it gets presented to the Advisory Committee to make a decision about whether or not to move it in for full evidence review.

So, let's see if I can move it on. So, in terms of the alternative approach to condition nomination, and again I've put this forth for the Committee to discuss, could be built on the process that the U.S. Preventive Services Task Force uses. And as I think many know, I was a former member of the Task Force, as was Dr. Calonge.

So, I'm going to describe how this might work, and one of the things that I want you to remember as I view it at least is that it's still critically important to have advocates engaged in the process that I'm going to describe.

Here we go. So, the way that I envision it is first of all that the Advisory Committee

website would allow advocates again, in the broadest sense, to nominate a condition with basic information about the nominated condition. So, a case definition, the screening method, the contact information of the nominator.

I put this up as an example for you all to consider, so you know the scope could obviously be, and I'm sure will be, modified if this process moves forward. Then, once that happens, the nomination and prioritization workgroup would review the material that was submitted to make sure that the nomination was sufficiently clear, and that it was in scope for the work of the Advisory Committee.

And then, after that, HHS through HRSA would develop the nomination package, so again instead of having the advocates develop the nomination package, that would move to HRSA to do, and that could either be done internally, or externally, and that process would involve feedback from the nominators and other subject matter experts.

Okay. I'm never quite sure where to - can you just go ahead and advance it? There we go. Number four, then the nomination and prioritization workgroup would consider the package with a recommendation to the Advisory Committee according to its usual process, so

again moving the bulk of the development of the nomination package from the advocates to some other process that HRSA would oversee.

Prioritization and Capacity Workgroup Interim Update

DR. CALONGE: So, I want to file that away, and I want to move to the second topic I told you I would talk about, which was the strategy for prioritizing nominated topics. This is something that we've discussed a couple times in the past. Here we go. Oops, now it went too far.

So the rationale for doing this is really to prepare for the possibility that multiple conditions could be eligible at the same time for referral to evidence-based review, to remind you all that prioritization is not meant to stop a condition if it meets the criteria for evidence-based review for moving forward, but just timing the flow if this happens.

And as the workgroup considered a process for doing this the key consideration was around the potential public health impact, and you'll see how that plays out in the scoring system we're going to show in a little bit. There we go. So, we developed a point system that was modeled on the previous work that the

American College of Medical Genetics, now the American College of Medical Genetics and Genomics developed, with the additional, very original formation of the recommended uniform screening panel, with the look back at how that was done and really modify that.

There we go. So, I'm just going to lay out here a few important points. First of all, the point system I'm going to show you was based on consensus, and you can argue about, you know, exactly how we assign points. It's difficult to do any sort of formal validation of a point system, but it sort of, you know, had face validity.

The other thing is it's not intended to capture all the elements of screening for the targeted conditions. Again, it's not a, you know, it's not supposed to be a large review in itself, but just a way to be able to prioritize conditions based on the potential public health impact.

As you see scores, as we pilot tested it, it was based on what was available in nomination packages. So, we went back in time and looked at some of the earlier nomination packages because the nomination package has evolved over time. Some of the things that we were looking for weren't exactly in there in the

way that the more recent one is.

And then the other thing is it relies on the values and the opinions of each person assigning the points. So, there's some things that are pretty straightforward in terms of the birth prevalence of the condition. But there are other things that really rely on the person's values and preferences around early detection. You'll see that in a second.

And the way that I envision it is the members of the nomination and prioritization workgroup would assign points, and I would fully expect that there's going to be differences for the reasons I've described before, and that that should lead to a conversation where things could be resolved by consensus.

There we go. And I think that the process is going to evolve over time with experience and further validation of the process. With the caveat that thus far it's never come up that more than one conditions had to be prioritized this way. And then finally the point system is different than the Advisory Committee recommendation process.

It's really only intended to prioritize. So, I think that if it comes into play you can imagine that the points would be assigned, prioritization would happen through

the transparent way to communicate that to stakeholders in the Advisory Committee process. But the point system wouldn't be carried over beyond that into anything related to evidence review.

There we go. So, if you put on your readers, because I apologize that this is so small, but I really did want to have this all in one slide. I'm going to go over this, but this is the final point system that we came with. So, what I'll say at a high level is that the approach prioritizes conditions with the clear case definition.

It gives greater weight to those that are presented significant public health burden, and where pre-symptomatic treatments is likely to be beneficial. The scoring system does consider implementation, but the points that are assigned to it are lower. And what I would like to do, and so, and you can see the mathematical formula, which is (A x B x C x D) + (E x F).

And I'm just going to at a very high level, go through the various categories. So, A is related to the case definition at the time of screening, and whether or not the nomination package included a clear case definition. B is the birth prevalence, and you can see that it's not linear. The score doesn't go up linear based

on the birth prevalence, but for conditions that are expected to have a birth prevalence of less than 1 per 500,000, that gives you a point 2 for points, so actually lowers the score when you multiply it out, all the way up to those conditions that are more than 50 per, or more than 1 per 50,000, which would go up to 4C. C is related to the natural history and asks the question about the likelihood of a poor outcome when treatment is initiated after clinical identification, and it's based on the judgements of the person reviewing it. D is related to outcomes from pre-symptomatic identification. Again, based on perspective of the person reviewing the nomination package.

E is related to the feasibility of screening, and F addresses issues of diagnostic certainty, or uncertainty. So, again I want to thank the workgroup for coming up with these categories, and the points, and let me just show you how this played out. There we go.

So, what we asked is for members of – so our plan is that members of nomination prioritization workgroup, would decide points differences resolved by discussion with the final score presented to the Advisory Committee. That's what I said a second ago.

But here's some lessons from pilot

testing the scoring system with our workgroup. What you can see is the overall rank of the nine conditions, beginning with the one that scored the highest was severe combined immunodeficiency, and the condition with the lowest score was Krabbe disease. What you can see is that for some conditions the scores were fairly broad, and the conditions that were nominated earlier tend to have the broadest score because there was less information that was directly tied to the things that I talked about before that was on the nomination form.

But in general, there was agreement, and like I said I would imagine that if this point system were used, that there would be, you know, all members of the nomination and prioritization workgroup would independently score things, and then if there is broad differences in how things were scored, that would be resolved by additional conversations.

But, you know, the system did seem to distinguish and at least spread things out. At the risk of repeating myself again, I want to say that these scores are not the same as the final decision that would happen, but is only to help prioritize things in the event that there are multiple conditions that need to be looked at, at the same time, and the Advisory Committee

decides to spread them out a little bit.

So, in terms of next steps, I'd like to put forth these considerations for the Advisory Committee. The first is modification of the process used for the nomination process, based on what I said before, around the Advisory Committee -- around the U.S. Preventative Services Task Force methods, and to give a greater specificity, I would imagine that there might be a, you know, nomination season, like January through August, and then a period of preparation time, and voting to keep things moving forward.

And then again, as I just went through in great detail, the scoring system when more than one nomination must be prioritized at the same time. Now depending upon what the Advisory Committee chooses to do with this, I think that there's an opportunity to update other Advisory Committee processes based on those decisions, including revision of the nomination form to better align with the point system that I just outlined, as well as potentially updating the decision matrix.

Again, I'm going to save my comments about the decision matrix until after the next Advisory Committee comment, or discussion period. Let's see if I can hopefully -- oh,

there we go. And I will stop there.

DR. CALONGE: Thanks Alex. I just wanted to pause long enough to say the prioritization ranking has nothing to do with whether or not an evidence review, a discussion from the Committee would or would not add an addition to the RUSP. It's a separate process that's intended for one purpose, which is if we have two conditions at the same time, which one would we take first.

So, I kept looking at the list, and I wanted to assure people the rank order of the list doesn't reflect what the evidence review discussion and decision of the Committee would be on any of the conditions. That's very important. Okay. To that, I'd like to open the issue for discussion. Janine?

Committee Discussion

DR. CODY: My first question is about the original slide about submission. So, I appreciate that having the advocates just do just an initial thing, and handing it to HRSA to complete takes the guess work out for the advocates, but at the same time it takes it out of their hands, and so is there a timeline for that?

Because the advocates could feel like

it just got buried in the bureaucracy, and never to be seen again.

DR. CALONGE: Yeah. So, I mean I think that's an important point, and since we have timelines for the other issues, I think trying to respond promptly, and with frequent, periodic updating of the nominators, and inclusion of them in the process, I think is kind of what we envisioned keeping it moving along, and not having it buried. Yeah. Michael?

DR. WARREN: Thank you. Appreciate that point. I think it's a really good one, and I think the sort of counterbalance will have to think of if that process becomes much more streamlined, and the input is much less, you could imagine a voluminous number of suggestions potentially. And so, thinking about how we match the reality of that with the capacity we'll need to just think through what the realistic expectations say.

I'm a firm believer in your point about good customer service and response, and just having a shared win and some resources, and thinking how we match that.

DR. CALONGE: I appreciate the comment on reality. So, I did want to make one other comment, and in the original days of the Advisory Committee, all of the nominations came

from the Advisory Committee. And so, the move to have the nomination package, and the early work all done by the nominator's advocates, and non-profit interest groups was a revision to the process.

And I think, as I've talked with advocates, and groups, it isn't an onerous task to request of -- especially advocates for conditions that may have less access to resources in order to put together a complete and compelling nomination package. I want to keep that in mind. Kyle?

DR. BROTHERS: I just wanted to express my support. I think obviously there's been a lot of attention given to make sure that we're not moving the goal post by making some of these changes, and I think that we're really trying to avoid doing that. think, you're having seen some of the nomination packages over the last couple of years. They are just super difficult to do.

I mean just the fundamental idea, the case definition, can be very hard to communicate, and try to you know, articulate in a nomination package, and so I think this is really a brilliant idea. I think, I mean, it provides technical support in the development of nomination packages, and still making it a process that the advocates and experts are very

active and giving feedback on, and participating in, I think is probably an ideal direction to go here.

And, you know, in terms of the prioritization's team, you know, if we were to be making decisions based on this we could probably pick at some of the details about what each thing is worth, but I think in a very general sense, a sense of this is really just a matter of what goes first. I think it really seems to work very, very well.

I would just want to be mindful of responding to Michael's comment just now, that we just want to look at this prioritization score very carefully to make sure that we could categorize the condition very early on in the process before a lot of detailed analysis has taken place, because ideally the prioritization would take place really early, and you know, I could think, you know, things like how common a condition is, that's probably relatively easy to come up with.

Whether or not there is a clear case definition is the kind of thing that you might need to dig a little bit deeper before you would be able to answer that question. So, I just think – not that we needed to do this and, you know, right now, and in conversation, but it

would be good to get a little background on that and just make sure do we think we can answer each of those questions without a completed nomination package, basically.

DR. CALONGE: Thanks Kyle. And Alex, I don't know if you wanted to respond to that question or? I do think one of the things I heard, Kyle, was that the prioritization number could change over time, and so thinking about updating those, especially when we have multiple conditions, might be something we need to build into the process.

DR. KEMPER: So, I agree with everything that Kyle said. You know, we wrestled with this issue of the case definition. What I can tell you is that on the evidence review side of things when the case definition is not crystal clear, it ends up really sort of slowing down our side, so that was why we really embedded it into the process.

The way that I'm envisioning the prioritization score, is that these are all conditions that are, you know, couldn't be referred for evidence-based review, so it's just an issue of the timing. And so, I would encourage the Advisory Committee, you know, if another condition comes in that happens to have a higher score, but there's been one with a

lower score that's been in the queue, you know, I wouldn't want to disadvantage that other one that's been waiting because you can imagine that there might be something that would never come up.

Now I said that again with the caveat that this has never actually happened before in the past, so it's hard to know whether that what happened. But the way I envisioned it, at least it wasn't that the prioritization score would be redone on a regular basis, like once it was assigned, and the thing was in the queue, it's allowed to move through in a timely way. Did that make sense?

DR. CALONGE: Yeah. That's very helpful. Thanks for the clarification. Okay. Sir, do you want to sit there?

DR. KEMPER: Am I getting put in the corner? I'll stand over here.

DR. CALONGE: No, no. Ash?

DR. LAL: Thank you. So, my one comment is about the alternative approach to condition nomination once that condition moves forward, you know, the proposal is that a person would vote the nomination package internally extremely with feedback from nominators and subject matter experts.

