THE ADVISORY COMMITTEE ON HERITABLE DISORDERS

IN NEWBORNS AND CHILDREN

IN-PERSON/WEBINAR

HRSA HEADQUARTERS

5600 FISHERS LANE

ROCKVILLE, MARYLAND 20852 (Pavilion)

Thursday, August 8, 2024

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P R O C E E D I N G S

Welcome, Roll Call, Opening Remarks, and Committee Business

DR. CALONGE: Good morning. I want to welcome everyone to the August Advisory Committee on Heritable Disorders in Newborns and Children in 2024. As we gather here in person at 5600 Fishers Lane, Rockville, Maryland, I want to open the meeting by taking a moment to acknowledge the land we gather on today.

We acknowledge that the land and water on which our meeting is taking place was and still -- is still inhabited and cared for by the Susquehannock Tribe, and the Piscataway peoples, including the Piscataway Conoy Tribe, and Choptico Band of the Piscataway Indian Nation.

We are grateful for their past and continued stewardship of this land, and we pay our respects to Maryland's indigenous community and their elders, past

and present, as well as future generations. And we are very excited today to welcome two Committee Members. That also means we're saying farewell to two more.

But let me start with our new member Robyn Sagatov -- I'll get it wrong, Sagatov. Dr. Robyn Sagatov, finally enough times, Sagatov will be the new Committee Member representing the Agency for Healthcare Research and Quality. She's a Senior Advisor for Children's Health in the Division of Priority Populations in the Office of Extramural Research, Education and Priority Populations at the Agency for Health Research and Equality.

She has over 15 years of experience in health research, with a focus on maternal and child health, and please help me welcome Dr. Sagatov. So that means we would like to thank Dr. Kamila Mistry from AHRQ for her services and dedication to this Advisory Committee for almost a decade, and Kamila, I wonder if you would just come up for a moment.

This is a HRSA service award --

DR. CALONGE: DR. MISTRY: Thank you.

DR. CALONGE: DR. CALONGE: And I don't know if you would like to say a couple of words. Thanks.

DR. MISTRY: Well, I will miss all of you very, very much, and this meeting has always had a special place in my heart in terms of the work that we do together. We've done a lot, and miles to go, so I'll definitely be watching, a little bit from afar, and also hearing from Robyn how everything is going, but welcome Robyn, and thank you all. It's a great opportunity, thank you.

DR. CALONGE: Robyn, I didn't give you a chance to make a comment if you'd like. You have to push the button.

DR. SAGATOV: All right. Is it working?

DR. CALONGE: Yes.

DR. SAGATOV: I just want to thank you for welcoming me to this Committee. I got to sit in on the

last meeting, and I was very impressed by all of the information everybody considers for, you know, these meetings, so thank you for the opportunity.

DR. CALONGE: We're looking forward to working with you, and thanks for being here. Next, I'd like to turn to Jeff Brosco. You're probably familiar with our next new member. He'll be serving as a Committee Member for the Health Resources and Services Administration. Jeff is a pediatrician and historian who serves as the Director for the Division of Services for Children with Special Health Needs, or DSCSHN, in HRSA's Maternal and Child Health Bureau.

He also teaches and practices developmental behavior of pediatrics at the University of Miami, where he contributes to scholarship through UM's Institute for Bioethics and Health Policy. As the DSCSHN Director, Dr. Brosco leads an interdisciplinary team, tasked with ensuring that every child in the U.S. receives the services they need to play, go to school, and grow up to

be healthy and productive adults.

So, welcome Jeff. Do you have a comment or two to make in your new role?

DR. BROSCO: No.

DR. CALONGE: A man of few words. That means we would like to just pause and thank Dr. Michael Warren. He's not with us today, but he, you know, served as the Committee Member for a number of years, a very valued proponent and supporter of the work of the Advisory Committee on Heritable Disorders in Newborns and Children.

He will continue to support us in his role with the Secretary and the Administrator, and we really do appreciate what he's meant to us. Jeff?

DR. BROSCO: This is Jeff Brosco. I just want to say a word about Dr. Warren. He has vast responsibility across the entire Maternal Child Health Bureau, and I will tell you he is deeply involved in what happens in this Committee. When we go to brief

him, he's usually briefing us.

He's been through every page of the briefing book. He knows exactly what's going on. He is absolutely going to be continuing to be part of this, so when Debi and I meet with him, he always wants to know what's happening in the Committee. He always has ideas, and he will continue to be very involved.

DR. CALONGE: Thanks, Jeff. We also have a new member in our Organizational Representative group, someone who is a familiar face, I think to many people who work in newborn screening, and members of the Committee and staff. Amy Gavigilio, is a certified genetic counselor, and founder of Connetics Consulting, LLC.

It provides newborn screening, public health genomics, and rare disease services in the U.S. and globally. Amy has worked in the newborn screening and rare disease space for