And I think that from where we are

today to go to this process is that it seems like a very big change to me, and I was wondering if we could change this a little bit and say that HRSA would partner with the nominators and the advocates, in having them an external group that is just providing feedback, but to actually have a creative voice in how the process moves forward. Thank you.

DR. CALONGE: Yeah. I do believe that the idea was to not take voice or power away from the advocates. And to turn away, or not fully include the guidance direction expertise, and skills of experts. And so, I think how we describe that relationship in a partnership makes a lot of sense, and I think that, Ash, to me you bring up the issue that the success will be in the details, of how that's done.

I do believe fairly strongly that the advocates and parents and experts will tell us if we're not being responsive. And the hope is that those relationships will prove themselves over time, but I appreciate that comment, and as we think about implementation, thinking about the locus of control being a partnership is an important point, thanks. Anyone -- everyone feel okay with that? Jennifer?

DR. KWON: Just to add to that. You had just alluded to the fact that there's been a

shift on how nomination packages have been put together, and I don't really understand the background, and I think that just to maybe help people like Ash and myself, if there was like -- if it was clear what the background was for going from HRSA to the advocacy groups putting together the nomination package, and now that, that might be helpful to understand.

DR. CALONGE: So, I can only make sure that people like Jeff, or others can validate this. I think the issue is that the Committee themselves were very comfortable when we were working in the space of A level recommendations. And once, we, if you will, had worked through the A's, the evidence and the clarity of nominating a condition became less clear, and I think that's when the separation occurred, and was turned the nominating process over to the advocates and the experts.

And while I understand that, it does seem like it was a shift from an area, from a partner that had resources, to a partner that may not have resources. And so, that's I think that's what we're trying to shift back towards. Melissa?

DR. PARISI: Melissa Parisi, NIH. So, first of all I like the efforts to try to provide some case definition to the disorders

that are being nominated, and I think that that's really helpful, and I think that's actually been a key component that has allowed for better clarity of some of the conditions that have been discussed recently, when we really understand what it is that's being proposed for review.

I guess I do have a couple of comments and/or questions related to this new process. One of them is actually kind of a question for Alex. So, my understanding is that your evidence review group has the capacity to do up to two nominations per year, or evidence reviews per year, is that an overstatement maybe you want to omit.

DR. KEMPER: I mean, we've never had more than two at once. My personal believe is we would scale up based on what was needed, but I think that there are other considerations that came into play, including the ability of the Advisory Committee to do the kind of complex decision making around multiple decisions and that kind of thing, but it just really hasn't come up.

DR. PARISI: I mean I guess I'm reflecting the fact that if you only have a certain window for nominations, and everything gets bunched up, then that could end up creating

some disparities in workload, and then you might have something that's been languishing since they were submitted in January until being considered, so maybe rethink the number of windows of nomination periods that you might want to consider, leaving them at two.

DR. KEMPER: I put that window in just as a straw person. I termed that to be gender specific here, but just as a point of debate. And I was thinking that that would allow, you know, HRSA, and the Advisory Committee, the Nomination Committee, to be able to you know, just take stock of what was there. But it may be that it would just be a continuous process as well.

So, I don't know if that's the right thing or not, but just wanted to put that out there to make sure that it entered into the debate.

DR. PARISI: Got it. I don't know – do you have a comment on that specifically? Because I had another question, but it was a different topic. So, my other comment is really around the scoring matrix used for the prioritization, and I worry a little bit about the disadvantage, at least the straw person's scoring matrix as you've just showed, that rare disorders will be at a significant disadvantage if they're only

allowed a point two weighting.

And again, you know, I think I need more time to digest that, and of course there's going to be more discussion around the points assigned. But in the past, the rarity of the condition has not been a major consideration for how conditions are reviewed for addition to the RUSP.

And if that is going to start becoming an important consideration, then I think there needs to be significant discussion about that.

DR. KEMPER: Let me just give you insight into the conversation that we had because this was a, we had like multiple calls about this particular thing. So, the issue was not whether or not the condition would go to evidence review, but which one would go to evidence review first.

And the feeling was that if a condition were to potentially impact more newborns, than that one should go ahead of one that could potentially impact fewer newborns, knowing that both conditions would ultimately move forward, so it wasn't to put like a value judgement on whether or not, you know, condition A or condition B should be added to the RUSP, but just which one should go first to evidence review if a decision needed to be made on that.

And that's where the public health perspective came into play. So, both conditions would go through, but the one that could potentially impact more individuals would go through first, and that's what the rush in offer that was for.

DR. PARISI: Right. Although you could envision a situation where you have rare condition like GAMT that could be languishing even though it's got a very robust algorithm, you know, screening algorithm, and a pretty effective treatment.

DR. KEMPER: Yeah.

DR. PARISI: Because it's less common, and something that may have.

DR. KEMPER: GAMT actually didn't - and now I can't remember where it was, and one of the things that I would hope again that came of the process is that really nothing would be languishing. It's just a matter of the rapidity which it would go through. And again, it just hasn't been an issue in the past, but I mean your points are well taken, and they were things that we argued with as a group.

DR. PARISI: My final comment, and then I'll pass on the microphone, is that in this process I wonder if there would be an opportunity for the nominators to also give

feedback with regard to the final prioritization score before it was formally presented?

And the reason I say that is recognizing all the caveats that you gave, when you looked at those sample conditions there were really quite wide ranges for quite a few of the conditions. A range of 6 to 105 is huge, and so if there is that much discrepancy among the prioritization workgroup, it seems like the nominators should have an opportunity to potentially weigh in on that and give some feedback, so that's my final thought. Thank you.

DR. CALONGE: Shawn?

DR. MCCANDLESS: Very quickly. The concept of moving the goal post in the process has been mentioned several times this morning. I think this is just -- I would just like to point out that what appears to one person as moving the goal post really is a process that's in evolution, and this process has been evolving constantly since it started.

And I think that the new system for prioritization that you're providing actually really helps interest groups to better understand where the process is at the time that they're making the nomination, so I think that's a very valuable point, especially to follow up on Melissa's point that assuming that it's an

interactive process between the HRSA team and the nominators.

The second is another point that Melissa brought up, but I think needs to be re-emphasized. And that is that this is a great approach to prioritization, but it really doesn't address the problem of the timeline and the capacity for evidence review.

So I think we just need to keep that at the forefront of our thoughts and be -- we don't have to make decisions now, but just be seeking about what that might look like if we do reach a point that there are five or eight conditions backed up waiting for evidence review.

DR. CALONGE: Thanks Shawn, Michael?

DR. WARREN: Thank you. Just to add a clarification point. I appreciate all of these perspectives because I think it's helpful, as our team formulates and works with Ned to think about a proposal, a strong proposal for the committee to react to.

A couple of things that come to mind for me. One, this notion of a partnership with nominators. I think it's really important that this not be something that administratively we take on, but there is this ongoing dialogue back and forth that may actually smooth the process from some of the burden that nominators have

experienced before, but not to take away that opportunity for folks to engage.

The other I would go back to is you know, I think the part of my brain that then goes to how do we balance the budget, also thinks about the resource limitations that go with this, and so I do think the feedback that you all are sharing today is really helpful, and as our team works with Ned to come back with a more concrete proposal for this whole process, thank you.

DR. CALONGE: Thanks Michael. Christine?

DR. DORLEY: Yes. So, this is a question that I have regarding the natural history. I just wonder why a low likelihood scoring was not included. It seemed like a huge jump from one to five. And then a second question is surrounding the feasibility of screening. I would just like a little bit more clarity on what you mean by an additional sample, or additional punch from the dry blood spot.

Coming from the screening perspective, that does not seem like that should be a huge issue in implementing the screening process.

DR. KEMPER: Yeah. So, let me take those questions in order, so that the first is

about the natural history, and then why weren't the points system flushed out more? So, I'll be the first person to say that the point assignment system was not based on any particular science, but the input from the workgroup and trying different scales and different mathematical functions to get to the final score, and it seemed to work. I'd be happy to, you know, refine it further and have more levels.

What I would say is even with that like very simplistic dichotomist thing it seemed to serve the role of separating the conditions out enough to move forward to the nomination process. So, you know, again it had face validity, and just sort of seemed to work.

What I can tell you on the feasibility side of things, that was a relatively small part of the overall score, and for the conditions that we run through it didn't really make a big difference in terms of if a condition would be prioritized more than another. There were members of our workgroup who pointed out that as you ask for additional punches from the dry blood spot, there's a, you know, a limited number of samples that you could take that it was a precious commodity, and that there is some worry that that could impact things.

But I can tell you just from playing around with the score and the conditions that we looked at it really didn't make much of a difference one way or another, but that was the rationale for where that came from.

DR. CALONGE: Natasha?

MS. BONHOMME: Natasha Bonhomme, Genetic Alliance. I have a couple of things to go through as a response to many things that have come up, so sorry if this seems like a laundry list. One, for just to add to the context of history. Years, and years and years ago Genetic Alliance actually got a very small bit of funds from HRSA to do technical assistance with advocacy groups who were doing nominations.

So, just to say that, that that was also part of the model that I think a lot of the people didn't really see, and again, that was really going more towards consistency, our role of being in the room, since many times advocates feel like they're not in the room to see how things are happening, to poorly quote Hamilton.

But so, there have been different models of support, which we're happy to again, talk about. A question I have is will there be time for advocates, and as you said the broader sense of advocates to give feedback on this

process. Again, they're not necessarily in the room to be part of this discussion, and what would that look like?

Is it just, you know, you're just anticipating at the next committee meeting, or will it be through public comments, or will there be a more engaged dialogue, not just you know, advocates reporting out and then taking that information, but an opportunity for actual dialogue around this, or is that something you're determining, not trying to put anyone on the spot.

DR. CALONGE: Yeah. I think when we originally thought about it was to involve the voice of the interest groups through the organizational reps the way we do today. I think if there are alternative routes that we can make sure fit within the confines of the time we allot discussion and meetings, and I would welcome that.

And hopefully, we'll be transparent enough with what we propose that there will be ample time for at least written comments, if not public comments, during this session.

MS. BONHOMME: I think that would be really important because even the Committee, or workgroup, or ad hoc group, I can't remember which term was used, that was pulled together

for this. I did see that there were two, if I remember correctly, people who represent advocacy, which is great. I don't think they would necessarily put themselves in the categories of more on the under resourced side, or the ultra-rear side, so even from that beginning there's that.

To the scoring, I know it's been said many times that the score is not going to impact or determine anything in terms of the actual review of the condition. That's great. I think that's also something to test, and to see, and to see if there may even be an unconscious bias towards a particularly low score compared to a particularly high score, and that's not an issue of just one person.

It's just you know, we're humans, and how our brain works, and if we really like the higher scores, and then we have something coming in at a lower score, just I don't know how to track that, but I think just to say oh, there won't be an impact isn't necessarily enough, so just something to watch.

And then again, sorry I'm trying to track as I was tracking the conversation here. Have we had an opportunity to go back to nominators and systematically collect what their experience has been, and what they think would

be a better approach forward? Like have we done that type of an analysis?

DR. CALONGE: Not systematically.

MS. BONHOMME: Okay.

DR. CALONGE: We did ask the participants in the process.

MS. BONHOMME: And I know that many of the Committee members have been really gracious with their time, and coming to meetings, coming to the boot camp that we put on with EveryLife Foundation, and we really appreciate those opportunities. I'm just trying to think how do we bring that into this room here. And then again, sorry for the laundry list, I guess my last point would be to the discussion about moving the goal post, and just trying to help that. I think one of the issues with the moving of the goal post is not that it's just a oh, an evolution. It's that the goal posts are moving in the middle of the discussion.

So, the conversations that groups have been having with this Committee, with HRSA, with different people for years, then in this room it seems things are changing, so it's just a little bit of a difference between that evolution. It isn't as though oh, we haven't thought about that, let's go back and really process it.

It's that evolution is happening in

real time, just saying that's just a bit of a different nuance, why it really feels like a moving of a goal post as opposed to just a yeah, things move forward, things evolve, we learn, and we build. Thank you. I appreciate all the time.

DR. CALONGE: Thanks, Natasha. So, to wrap up this discussion I think working with HRSA staff, and prior prioritization group sorry -- oh I'm sorry, Sue, we're just behind, but I'm going to let you go.

DR. BERRY: I'll make it brief. I just wanted, the one thing that I take away from this that I find particularly important is that I feel like it offers a better opportunity for those small group for people who just don't have a lot of expertise to have a comparable packet put together, and that serves some elements of justice that we otherwise haven't.

So, there are other things to fix. I hear all this, but I like the idea that it's more of an even playing field if we take that responsibility and get a better packet from everybody, so a fairness thing from my point of view.

DR. CALONGE: I'm sorry, Karin?

MS. DOWNS: Thank you. I wasn't quite sure where to put my thing. This is a very -

this is just a quick question. I'm fairly new to the Committee, and so, and I'm coming from a public health perspective here. But I just wondered in the prioritization if there was any consideration of how to measure equity, health equity in terms of which might be given a little more priority because it is, maybe more linked to groups that are under resourced.

And I just had to ask that question, so I just wanted to know.

DR. CALONGE: Well, I'm glad you did, and I apologize that Alex didn't include that part in the discussion.

DR. KEMPER: I should have added that in, and I think you're 100 percent correct. We really struggled with how to put it into the point system. There's no clear way for us to get it, and to capture that in a meaningful way. And all I can say is that, you know, it's not to delay any condition from moving forward, but if this kind of process is adopted, I shouldn't speak for the Advisory Committee, but I'm sure everyone would be very interested, and if you could come up with a strategy.

We just couldn't figure out how to do it in a way that drew naturally from the information that was on the nomination form, but I think you're exactly correct.

DR. CALONGE: Marc, I'm going to have to cut off the discussion. I apologize, but we're 15 minutes behind, and need to catch up, so if you want to make sure you write your comment, and we'll make sure that it's considered going forward. We will work together on more formal proposal for discussion by the Committee in a future meeting, and really appreciate the discussion and the guidance, and suggestions that have been put forward. And Alex, I wonder if you would move on towards the decision matrix.

ACHDNC Decision Matrix

DR. KEMPER: Yeah. I'll be able to do this quickly I believe. There we go. So, this conversation is really to tee up a conversation about potential changes in the decision matrix, and so this is like a visit into the way back machine. So, first I'm going to begin way back in the Jurassic pre-matrix era, so in June of 2004, before I was born, was the first meeting of the Advisory Committee, which included a consideration of the uniform panel and then in 2005 the ACMG, the ACMG at the time, expert in the panel recommended 29 core conditions and 25 additional conditions as secondary targets.

They used the point system that was

based on the incidents, signs, and symptoms for the first 48 hours for the disease. Benefits of early intervention, family and societal benefits or early intervention, prevention and mortality, accurate and feasible screen test available in treatment, cost of treatment, efficacy of existing treatment, ability to make diagnoses, and availability of services for key management and simplicity of therapy.

So, those were all the components that led to the score. And this is a figure from the report that was generated showing MCAD on the left with the highest score, and then if you read closely in there, I believe it's cystic fibrosis where there was a sort of break point in terms of where things were included. And you can see their score went from 400 to 2,000.

Can you just advance me? There we go. So, in May of 2010 the Secretary of Health and Human Services accepted the recommendation which created the original recommendation for the screening panel. And I'm going to move up and talk about the developments of the decision matrix.

So, originally it was based on this assessment and net benefit following the matrix's used by the U.S. Preventative Services Task Force where on the top you can see the

magnitude of that benefit, and on the left you can see certainty and net benefit, and you sort of find out where you are on that grid and end up with A, B, C, D or an insufficient, if there's a low certainty of net benefit.

And this is language from the U.S. Preventative Services Task Force, and I think it's helpful to think about that as we reflect back on the matrix. Again, for those of you who don't know, the U.S. Preventative Services Task Force makes recommendations to primary care clinicians about things they should do with their patients in the primary care setting related to prevention.

And it's the A's and B's where the suggestion for practice is to offer it to patients, or to provide this service. These are the ones that where the service is discouraged because there's the potential harm with no potential upside. The C recommendations are where the benefits of the likelihood of benefit, and the likelihood of harm are more equally balanced with a little bit more likelihood of benefit than harm.

And in those situations, that's where you're supposed to have a conversation. I think it was C standing for conversation with the family to figure out what to do. And then an I

statement is when the evidence just isn't there to make a decision for or against something, and that's where you should turn to other references, assess patient preferences, use your expertise to figure out what to do.

And there's often times confusion between the C's and I's, and I just want to take a moment to explain it again because you'll see how it plays out on the matrix. So, and I is -- there's just no evidence, and look other places. And the C is there might be a benefit, and that's where you want to have a conversation with the patient or the family about what to do.

Next slide please. There we go. So, then there was an expert panel held in 2012, that was ultimately approved in 2013, that led to this matrix, and you can see how the matrix is essentially the same as the U.S. Preventative Services Task Force, one, but it has glued onto it assessments of laboratory feasibility and readiness.

And there was a lot of discussion about whether or not there should be a two-step process where net benefit was considered first, and then issues of laboratory, or newborn screening readiness, and feasibility. And ultimately, it was decided to combine those things because to really speed up the process

and not have this like drag down more complicated decision-making process where the assessment of feasibility and readiness wouldn't happen until after net benefit was assessed. And so, that's why these things were put together.

So, I do want to highlight in the original article the description of the recommendation process, and again, this was written before there was much experience with using the matrix, and you know, as you might expect things change. So, in the original documentation that came forth from the expert panel, and then approved by the Advisory Committee, was that things that were in the A-1 or A-2, would lead to recommendation to the Secretary.

Things that were in A-3 or 4 would be recommended to the Secretary for addition to the RUSP at the discretion of the Advisory Committee. Anything with a B, C, D, or an L was not recommended. Now in terms of the assessments of newborn screening feasibility and readiness, that really came into play in 2013 in a formal way when there was a survey that was developed, and that's the part that's managed currently by the Association of Public Health Laboratories, so it wasn't until 2013 that that survey was really implemented.

Can you just advance for me? Thank you. So, here's the recommendations based on the matrix from 2013, with Pompe disease through 2023 with Krabbe disease. You can see the matrix ratings in the third column, ranging from NA to a B-3. All of these conditions, except for Krabbe Disease were recommended for the recommended uniform screening panel.

So again, there's been sort of evolution in terms of how the matrix has been used leading to recommendations, and the matrix now is used to help communicate from my perspective at least, to help communicate amongst members of the Advisory Committee where they think the evidence is, and then to come to consensus with the rating, and then moving from the rating to the recommendations is a separate consideration.

So, here's some considerations for discussion. Next slide. So, again, as the matrix has evolved the question is, is it a decision aid, or is it a prescriptive tool to help decide whether or not to move something to the Advisory to recommend to the Secretary for the recommended uniform screening panel.

I think the questions come up multiple times of whether or not feasibility readiness really should be separated out from the matrix

and be a separate consideration. I mean obviously that can be done in the same meeting versus at another time. I think that there's an opportunity to clarify the language throughout, including how the Advisory Committee now considers benefits and harms, as well as issues of feasibility and readiness.

Or it could be that the Advisory Committee wants to adopt an alternative approach, but I hope that this, you know, brief walk through memory lane, helps begin the conversation about the future of the matrix. Taking into account, of course, as multiple people said is, you know, there's no interest in changing the goal post, but really to clarify the process, and make it more transparent. Next slide please.

Oh, that's the end of it. Very good. Thank you very much.

DR. CALONGE: Thanks Alex. Bring up the next set of slides. So, no? I do, as the slides are coming up, tell you that this is a preliminary discussion, recognizing that input from Committee members, organizational reps, and interest groups will be important in the decision-making process for new changes to the matrix.

And I thought we could start somewhere.

Okay. Next slide please. Could we go back? Go back. Thanks. Okay. Now advance. So, suggested changes if I was going to summarize them is I think thinking about separating out the elements of readiness and feasibility are important. Actually, looking back at the decisions that have been made, especially in the last few years, the public health readiness and feasibility has not really had a big influence on what was voted to move to the RUSP or not.

I'm not saying that it's not a very important piece of information, but I will say that the answers tend to be about the same for every condition, and again, they don't seem to have impacted decision making at the level of the Advisory Committee. I think there could be better approaches to looking at barriers to implementation that should be evaluated separately from the evidence-based decision to add or not add a condition.

I think once that decision is made, it should be made on the basis of the evidence looking at the balance of benefits and harms. It's the best way to make that decision, and then figuring out how to best engage states, state laboratories, state newborn screening systems, which include interaction with clinicians, the health care system, and more

than the state laboratory are things that can occur driven by the evidence-based decision to add a condition to the RUSP.

I think then that gets us to a single A grade, which would propose that would be a high certainty of net benefit, and then a B grade that is now inclusive of moderate certainty of substantial net benefit, or a high certainty of a moderate net benefit.

So let me say that again. We're moderately sure there's a significant net benefit, or we have a high certainty that there's a moderate net benefit. The C grade would then be inclusive of moderate to high certainty of a zero or small net benefit, or net harm. And the I grade, which we do not currently have would be a low certainty grade indicating that the evidence is currently insufficient to assign one of the other grades. Next slide please.

Now what happens to the decisions is predicated on what grade you get, so like in the past conditions with an A grade would be forwarded to the Secretary with a recommendation to add to the RUSP. Now we would look at these differently than the matrix is written, but more in line with how we practice on the Committee.

So, B grades will be discussed by the

Committee, and on the basis of a second vote, will be forwarded or not to the Secretary. So, this is kind of where we are with most of our conditions now, is that we have B's that the Committee discusses, and rather than the original matrix, when those weren't forwarded, we have an additional discussion about whether to add those. That gets C's back to conditions that would not be forwarded to the Secretary, and the I grade assignment allows us to tell the research community and interest groups that the data are currently insufficient, and where the gaps are that would need to be filled in order to assign another letter grade.

Next slide. So, this is the last kind of summary slide, which puts out altogether. You have the certainty of net benefit and magnitude of net benefit in the matrix above, so a simplified matrix. And then the translation of the letter grade in terms of its description, and then action in terms of the addition to the RUSP, so we have the matrix and the decisions in one place. Next slide please.

Now that's the simple piece is creating the matrix, presenting it, thinking about what happens. But I want to point out that evidence-based decision making involves judgment. And one of the ways you get to votes that aren't

unanimous is that it's hard to create criteria that says, oh yeah, that's evidence based. There are judgments along the way around the key elements, and one of the key elements is certainty.

And so, the bar for different experts around the table based on their experience, knowledge and interaction with evidence-based medicine could vary around the level of certainty. And I was talking about certainty as it's the opposite of the risk. It's trying to capture the risk of being wrong. So, a high certainty means a very low risk of being wrong.

And moderate certainty says well, it's not that there isn't the risk of being wrong, but we think we're certain enough that we're less worried about that risk. So, that judgment is very important. There are established approaches for the decision that are based on epidemiology, risk of bias assessments, strength of evidence. There's a rich and evolving science around certainty, and how we can most objectively make those judgments over time, or at least make the judgments with an agreement around the elements that go into it. On the other hand, the magnitude of net benefit is more complex, and so I think even in the last day, the last two days, and the last meeting, you see

the complexity of the magnitude of net benefit decision.

And it becomes more complex in adding a second level of net benefit. So, one of the reasons the original matrix did not include this, was this issue of what is the difference between significant and moderate net benefit? However, I will tell you in my experience on the short time of being on the Committee a second time, people are already using those phrases to describe benefit.

And so, I think trying to, if we adopt something similar to what I presented outlining the criteria, or at least rough criteria, that we can use to make the judgment consistently over topics and time will be a challenge and will be something that's important for us to spend additional time on. And I think that's my last slide. Oh, sorry. I wanted to come back to this. I think we do want to talk about what we want to achieve with the determination of public health feasibility and readiness. The most common answer to get back from the assessment is that we can implement this within three years.

And the reality is then becomes most states do not implement a newly added condition within three years. And there are lots of reasons for that, and we've heard individuals

involved in the system eloquently talk about the complexity of moving from something you're not doing to something you are doing at the state level.

And the state public health laboratory in the context of a system that then requires, or could require diagnostic confirmation, secondary testing, referral to specialists for treatment, and follow through, through the rest of the system.

And I think as eloquent as the current system and survey is, I worry that we're not getting the information that's useful to the Committee in moving forward. So, I think talking about the support that the Advisory Committee, our partners at CDC, and other agencies, by bringing to bear, and helping states implement new conditions would be a good thing to consider.

And then really think about the level of support and prioritization from the decision makers in the individual states. And they're complex, and we tend -- I agree, we tend to, because they're in the room, talk to our laboratory directors. But they're the newborn screening advisory committees. There's the state public health laboratory director, who may not be the same person as the person running the

program. There's the state public health department executive directors who are balancing their topics and issues for legislative discussion and requests for resources.

There's the Governor's office, and the executive directors of the health departments work for the Governors, and so where is their prioritization? And then the key legislators who hold the votes necessary to do appropriations, or make decisions, increase FTE, buy new equipment, and implement projects.

So, I think thinking about the level of support at multiple levels, if this is something the Committee believes we need to be assessing versus on the other side, thinking about how to provide effective support for implementation, are discussions I would like to have.

And I think the idea would be to create a set of actions that any assessment we make would be able to prompt, or help us make better decisions, or bring other resources to bear. Next slide. So, again, recognizing the importance of this, and the importance of input from interest groups and experts, I'm suggesting we consider creating an ad hoc topic workgroup to review possible revisions to the matrix, including the assessment of public health, feasibility and readiness should include

interested Committee members, organizational representatives, and members of the public.

Our future meetings could include the topic groups' progress and time designated for public feedback. So, that's kind of the proposal for moving forward, and I'll open the floor to discussion. Let's start with Kyle. Hi Kyle.

Committee Discussion

DR. BROTHERS: Hey. Thank you so much. I may have said this before, but I'm just going to repeat it, I guess. I'm a little skeptical of the use of a decision matrix that we're sort of all expected to agree upon. My understanding of the way the U.S. Preventative Task Force's recommendations work is its classification is actually policy relevant.

So, in an A it's treated differently in practice than in policy than a B does. For us, our decision is dichotomous. Either yes, we recommend it, or no, we don't recommend it. And I would be happy to be proven wrong, but I don't think the states or other folks are implementing the RUSP say oh, well we just don't do B's or things like that, right?

I don't think they'd use the decision matrix classification after a recommendation is even made or is not made. If it's on the RUSP

then it's a thing, right? So, that raises the question of what function does the decision matrix serve? And this is a topic that we discussed last time quite a bit, which is you know, Dr. Warren and I disagree about where a condition fits on the matrix.

I think that's totally okay, right? Because you know, if I think the evidence is high, is a good quality, the doctor warrants these weaknesses there, our votes are going to reflect that. So, it seems to me that it's not that the matrix serves no purpose, it does serve a really great purpose for me individually when I'm thinking about whether I'm going to vote yes or no, for a doctor were to think about this vote, et cetera.

But I'm not sure as a Committee we need to agree upon a classification because I'm not sure it serves a purpose afterwards, and because any disagreements about where it falls are still going to be reflected in our individual votes.

So, I guess what I'm asking for is in addition to thinking about how we structure, I think we should be coming to a decision on whether we think the classification is something we need to sort of reach consensus on, or it's a tool for our individual votes.

And I do think, as something you

suggested Ned, which is sort of digging a bit deeper, and start to define what's the level of evidence that we think classifies as a B, you know, is it are we looking for some comparison in siblings, or some other kind of piece of evidence that would be relatively concrete?

Because I think, you know, even though picking up a single person in a pilot is a controversial requirement, you know, in my mind it's at least concrete, and it really helps groups decision where are fitting right now into what the Committee says it expects, right? Our individual votes still need to be individual votes, but I think getting that more concrete guidance is what's valuable to folks who are thinking about whether it's time to nominate or not. So, thanks so much.

DR. CALONGE: I appreciate that Kyle, and I'm not trying to correct you. It just going to sound that way, but the USPSTF A's and B's are not different. They are different from the standpoint of the magnitude of certainty and benefit, but they're not treated differently in terms of implementation.

All A's and B's are covered with first dollar coverage under the Affordable Care Act, and those become the do's. The D's and I's, the D's become the do not's. We don't have a D who

kind of rolled them into the C's, and the C's become kind of where we are at, with these B's.

It's like well, originally the C was should not be routinely provided, and now depending on the topic, and the sensitivity of the topic, the C's have become you should ask the patient about their preferences and values, and then make a shared decision.

So, in some ways, if you just took the B's and the C's and the I's, you get down to the simplified decision matrix, which I think you're talking about the issue about prescriptive versus decision tool. Our decision assist tool, which I think is important. But I do want to point out that I mean I think the A's need to continue to be on the matrix because I don't know what the future holds in terms of either identification and diagnoses of conditions, or the availability of novel, new effective therapies.

And so, that's why I think the A kind of sits there. I think most of our decisions are now more likely to be in the area of B's, and you're right. At that point it's like yep, we have a sense that there's a benefit that's different than small, and we want to have a discussion and a vote about whether to move that forward. So, I appreciate those comments, and I

hope that helps clarify a little. Shawn?

DR. MCCANDLESS: Thanks. If there's other comments about that particular topic, I'm going to change topics. I'd be happy to defer. Okay. I wanted to address the issue of feasibility and readiness, which to me seemed very different topics. Readiness seems to me at least is the question of whether the states and laboratories are equipped to do the testing, whereas feasibility to me seems more about a technical issue of whether there's an adequate screening test, than is it broadly applicable. And I would be hesitant to remove that feasibility from the decision-making about proposing the addition of something to the RUSP because I think it's very important that there has to be a good and reliable screening test, and I don't know how else that would be captured in the decision making process for the Committee.

DR. CALONGE: That's a great point, and Scott, I think it is -- I'm sorry Shawn, I think it is captured within the nomination package when you say there's an available I through put task that identifies the condition with acceptable screening tests attributes, false positives, false negatives, and predictive value.

So, I think we are capturing that feasibility, and we discussed that, and at least for -- well I think for both A and D and D we had discussions specifically about the feasibility of an availability of testing.

DR. MCCANDLESS: I guess my point is not so much the question of are we capturing the information, it's how do we use it. And so, it would seem to me that actually, feasibility should be the first discussion because if there's not a feasible screening method, then there's really not a lot of point in discussing the rest of the issue.

So I would see it as feasibility first, and maybe even that occurs during nomination prioritization with a conversation with the nominators, and so that the assumption of the Committee is that anything that comes to them that's already been documented feasibility for screening, and so now it's coming to assess the rest of the issues.

DR. CALONGE: Thanks. I'm going to do Michele next. Sorry if I missed the order.

DR. CAGGANA: No that's okay because putting Shawn before me exactly what was one of the things that I was going to mention, that the feasibility is key for programs. And I think one of the other things is when I totally remember

Scott saying all the time about the readiness tool, and that we all say the same thing.

But I think, getting at the implementation barriers is really important, and that the Committee needs to understand what those are, you know, on a granular level, because they're variable throughout the different state programs. And if you're going to be going to different parts of the health department from the Governor's office to ask about readiness, I think you also have to engage the program directors, because they're the ones on the ground that actually know that the true readiness is, and can give you the reasons or the rationale as why.

And then those other people are decision makers, but I think we need to go to those decision makers with a set- set of concerns, and that will help. The other thing I just sort of a question between the C and the I. C, I seems like it's a no go, but will tell you all the things you need to fill in.

So, I don't see the distinction between a C where you're saying no go, and an I where you're saying no go. I would assume a C would also give you, you know, identify what those gaps are and encourage people to come back maybe.

DR. CALONGE: So, I feel a little bit different than that.

DR. CAGGANA: Okay.

DR. CALONGE: There's a level of certainty that the net benefits are either small, zero or negative.

DR. CAGGANA: Okay.

DR. CALONGE: So, you've actually made a decision because you're a C there's not sufficient benefit, net benefits, benefits minus R.

DR. CAGGANA: Yeah. I see that. I guess my point is what you said just previous where you can give somebody a C today, but now all of a sudden there's a new development, and you would encourage those people to come back, so that's what I'm struggling with the whole grading system on the lower levels to be able to give people guidance on what's needed.

So, SMA was not treatable at all a few years ago, and now all of a sudden is inherently treatable, and that you know, that ricocheted it to the top, right, so these are all influx. So, I think giving people some guidance on what the decision was is important.

DR. CALONGE: Okay. So, let me try it one more time. If there is no treatment available, then it would end up in the

insufficient. So, in order to get to a C, you actually have to have at least moderate certainty of the net benefit. If you don't have the least moderate certainty of the net benefit, you're in an I.

So, it's likely to rarely happen, just like the A's are trying to stay optimistic about A's coming, but this is like the proof that it doesn't work. That's what you're talking about, and at least in a period of time there's sufficient proof, or sufficient evidence to raise the level of certainty that it doesn't work.

DR. CAGGANA: Okay. I think I get it.

DR. CALONGE: Those of us it's like, so one of the things that I always say is where there's an I, there's hope. I never minded insufficient evidence when I was in the job of actually implementing prevention programs, because that was an area where you could bring in a lot of information around where does it fit in the broader stream of health care systems, and patient preferences, and how do you work around that while you're waiting for the evidence to fill in. Yeah, thanks.

I have Carla next, and then Melissa.

DR. CUTHBERT: I just wanted to follow up on what Shawn and some of what Michele was

talking about. This is Carla Cuthbert, CDC. And as a federal agency, I just want to indicate we do provide some funding for state programs. This is something that we will continue to do.

We recognize that it's, you know, in terms of how much money is probably needed, it's a modest -- it's a small amount, but it's still there, and we'll continue to do that. One of the things that we've also found that has been helpful recently is being able to provide onsite technical support.

We've been hearing that some of the states have needed some help in sort of developing methods, and you know, many of the states don't necessarily have someone dedicated, a chemist dedicated to being able to implement new methods internally, and we do have some staff within our program that are able to travel to states, spend a week there, and implement a new condition.

You know, take a look and help troubleshoot and so on, just to, you know, I just wanted to make sure that I mention that as possible areas of support that we could actually provide. We also, together with APHL, there is an on-site at CDC training opportunity that we have for both molecular testing, and for Mass spec technology, and we're starting that up

again post-COVID.

So, there's going to be opportunity for them to do that. The one thing that I really, you know, was thinking about when I was hearing the issues of sort of separating out implementation and that sort of thing, is my mind just immediately goes to the what if, or what happens when, an application comes that is not using a dry blood spot matrix.

What if saliva, its urine, and there may be some pilot that was created that shows a really great benefit, and so on and that may rank highly, but we're just literally not set up to be able to do any kind of testing that would require significant reworking of our workflow, not impossible. But would require significant workflow.

My mind just goes to that wondering what will that mean for our programs to be able to make that happen? You know, in some cases it may not fit the three-year timeframe, and that's my concern. Again, I'm not in a state program, so I don't know how quickly, or how easily that will translate.

So that's one thing that I've been thinking about, and again I always say to people that I'm a biochemical geneticist at heart, if we ever get urine and if we ever get saliva,

that would open up a whole area of biomarkers that would be amazingly fascinating, and would be wonderful in terms of being able to identify new diseases.

The second thing has to do with newborn sequencing, and the very strong movement that exists currently, but really wants to get that happening, and again if that should happen within a pilot program, how does that translate here, because we know that many of our programs, most of our programs are not able to move forward in that regard.

So again, readiness, feasibility, implementation, all be an issue, and that's what I see when I think about this area.

DR. CALONGE: I really appreciate that, Carla, and Shawn's comments as well. I think, and I don't know if this is helpful or not. We have laboratory people, both on the Committee and on the organizational reps. And back when we had the matrix that didn't include implementation, it was those voices where we considered whether or not it was a test we could do, we could pull off.

And I think that would continue. I think while I appreciate the comment about program directors, so well said, I appreciate that. I think for me, perturbing the decision

route evidence with the decision's route implementation are where I think there's a little -- for me there's a gap. It's like okay, we know this is going to work, so then let's figure out how to do it, and maybe that's an issue about what does it mean to have a condition on the RUSP?

I will tell you what it means today is that unless you have legislation that says you'll do it within a couple years, or three years, it does not translate the implementation in every state. And I don't know, I do know, sorry I feel that states start to think about implementation when the conditions had it.

So, I think again, they seem to me to be two separate decisions, and while they're linked to implementation and translation, and to improve public health, requires implementation, I think the science about whether or not the net benefit is moderate or significant should remain the same.

We should be able to say yeah, we think this works, and we should implement it. So, thinking about those is not -- it's related, but not perturb the decision about evidence based on feasibility and implementation is what I'm trying to advocate for. And we don't have to do it by the way, but I just would advocate it.

Melissa?

DR. PARISI: Melissa Parisi, NIH. So, I have three points like I always do, but fortunately the first point was just made by my colleague, so you get spared one of my points. But just to reiterate that I think feasibility and implementation need to be separated, and the feasibility of the assay needs to be considered because if someone comes up with a brilliant assay, but it involves a substrate like urine or saliva, that's just not doable by the state program, so just a reminder to keep that separate.

I think my most important point and feedback from all of this discussion is really an agreement with you that the key works here in this revised matrix proposal are certainty, and net benefit. And I think that those are intrinsically subjective terms at a certain level, and I think this is where the crux of the matter really lies.

And I do have some concerns about using this graded system when we may not agree on what a benefit really is. And I'm thinking specifically around the space of whether being alive versus dead is considered a net benefit. Being alive with some disabilities is considered a net benefit maybe to maybe being alive but

having full functional capacity.

And I worry a little bit about ableism potentially creeping into these discussions as well. And, I'll be the first to admit that I'm still learning about this concept, and I think that this is a point that we all need to educate ourselves on, and for those of you who may not be as familiar with this term, it's really the assumption that people with disabilities are less valued in society, that they don't have as much offer and that there's this subtle prejudice that enters thinking, myself included, around being able, versus being disabled.

And as a side point if you're very interested in learning more about this the NIH hosted a two-day workshop webinar, Ableism and Medicine in Clinical Research on April 27 and 28th, just like a week and a half ago, or two weeks ago. Actually, that was just a week ago. We're already in May, oh my goodness.

So, last week, and the full recordings are available on the NIH videocast website, so if you want to learn about this topic, it was incredibly eye opening for me, and I feel like I need to go back and listen to it again, but go to videocast.nih.gov if you're interested.

So I do think we need to be having more discussions around this topic of what benefit

really means for newborn screening conditions, and I would suggest that in convening an ad hoc committee of public members, and laboratory representatives, and advocacy groups to discuss these proposed revisions to the matrix, that we don't just focus on feasibility and implementation, but that we also talk about this really critical component of what net benefit means. So, that's my second point.

My third point is I also worry a little bit about the C versus I grades, and this is kind of based on my own experience, and I'm not an expert in USPSTF formulation and process, and I really believe that it's an important system for evidence review.

But I've also seen that it hasn't served pediatric disability conditions terribly well. And for example, the screening for autism, which most pediatricians would advocate for by the age of two years, is still languishing as an I grade, insufficient evidence. And I think that's really tragic because I think most individuals would agree how important it is to really be screening for this condition.

But because there has not been adequate evidence as predicated by the process, and trying to do a randomized control trial would be unethical. We're really not able to get out of

that categorization.

So I worry that a C grade might not mean that there would be any discussion of a condition for newborn screening if we apply this gradation process, and I hope that there would be at least allowance for discussion of such a nomination, particularly since our experience in our last meeting in February there was actually discussion, and a change from what the recommended grade of C to a B, and I think there's always value in having discussion of this Committee, and I also worry that an I grade could mean kind of a kiss of death, and that it might not necessarily result in meaningful ability to progress up the gradation, so that's my third point, and thank you very much.

DR. CALONGE: Thanks Melissa. I think you know being someone who worked with the USPSTF and the CPS for a long period of time, things do move out of the I actually quite frequently, and I've seen D's become B's over time, so as evidence fills in, things change.

There are a lot of ways to make decisions, and I think I often say this. Only one of them is evidence-based approach, and that's what the Committee is charged with today, is to use evidence-based approaches to decision making in whether to add conditions to the RUSP.

How we structure that evidence-based decision is up to the Committee, so that's within our purview, and I think that's the thing I proposed was trying to do two things, separate out the readiness and feasibility, not that that's important. And then to move towards simplification. It doesn't mean that there's not additional simplification, or other approaches, and that's why I think taking on the issue with an ad hoc committee that is inclusive, could help us move forward and make our discussions richer and again, hopefully a little bit more consistent.

I don't expect because of the expertise and differences and experience of people around the table that this will translate to votes that aren't split because I think we do bring different judgments, experiences, and values to the table, and that's why we have a big Committee.

And I think trying to provide structure that the interest groups, the public understands, and the Secretary of Health can have faith in about the discussion around the evidence of we believe that implementing this is worth it because it's going to provide more benefit than harm is important.

And then to your last point, deciding

how those are. I mean we had sessions on it yesterday. I think one of the things that USPSTF when I was there continue to struggle with, is that the currency of benefits and harms is often different. And so, how do you balance a life saved, which is a pretty dramatic benefit that accrues to very few, to a harm that less, but accrues to a whole lot of people.

And that's a -- I know it sounds easy, maybe it sounds easy, but I think that's an issue where people start thinking about voting differently. And wrestling with that and doing it in discussions is important. Jennifer?

DR. KWON: I mean I agree with Melissa that the B category is going to, I mean that's the category where we're going to have a lot of differences in opinion. And I think it's in looking at those sort of relatively manageable harms, but that affect a large number of people, one of the ways that we justify it is by looking at the outcomes.

Is it survival? Is it survival with near normal abilities? Is it -- I mean we treat, if we didn't treat PKU they would live a long time, and they would be pretty disabled, but we treat it, and we hope that their abilities would allow them to be independent, and you know, have just more independent and abilities.

So, I think it's those outcomes that kind of help us jump over the unknowns of the harms, and it's also those outcomes that drive clinicians to be more involved. I think what's happened in the world of SMA, and I remember that part of the issue with SMA is the evidence wasn't great. You know, we were very optimistic, and I feel like the optimism has paid off, but it may not have paid off, and so that's where a lot of the discussion there was. And I thought that was fair. But I think now we have a disease where honestly, I don't, I mean I haven't had a family refuse treatment, but we would do a lot of things to prevent them from refusing treatment, because you know, because it would so irreversibly change the outcome of this child's life. It just doesn't seem right.

Whereas there are disorders where we do let families make those choices because the outcomes are challenging. And those are the situations where it would -- that's where it would be helpful to have the harm, but yeah, I think B is going to always be a tough one.

DR. CALONGE: Marc?

DR. WILLIAMS: Thank you. A couple of observations. Most of yesterday mentioned ClinGen, and I wanted to talk a little bit about the actionability work, and the way we approach

this as a possibility to deal with some of the courses that come up in discussion.

The first thing that we do we consider a condition that has an established validity, is to say and if we were to identify it early, what would be the particular outcomes of interest, and what would be the interventions that would be needed to achieve those outcomes?

And so those are predefined. And I think listening to, and reflecting on the comments from yesterday, this would be a really great place to engage with our advocacy groups or patients and our clinicians to sort of co-define what do we consider to be the important outcomes, and what do we think the interventions are that should be evaluated?

We then, as we would move forward, look across categories, much like you do in the matrix, for things like how frequently does this occur? What's the severity of the disease? Is it death? Is it long-term disability, et cetera? What's the nature of the intervention?

How onerous is it to do the intervention? And you know, those are all E's, but you would define those differently for the task for the Committee. And then evidence is developed for each of those, and presented for each of those separately, rather than combined,

and there's an evidence grading that goes along with it.

So, we look at the prevalence and say well is this a registry? Is this an independent population assessment? And you can grade that evidence. Do you have evidence grading directly relating to each of the questions that you're specifically asking that helps to focus on the individual component? And we look, and we generally come to reasonable consensus, with some differences, but we're not trying to eat the whole elephant at the same time.

Of course, we don't come up with a recommendation. That's not the whole of the action of the working group. We come up with transparency. But one of the things that we recognize is that we reducing the formula that sounds like it's going to in year two, is that we have these cognitive differences with what the torch levels and what we really think.

And so, introduce the second concept proposing that, you know, our assertion with maybe the certainty metrics that you are looking at Ned, which is to say do we agree with what those four are telling us? And if we don't agree, why? What are the issues that we are, you know, that are causing this disagreement?

And that's been very useful in certain

circumstances to really paint a -- move away from I just don't feel this is right, and we can articulate it a little bit better. And so, I think perhaps, some adjustment to, but use of that type of a framework as we do these considerations it would be useful, and it might be useful to have somebody from the actual working group walk through the tenures that we've been developing that.

So, the second point will be much shorter because it's been stated before. I agree with people that are saying the feasibility implementation at the state level needs to be set with a process. I haven't gotten into the charter in great detail, but I have a fundamental question as to whether it is the remit of this Committee to actually do these state-by-state assessment of feasibility.

Because I'm not sure that it is. And I understand it's difficult to separate out, and it's all going to say yeah, this is great, we should do it, and then it's impossible to do at the state level. But it does seem, and I would endorse the suggestions that several have made that that has to be a separate process.

And it might be a separate process by a different entity that develops a feasibility assessment that goes in parallel with the

Committee's recommendation in the second.

DR. CALONGE: Thanks Marc. I think it's been a rich discussion, very useful. I think what I would propose, so let me try to summarize a few points. So, the first one is that I don't think we're pleased with the current matrix. So, I think we would like to move away from that. So, that's one point that I think I feel we've made.

The second point is that feasibility is an important assessment that needs to occur if implementation of conditions that we vote to add to the RUSP are going to actually be implemented. So, I think that's an important point. The readiness issue, while important, I felt less enthusiasm, or I'm sorry, less passionate around discussion.

And the third point is an acknowledgement that the matrix approach, the grading approach we may want to not constrain ourselves to the thought that we'll have a matrix, right? That we might want to have a decision approach that does or does not involve grading, but that does work hard on trying to identify and with as high a certainty as possible, determine the certainty of benefit, the certainty of harms, and a feeling around the certainty of net benefit.

And that that would translate to a discussion and a vote of adding a condition, or not adding a condition. So, that the decision point isn't what grade are you, but based on those important factors, what does the Committee vote to do?

So, we may end up with a grading system, but as I've listened to people talk I think this issue about feeling constrained by assigning a grade is something we may or may not want to continue, and I think we'd be more open to other approaches, other decision approaches if I hadn't done what I did, which is just present you with a different matrix, and say let's do this.

So, I want to make sure that as we put this, I think we want to change. I think any change should be with a process that's inclusive of the public's interests and experts, and the Committee, and that will kind of move forward in that realm. Scott, I did see your card up and wondered if you're okay.

So, is that a reasonable summary of where we are? And would it be okay to move forward and try and do assemble a group, an ad hoc workgroup to discuss decision making for the Advisory Committee on voting to add conditions to the RUSP? Okay. I think Michael and Jeff,

Leticia, I think we'll move forward.

In thinking about the group, I think knowing that people are busy, I think having a group that can make every meeting, or almost every meeting will be important because otherwise you end up re-adjudicating the same points over and over again.

But we'll get started, and we'll figure out ways to schedule that group, and figure out how to recruit members because I think there will be a lot of interest from both the Committee and the public, so. Great.

I do want to take an opportunity before we break for lunch to just ask Carla if she might have a comment about the recent shooting that involved CDC.

DR. CUTHBERT: Thank you. Thank you for this opportunity to acknowledge what's happened recently in Atlanta. You may have heard that earlier this week there was a shooting at a medical facility in midtown Atlanta, and the victim in this instance was a CDC employee, called Amy St. Pierre.

And while I did not know her personally, Amy was a very valued member of the CDC family, and she worked in the division of reproductive health in a building just opposite our own branch buildings in our quadrangle.

In a statement put out by Amy's family, Amy was a loving wife, mother of two, she was an Emory honors graduate, had a Georgia State MBA, and traveled the world with curiosity and courage. She was driven by compassion both in her work in the field of maternal mortality, and in her everyday life.

Amy was selfless always. She wanted more for others, but never for herself. A generous supporter of worthy causes. She was a social conscience of her own family. As a very valued member of our CDC family, we feel a tremendous loss over her death. To Amy's family, and for the others who were injured during this shooting, and their own families, are hearts are with them, and we wish them strength and comfort during this time of immense grief. Thank you.

DR. CALONGE: Thanks Carla. Leticia?

MS. MANNING: And now we're going to shift to our lunch break. We will reconvene at 12:45, and I'll see you then. I'm sorry, 12:15. My apologies.

DR. CALONGE: Yeah, you don't get that long.

MS. MANNING: No. 12:15.

(Lunch break)

Ad-Hoc Topic Group Ideas

DR. CALONGE: Let's all find our ways back if we could finish up with, I think some interesting topics, and what we want to do is talk about the move from standing workgroups to ad hoc topic groups, and we want to get started on that process. We talked about one already in terms of decision making for the Committee, about recommendations to add conditions to the RUSP.

We have a couple we want to talk about specifically, sorry including one on conflicts of interest, but we also know that from the new business if we have time to get to a discussion around secondary conditions, screening outside of the newborn period, and counting conditions.

And so, what I think I'd like to do is start with I don't know, where am I going to start Leticia? COI. Okay. Yeah. I'm ready to do that. Next slide please. If you can advance for me that would be so great, or I'll try it again. Oh, it's different okay. So, we do do some conflict of interest, but we have two assessments.

One is this truly wonderful form that everyone in the room should get to experience at some point. The OGE Form 450 Financial Disclosure Report, which is reviewed by HRSA staff, and discussed specifically with the

person if there are issues of concern or questions.

The one good thing I will tell you about the form is that when I first started filling it out for the Committee, it was the PDF that you could not enter data into. And so, when you had to repeat it every year, you had to start from new every year, so that's gotten better at least, but anyway.

So, then the second point is the decision by a specific Committee member based on their own assessment of any potential conflicts, for a specific topic vote. And currently there's no assessment of potential conflicts for organizational representatives. So, these are issues that I want to have, be able to discuss.

I feel when I think about the other groups I work with, community guide, the USPSTF, which I've done in the past, and the National Academy of Science Engineering and Medicine, all have moved to a much more formal and detailed conflict of interest approach.

And so, I would like to present one, at least for us to think about moving forward with, and hopefully put an ad hoc group together for. Next slide please. Next slide please. So, I'm going to rely on the group that I've worked the most with, the most recently, I rotated off the

community improvement of services Task Force at CDC at the end of last year.

And we had implemented this project, I think around the second year of my Chairpersonship, where based on working with other federal agencies, and with the USPSTF staff, came to disclosure forms that talked about three different kinds of potential conflicts.

The easiest one is always the financial conflict of interest, and this is what the OG 450 is supposed to do. Do I have stocks or bonds where a decision made by the Committee might benefit me financially? But financial COI can be expanded to different areas, and the level at which you have to disclose is an important issue.

The second area was business and professional conflicts, and then the last was potential intellectual conflicts. The way it works at the CPSTF is that the DBC staff, which includes the Office Director, legal advisor, and the Task Force Chair and Vice Chair, review the statements prior to every meeting, and decide whether or not the members should have some sort of restricted participation.

The restrictions are not all total recusals, so they can include no restrictions,

and no public disclosure, no restrictions but public disclosure. That would mean in the meeting we consciously talk about those potential conflicts. Participation in discussion, but restriction from voting, or recusal and restriction from all parts of the topic presentation and discussion, so those are pretty uniform levels across different groups.

I think it's really important, this last point, maybe I should have bolded it, that disclosure and actions are separate processes, so I think one of the most important things in COI to do is to disclose, and if it could create an appearance of a potential conflict, make sure that it's transparent to the public, and to the groups that we're serving.

However, a disclosure may also not lead to any restriction, and may not be publicly shared if in the decision-making process of the staff and the Chairs, that information is not something that is required to be shared publicly. Next slide please.

If I'm talking about financial interests, investments, or entities that could influence, or give the appearance of influencing the outcome of a decision, those entities could be individuals, organizations, or corporations, or other groups with established or future

business in the matter of a decision.

A relevant financial interest is a situation where a Committee member has the potential for direct or indirect financial gain or loss related to a recommendation vote, and so members need to disclose their own financial relationships, those of their spouse or close personal relation, and their dependent children.

And the cut off that was set by the USPSTF and adopted by CPSTF was $1,000.00 or greater in the previous 12-month period. And I will tell you I feel that's a pretty low level, and I think it assures that you err on the side of disclosure, rather than not disclosing. Next slide please.

This is a long list of potential interests, but they include stocks, employment, patents, royalties, licensing fees, a research grant not from the fed, so we excluded those, but our search grant from a corporation or proprietary business, compensation for being on a governing board, or advisory council of a private business, although we included non-profits, if they're paid.

I'm sorry, I've got to get back to that paid, participating in a speaker's bureau for a proprietary business entity, honorary travel or gifts from a private business, payment as an

expert witness, and receiving compensation for services be parties having a financial interest of the outcome of a decision.

So that's a long list. It's meant to be comprehensive, and it's to try to make sure we raise up any financial issues. Next slide please. Now business and professional interests are different. So, now we've moved away from the area where everyone seems to agree, and where we're trying to move into areas that we think are important for disclosure, and potential action in a decision making that have kind of federal and public potential impacts.

So, a business or a professional conflict is a bit relationship or activities that aren't disclosed as financial but could influence or give the appearance of influencing a decision. It's a situation where the member has the potential for business, or professional gain or loss, related to the finding, the outcome of the decision could positively, or negatively affect that organization's ability to receive funding.

So, you need to disclose your own business or professional relationships, those of your spouse, and dependent children. Next slide. So, here are examples, public comment and testimony, like an expert witness made on behalf

of a business, or a professional organization, leadership roles, panel associations, society journal or certification body, advocacy or policy positions on behalf of an entity, so I've made an advocacy statement, or have a position on behalf of an entity.

Relationships with government organizations, non-government organizations, private organizations, professional societies, or other organizations that you have a reason to believe may benefit or be harmed by the findings, and these could include being a board member, a director, expert adviser, a leadership position, officer, owner, or principal investigator.

So, again these are disclosure requirements that may or may not lead to public disclosure, or restriction of participation. Next slide. The last category is potential intellectual interests. These are potential interests, likely to be numerous, because we're actually selected because of our expertise, and so we have intellectual interests.

The work may be sufficiently well-known that different audiences might question the objectivity of the process. If members are known to have taken leadership roles in discussion, then sometimes even votes or recommendations

regarding that topic. A member may hold strong, personal views on the effectiveness of particular interventions, and may be unwilling to accept evidence to the contrary.

That's a very important phrase, and this is the way, something the National Academy gets at by actually asking the question if we found evidence that actually was contrary to your stated position, or your intellectual belief, would you be able to vote opposite of your intellectual interests, and that question needs to be asked.

Same holds true for strong moral convictions that can influence a member's scientific opinions. Potential intellectual conflicts of interest could be indicated by membership and lobbying, or advocacy organizations, again serving as an expert witness.

Public comments, or other indication of strongly held beliefs, or intellectual property rights, including books, journals, manuscripts, patents, and copyrights. Next slide. So, the organizational representatives do not vote, and as such do not need to be held to the same standard as I think voting members need to be held for.

On the other hand, I do believe that

why they should not have any COI-related restrictions, they do have special status, and access to participation and Committee discussions, as meeting times allows, and at the discretion of the Chair.

And so, the proposal to consider as we move forward is whether board reps should annually disclose whether they receive any fundings from a proprietary private business entity, include that in that disclosure, how much and what percentage of their operating budget that's relevant such funding represents.

And that information should be available at least to the Committee members. This is completely new, and additional, but not with the idea of restricting participation, but disclosing potential, financial interests and conflicts. Next slide. So, this is complex, and sensitive, and the proposal is to consider creating an ad hoc topic work group to create a proposal to present to the Committee for consideration and adoption.

And I will stop and see if there are questions or comments.

DR. WILLIAMS: I'm online Ned.

DR. CALONGE: Thanks Marc. Let me start with you then.

DR. WILLIAMS: All right. I think this

is excellent. I've been as part of the Presidential, or elected President role of the college we have a conflict-of-interest committee, and so I spent a lot of time with this. And I would make three recommendations in addition to yours, which I, by the way, agree with.

The first is that we specifically for the college include federal grants and contracts as part of the disclosure. And the reason for that is that these can represent significant conflicts for some businesses, and in particular, if you think about grants and contracts for example, that I'm on, like NBSTRN that directly relates to work that the Advisory Committee does.

And I think that case could be made for Propel, Excel and others. And I think it's also important to disclose for specific topic areas if you have funded research, whether its federal or industry related, it's specifically conditioned, I think that needs to be disclosed, so that's recommendation one.

Recommendation two is I completely agree with the disclosure for organizational representatives. I think that that's very important for many of the same reasons that I just articulated. The third recommendation I

would make, and this maybe is presuming a discussion is going to happen in the ad hoc discussion that's upcoming, but I think there should be a separate disclosure for participation at any of the ad hoc working groups.

That's a practice that we do at the college for all of our evidence-based guidelines, working groups, committees, et cetera, because there may be specific conflicts that are not relevant to the committee as a whole, but would be relevant for as ad hoc working group.

Now, you've talked about how onerous this is, and there's no question that it is. I fill out about one a month, but if the information could be persisted such that all one would need to do is to go in and make edits, when that was asked for that would be, it reduces the work considerable. And I think this is the most rigorous way to ensure that we're doing our business transparently.

DR. CALONGE: Thanks Marc, and I agree the issue about trying to make it as easy as possible as we were talking. There were things, the CPSTF approach, and the USPSTF approach I left out on the slides, which is that you do the COI assessment prior to a meeting based on the

topics that are going to arise in the meeting.

And so, it is the topic specific assessment and action taking. The second thing you reminded me is something we didn't get to the slide sets, but I appreciate Don, in your presentation, including a slide for all presenters about their own assessment of any conflicts of interest when they present in front of the Committee. Shawn?

DR. MCCANDLESS: Thanks. I think this is a good idea, and I think I just wanted to ask if the intention is also to include the evidence review group, and the expert panels that assist the evidence review group?

DR. CALONGE: So, I think that's another expansion of the process that I think should be under the consideration of a topic work group. I would like to at least get it done for these discussions and think about how to most appropriately. And again, you know, it's funny as you get involved in this work because there's always a worry that we're saying if you have a financial, or an interest, you're not a good person.

And I don't know how to get around that except we're people, and that is a completely different discussion. It's like yes, I have these interests, that might be a conflict, and I

wanted to declare them. So, as we think about experts especially in evidence review, and other settings, it's not saying that it's not okay to have conflicts, including financial conflicts.

It's that people should know about them when you're in a decision making or advice providing mode. Okay. Susan?

DR. TANKSLEY: Thank you. Susan Tanksley, Association of Public Health Laboratories. So, as organizational representatives, would you also want disclosure of any grants, or things like that that the organization itself has? Like is that – these are all personal, or would there be any need for any expansion into the actual organizations? Thank you.

DR. CALONGE: Yeah. I think that's a great discussion again for the ad hoc group of where conflicts might come. I was really specifically thinking about the issue about corporate funding as the most important assessment. And not at the personal level for the org rep, but at the organizational level. Does that make sense? Yeah okay. All right. Sorry Jane.

DR. DELUCA: Jane DeLuca, Committee Member. We do this a lot, right, in our professional lives. We disclose lots of

different types of information, but I've actually never seen anyone pulled from anything because of a conflict, so I wanted to know what is sort of the watchdog process that goes into that? You know, and then what happens to someone if there is a conflict that they don't see it as a conflict, but an organization may?

So, I'm just wanting to hear a little bit more about that in terms of maybe your experience, or other people's experience.

DR. CALONGE: Yeah. So, well I can tell you about the way the CPSTF works because I was most involved with that. So, the forms were sent out, and had to come back by a specific date. They were then reviewed by the agency, including their legal advisor, and then in this regard it would be someone at like Michael's level, and then someone at Leticia and Jeff's level as well.

And they made separate conclusions about what actions might take place. And then they brought the Chairs in, and we had the Vice Chair of USPSTF, and we went through the same discussion, and then came up with a final determination. There were times when a person was asked to recuse. And recusal was leave the room. In this setting it could be that the conflict is not raises to the level of recusal,

but it might limit the ability to serve on a topic work group or a nomination group because of the potential conflict of interest, or the appearance of the conflict. And that would not necessarily restrict discussion and vote.

So, all levels kind of have occurred in my experience.

DR. DELUCA: And just to follow that up, you know, I think there's a very nice packet of education materials that go along with our yearly, and are there plans to actually look at that? Have Committee members look at that, update, et cetera.

DR. CALONGE: I think that's a really good point, and I think it's something we can definitely do. Ash?

DR. LAL: I have a comment about the intellectual conflict of interest. And I think the Committee is not assembled to bring in subject expertise for different conditions if that's my part. Relying on an expert testimony when the condition has been discussion for inclusion, but I wonder if it could be that there's some sort of having one expert it could be a panel of experts that could be invited, based on the testament of the evidence review group.

Based on your evidencing field, and not one person, but maybe a panel of three people. And then the Committee just accepts the recommendation made by that expert panel. Because that could avoid any, you know, potential for an intellectual conflict.

DR. CALONGE: So, could I, I'm sorry, so just so I understand. Are you talking about the decision process, or the decision around whether there's a conflict?

DR. LAL: So, no, it's the appearance of a conflict for when a subject is being reviewed, and we would you know, whether we judge as experts for something the evidence is there for a certain thing, and we hear from experts from outside, which are brought in by the advocacy groups, so during the nomination package.

But I was wondering if that process would be such that the experts could be invited by the Committee, chosen based on the national reputation.

DR. CALONGE: Okay.

DR. LAL: And then we just accept the recommendation as the expert recommendation.

DR. CALONGE: So again, and I'm not trying to be dense. When you say -- sorry? When you say adopt the recommendation, what

recommendation?

DR. LAL: That the evidence for moving conditions forward.

DR. CALONGE: So that would be yielding the responsibility for decision making from the Committee to experts?

DR. LAL: Well, that's not the fact recommendation, I mean it's one part of it.

DR. CALONGE: Okay.

DR. LAL: The subject matter expert's recommendation is that this is yes, this should move forward, or whether this should not move forward, and the Committee would accept that part of the recommendation.

DR. CALONGE: Okay. So, again so, very important, so now I understand. So, I think you're actually talking about the decision-making process and are there better ways to include subject matter expertise than occurs through one, the evidence review group and report, and then the assessment and presentation by Committee members in the decision-making process. Is that fair? Got it. Thank you. All right.

DR. WILLIAMS: I'm sorry. If I could add on to that. That specifically is addressed by the Institute of Medicine, now National Academy of Medicine's guidelines. You can trust

the use of experts and addressing conflicts of experts in evidence-based assessment, and so that would be something I would also refer to this working group for consideration and consent. I think the inclusion of experts in the evidence process is critically important.

DR. CALONGE: Right. And I just want to point out that they are included in the process, and what Dr. Lal was suggesting was that they have a different role in the actual presentation of evidence to the Committee. So, Marc, there are subject matter experts that sit on the ERG for a specific topic to bring that level of expertise to the table.

And I think Ash is talking about how that gets translated to the Committee for consideration and discussion. I'm sorry Melissa? When your card turns sideways, I can't see it.

DR. PARISI: It's the wrong angle, right? Yeah. Just a quick comment, and I think this was just raised a moment ago but I think for intellectual conflicts of interest where it's a little more subjective, it's I think making sure that the person is still present and able to provide feedback is really important, and to answer questions because they have the expertise and the knowledge that could actually be very beneficial in some of the deliberations.

DR. CALONGE: Absolutely. And that gets to the point where disclosure and action are different, and you have to have the action match the level of potential conflict, and you're all at the table because of your specific expertise, and we wouldn't want to lose that.

So, we'll move ahead, it seemed kind of -- I'm sorry Jeff.

DR. BROSCO: Just one last comment. It's Jeff Brosco. Is that this Committee makes such important decisions, and there's so much scrutiny of the work that we do, that it seems that one of the ways to build our legitimacy is to say everything is open. We're going to let you know what it is.

And so, whether it comes out as a specific process from the ad hoc topic group, part of the idea is to build the legitimacy of our decision-making process and transparency.

DR. CALONGE: So, I am going to move ahead with trying to recruit interested people and serving on a COI Committee. We'll start with kind of place that I'm trying to present today, and expand it based on the questions and discussion that we've had.

I wonder if we have the lists developed by the work groups at our last meeting to put up on a slide. Thank you. So, in the spirit of

transparency, I've discussed this issues with staff at HRSA to think about where could we get started, and given that we just now created two work groups, and I thought maybe we could create two more, and work through the -- and the ones that we thought about adding.

But this is open to discussion from the Committee- is an ad hoc work group on the blueprint for follow-up and treatment of RUSP conditions, and then laboratory best practices for utilization of second tier testing. So, those were two specific comments that were lifted up, even though the planned tool for implementation is listed first, I think at the last meeting, at least my notes said that the highest priority was second tier testing.

And so, not losing the other elements on the list, I wanted to ask whether or not the Committee felt these would be a couple of working groups we could get started with, that would contribute to the knowledge work of the Committee, and I'll pause and let people think about that. Jeff?

DR. BROSCO: How do I get a chance to try to put that up, and get all three to balance? Jeff Brosco, I can make things easy for the follow-up and treatment as we tried to present yesterday, my colleagues from CDC. We as

federal partners have a sort of plan for moving forward that will includes folks, so my sense is that we probably don't need a separate ad hoc Task Force for that, that we can involve folks, and we have a way forward to try to implement that.

DR. CALONGE: Well, that makes it easy, so we don't need to do that one. How about second tier testing? Hi Kellie.

DR. KELM: Kellie Kelm, Committee member. Yeah, I mean I think the top two items, I mean I don't want to volunteer people because I'm rolling off. But I mean, I definitely think that there was a lot of discussion around this space, and it would probably be a valued product that people would like.

Because I also know there were some similar types of things, I think being worked on for the first thing that labs had available for the first bullet, so.

DR. CALONGE: Okay. Yes, Carla?

DR. CUTHBERT: I would agree with Kellie. Second tier testing is a very good approach to a good project to discuss for our groups.

DR. CALONGE: Melissa?

DR. PARISI: So, I have a - Melissa Parisi, NIH, I have a question for my laboratory

experts, and I'm reflecting on yesterday's comments from Susan Tanksley about counting conditions, and whether sorry -- whether that's an activity that should be taken up by a specific work group, or that can be addressed by other means, but it seems like that's also a high priority, and something that maybe should be addressed, and I don't know whether the laboratory standards and procedures would be the right group to consider that, but that seems really important.

And I'm wondering if other people think that that's also important.

DR. CALONGE: Well, I know that Susan is planning to bring this up in new business, and I guess I might look at her and say do you think the same group could look at both issues?

DR. TANKSLEY: So, Susan Tanksley, Association of Public Health Laboratories. I think that this topic would benefit from a cross section of experts, not just laboratory for certain and really needing the input of experts in the other areas.

DR. CALONGE: Shawn?

DR. MCCANDLESS: Thank you. I just want to follow up with what Susan said. That to the extent -- sorry, Shawn McCandless. Just so I'm clear.

DR. CALONGE: There you go. Use Janine's because the battery must be weak.

DR. MCCANDLESS: Thank you. Shawn McCandless, member. Just so I'm clear, the work groups are no longer going to be active, correct?

DR. CALONGE: That's correct.

DR. MCCANDLESS: For creating ad hoc groups to address topics, so I think that would address Susan's important point, the discussion around the counting should include a variety of different groups input. I would suggest that the secondary targets issue also be added to that ad hoc committee's work group, so secondary targets, counting conditions, and then what was the suggestion that that also be the same group that works on second tier testing utilization, or is that a separate group?

DR. CALONGE: I'm sorry. I thought you just said that they would be together, so I'm missing the --

DR. MCCANDLESS: I'm just not clear. To me it seems like best practices for utilization of second tier testing should be a second group.

DR. CALONGE: Right. Got it.

DR. MCCANDLESS: And an accounting, and the counting and secondary targets group.

DR. CALONGE: Right. And then what I

heard was that the secondary counting group needs to be cross sectional, cross expertise, whereas the best practices could be a laboratory led group.

DR. MCCANDLESS: Could be, but I think it would also benefit from --

DR. CALONGE: Oh, they always will yeah. All right. So, I'm sorry, Michele?

DR. CAGGANA: I'm Michele Caggana, member, which I always forget to say. I agree with Susan. I think APHL has made great strides for how many years this group? Two? I've been working on, and they've actually made quite a bit of progress in developing the framework, and so I think we need sort of two vet this through the entire Committee, rather than the group. Thanks.

DR. CALONGE: Great. That will be a successful ad hoc working group that will meet its charge within a 12-month period of time, which is what we're aiming for.

DR. CAGGANA: Yes.

DR. CALONGE: If the Committee is okay, we'll proceed with that group, and Jeff has said that he's already working on the blueprint, so. At this point I'd like to open things up for new business. I'm sorry, Melissa.

DR. PARISI: Can I just add one thing

to the blueprint for follow up with conditions, and I think this actually reflects the discussion that was initiated yesterday morning by Don Bailey and his colleagues. And if there is a way in which we can potentially build off of some of their work to bring early intervention into some of that blueprint for follow up, I think that might be something that would be a goal worth considering, and I'd love other people's feedback on that.

DR. CALONGE: Jeff?

DR. BROSCO: Yeah, it's Jeff Brosco. We already made a preface to figure that out. But it's down the road. It's a work in process.

New Business

DR. CALONGE: Great. I'd like to call on Shawn to bring up his issues of potential new business.

DR. MCCANDLESS: Thank you. Shawn McCandless, member. I think that one of the issues that I had mentioned has already been discussed, and there's been with the secondary targets and counting. The other issue that I had proposed we discuss is one that I've been thinking about a lot over the past two years, and that is related to the fact that newborn screening is a population based compulsory

public health system that every child is required to go through, essentially, in the U.S.

And every family that has a child that is required to go through, which creates a very high bar for both the evidence-based for decision making, and the requirement that we be incredibly thoughtful about all aspects of who will be impacted by the testing, and how they will be impacted.

And many of the things that come up really seem to be there probably are other opportunities for screening for conditions that would be valuable for a Committee whose charge is to think about inheritable disorders of newborns and children. There may be other times for screening that would not be compulsory, population based newborn screening, but would be very appropriate for some conditions and some targets.

And so, what I was proposing is that we have a discussion about what would be other naturally occurring opportunities for population based screening to occur on a voluntary basis that at least to start with on a voluntary basis, that we could also include in our discussion and thought processes, so that if a condition is proposed for newborn screening and the decision is made that it may not be

appropriate for newborn screening because of the high bar of evidence required, and the impact of the outcomes involved.

But that there may be another time for which screening would be appropriate for that condition that this Committee would then have an opportunity to say this is not appropriate for – we don't recommend adding this to the recommending uniform screen panel, but this would be very appropriate for screening at the one year well child check, or something like that.

So, the proposal would be that we develop a panel of other opportunities for screening so that there are then options for valuable conditions for screening, that maybe don't meet the high evidentiary bar that would be required for compulsory newborn screening.

DR. CALONGE: Thanks Shawn. And I have to say I was reminded during the lunch break that while Melissa is correct around the USPSTF, having a hard time with pediatric conditions is a completely separate process called Bright Futures, which has the same impact, in fact today has more of an impact because they weren't dismissed by a judge in Texas.

So Bright Futures, Shawn, to kind of your point, assures that recommendations made by

the Bright Futures Group actually have the same impact of a recommendation from the USPSTF in terms of funding for the testing of the follow-up. So, I only bring that up now first of all because I think it's important to recognize there is a separate process, and in some ways it would be a potential audience for recommendations around screening that could occur later in childhood, and so I'll just add that and then open it up for discussions, and I see Kellie has her hand up.

DR. KELM: Kellie Kelm, Committee member. I want to say that since I've been here 14 years, there was previously discussions and presentations at this Committee about thinking about screening at times other than birth, and maybe that's something that we can go back and look at, and I don't remember what came out of it.

But I think we had like, you know, a half day of some -- I don't know if anybody else remembers, but. Yeah, it was Don, so there you go. Anyway, it might also still be worthwhile to look back and see what we have previously discussed, and whether there are any outcomes there.

DR. CALONGE: Any other comments? Jeff?

DR. BOSCO: I think it's a question for

Shawn. Do you have particular things in mind, in your clinical experience and so on, that you were thinking boy, it would be great to screen for this at this time, or do you have some ideas already?

DR. MCCANDLESS: Yeah. I think something like Fragile X Syndrome would be a very appropriate thing to offer as a screen that would occur at the one year well child check because that's, you know, it's voluntary, so there's you know, that's a time when many families are concerned about their child's development, that their pediatrician may not yet be concerned.

So, it would give those families an opportunity to sort of drive the testing, and one could think about a lot of things like that. It's possible that Duchenne might be appropriate for one year -- for screening at one year of age, depending on how the data plays out in terms of the appropriate time to initiate therapy. It may be that that one is more appropriate. The other thought that I have is that this Committee could potentially help to drive the conversation around carrier screening, which I know has a lot of societal implications that, and maybe even some baggage associated with it, but the idea that carrier screening is

I believe going to become more and more important as we recognize that opportunities to treat many of these conditions, and I think Pompe, we now have very clear evidence that prenatal treatment is better than neonatal treatment.

I would be shocked if SMA doesn't end up in the same place. I think other conditions for which gene therapy is going to be appropriate are probably going to have significant advantages to prenatal therapy. And the opportunity for prenatal screening is the way we do prenatal carrier screening now is not good. It's very poorly counseled.

I think there are opportunities in the pediatric community to advance carrier screening during adolescent age visits that would be very appropriate, and empower young people to make sure that they have the knowledge they need for reproductive decisions later in life, so that we don't just focus on birth control, but focus on sort of long-term adult issues as well, that age group.

I recognize that there are issues about equity, who gets access to adolescent well child care, and other things, and those are all important considerations, but it just seems to me that off the top of my head adolescent well

child visits are an opportunity for carrier screening that this Committee could be advocating for, and making recommendations that might add to the conversation.

The one year well child check, lead poisoning and hematic screening are sometimes occurring, or have traditionally occurred would be two obvious opportunities.

DR. CALONGE: Natasha?

MS. BONHOMME: Natasha Bonhomme, Genetic Alliance. Just to give a little bit, because I think I've been to almost as many meetings as Kellie has, in terms of looking at more childhood screening, Don when he was on the Committee, did a lot of that work, and I can't remember who your co-chair was. But I think that Beth -- it was Beth, and that was an offshoot, I believe, of the Education and Training Committee, and I think there was a write up and a whole bunch that has been done on that, so it would be great to pull that, and the discussion. And I think, also, is that an opportunity maybe not to recreate that, but to see where that is, and to say what would we do next because I think that was a big thing.

A lot of thought went into that, and then I wouldn't say nothing happened, a lot happened. But just I think things happened

outside of the Committee, so I just wanted to call that out.

DR. CALONGE: Natasha, it's a very important point to recognize. A lot of really important things happen outside of the Committee, and we want to support those, and how those translate into heritable disorders of newborns and children. It's an important issue.

So how about the process would be to ask Don to help us identify what he did, and what's been done since then, and send it directly to Shawn McCandless, who will write up a set of slides for a proposal at the next meeting. Sorry, Jeff.

DR. BROSCO: I think it's a great idea. I was going to say that HRSA staff can also think about between maybe it's a presentation at our next meeting that would involve different folks.

DR. CALONGE: Shawn?

DR. MCCANDLESS: I defer to Dr. Brosco's proposal that the HRSA staff decide who's going to present, and if that's necessary. I would say though that it would be also valuable to -- we should probably think about who the other partners should be, AFP would be an obvious choice. The Academy for Family Practice would be an obvious choice, and likely

others.

DR. CALONGE: I also think, you know, reaching out to the Bright Futures process is important. It's a great process that actually was put in place to acknowledge the fact that the evidence based are for things like anticipatory guidance and some screenings in the pediatric population don't lend themselves well to methods that were specifically written around adults and RCTs.

I guess the one last thing I'll say, Melissa left, but you can get to the -- or a recommendation without an RCT at the USPSTF. There is a feeling that you can only get there with RCT and it just isn't the case, so I want to make sure people know that the world of research is broader than the RCT, although it's nice when you have them. Thanks. Okay Susan?

DR. TANKSLEY: Susan Tanksley, Association of Public Health Laboratories. So, I mean we've already talked about doing a work group on counting conditions, and including secondary targets, so I do want to stress I think that it should be a broad membership who is part of that work group.

DR. CALONGE: So, I suppose with that statement that it would be okay to start recruiting broadly for a work group whose

product would be a recommendation around counting conditions in uniform and structured approach. Yes Scott?

DR. SHONE: Just to add on to Susan. You know, I appreciate APHL bringing this to the forefront of the meeting, and also Michele and Shawn as Committee members vocalizing this. But you know, as a representative from ASTHO, you know the state health officials are going to play a critical role in making sure this happens uniformly across the country, and for all programs, whether they have a lab or not, right?

So, I want to pledge the support of ASTHO toward collaborate and work with APHL and in a broad swath of the community to make sure that this happens, and also collaborate with all of our partners across the different health departments to make sure that this can happen once this Committee makes a recommendation moving forward.

DR. CALONGE: Thanks. Natasha?

MS. BONHOMME: Natasha Bonhomme, Genetic Alliance. Like this is not me volunteering, but I think either as maybe not part of this work, but adjacent to it or right after really then saying how are we going to communicate this out? Because and I know a lot of times education and things gets added on to

the end, but that will be extremely difficult.

And I would say it's actually the communication around this that has also been a big push to have this Committee come together, and that that will take -- it's just not going to be easy, so I don't know if that would be another Committee, or bringing experts or what have you, but to really think that that's going to be a whole project upon itself. It's not just going to be an oh, let's update a website, so just to have that be in the mix.

DR. CALONGE: I appreciate that. Thanks for the comment, and as you put your tent up I was also thinking sure that we're -- no I was just, it just made me realize, you know, it's not unusual for the room to thin out on day two, which I recognize, especially when it's Friday afternoon.

And as we are thinking about recruitment for these groups to assure that interested member of the public, or interest groups know that we're doing this, and so we could have recommendations for potential interested members of the public, or interest groups.

And I know, I'm sorry, I feel that reading, looking at the website, and looking at announcements is one thing that happens, but a

structured outreach to those individuals who -- I see EveryLife is still with us, and Natasha, you're still with us. I've been thinking about how to make sure that those -- that the public, members of the public who have interests in these topics are aware that we're recruiting work groups.

And we have a process, which is Leticia, of gathering those names, and putting the groups together. Pardon me? Oh, Debra, I see you there.

DR. FREEDENBERG: I actually have to make a comment from the previous conversation. It's been up since then. I just wanted to say two things. One was that anything that would involve childhood screenings should absolutely, you should be involved in that discussion.

And then Marc may want to make a comment because ACMG has done a lot of work around the carrier screening issue, and I don't know if Marc wanted to make a further comment about that, or whether that would just be part of the joint opportunity.

DR. WILLIAMS: Thanks Deb. In our recently published carrier screening document we focused more on the methodology for how we would determine which conditions and screening were based on things like prevalence population, to

get away from some of ethnicity based screening approach to a more prevalence spaced offer to bring a little bit of rationality to a world where it often seems to be a selling point that more is better.

We did not specifically address timing, so I think the point that Shawn brings up is a good one and should be considered and lord knows there would be plenty of room to improve what we do for our adolescents and well child setting. Now the challenge, and I know the pediatricians in the room, and they had mentioned Bright Futures probably had a bit of a -- it's never been quantified like the Internists have, when they say we're supposed to do all the anticipatory guidance that was given in the internal medicine guidelines, and then take eight hours of visit. I suspect the same would be true for the Bright Futures recommendations, and so you tend to pick and choose, and I think that's part of the reasons that we see very spotty uptake in some of the recommendations for things like blood cell screening, and as you through Shawn, lab and those types of things.

We just don't do as great a job as we should because there's so much we have to get to. So, in some ways where screening becomes involved because it's the one time where we can

get everybody, which is not necessarily the best rationale for saying we should do things in that setting, but it is a pragmatic.

DR. CALONGE: Thanks. The next new business piece I'd like to bring up is the concept of reconsideration of a topic for which there's been an evidence review that is still fresh, and that the request for the nominators, or the evaluators has been to provide additional evidence in a specific area.

And my proposal for the group is that if those additional items are made available within a year of the prior Committee discussion, the entire evidence review would not have to be redone, only the new evidence would need to be incorporated into the discussion, into the review, the discussion and the vote, and that's those of us who know that that evidence is actually often rapidly changing.

This would keep from requiring gap analysis of the other evidence, and would provide for a much more I would say efficient and timely re-review discussion and vote for a specific topic, so I'd like to propose to the Committee that we adopt that approach to a rapid re-review in the setting of what I would call a fresh evidence review. Ash?

DR. LAL: I support that.

DR. CALONGE: And assuming that people would support that, I would entertain a motion and a vote. Oh, sorry. I'm reminded because we are a federal advisory committee. We cannot do what I just asked for, so what we will do is, we will put this on the agenda for our next meeting with a formal proposal and vote. Thank you, Debi, she's my conscious. I almost never look at her, but I was at this point, and I appreciate that.

So, yep, we have to follow the rules. So, we'll bring that up at the next time. Appreciate that. That ends my list of new business. Is there additional new business that the Committee would like to bring forward for consideration? Seeing none, I believe I can adjourn the meeting, and would do so.

I want to thank again everyone. Everyone who is not in the room, oh sorry? Oh, thanks, thanks, thanks, thanks. I could ask for a motion to approve the minutes. See I even wrote myself a note, but I ignored it. Is there a motion to approve the minutes?

DR. MCCANDLESS: Shawn McCandless. I move that we approve the minutes as provided this morning.

DR. CALONGE: Could I have a second?

DR. CODY: I second.

DR. CALONGE: Any further discussion? All those in favor of accepting the minutes please -- oh sorry, Michele.

DR. CAGGANA: I'm sorry. There's just a couple items that I sent in from what was provided yeah.

DR. CALONGE: Could you tell us what those were, sorry? So that we can approve it pending those revisions.

DR. CAGGANA: They were in the minutes. New York State began screening for Krabbe in 2006, not 2016.

DR. CALONGE: Okay.

DR. CAGGANA: I think you changed the one that had Hunter Kelly was eight and a half, but he passed away at that age. What else is there? The one case that was discussed was a false negative, not a false positive, with the psychosine that was low. Of course, now my computer is slow. And there was one more.

MS. MANNING: Michele, it was the one on page nine around the false negative.

DR. CAGGANA: Yes.

MS. MANNING: About the missed case?

DR. CAGGANA: Yes.

MS. MANNING: Okay. And I have these edits and will incorporate them.

DR. CAGGANA: And so, you got them,

okay.

MS. MANNING: Yes.

DR. CAGGANA: Okay.

DR. CALONGE: So, I just have to ask the mover and seconder, do you accept those changes?

DR. MCCANDLESS: Yes. I was just going to say I move to accept any sort of factual changes that were proposed in the meantime.

DR. CALONGE: Thanks.

DR. CAGGANA: Thank you.

DR. CALONGE: Now all those in favor please say aye.

CHORUS: Aye.

DR. CALONGE: Christine on the phone, if you could unmute, and Kyle unmute and just give us your vote, that would be so great.

DR. BROTHERS: Aye.

DR. DORLEY: I recuse to vote as I wasn't present for that meeting.

DR. CALONGE: That's a great answer, thank you Christine. With that the motion passes. Any further business? All right. Any other notes though? I declare the meeting adjourned, and look forward to our upcoming meeting in August, and thanks again for everyone who testified, engagement of Committee members, organizational reps, the passionate and

articulate, and moving testimony of those providing public comments.

And of course, the herds of staff that make the meetings possible, and Leticia, great job. Thanks everyone.

(Whereupon the Meeting of the Health Resources and Service Administration concluded at 1:20 p.m.)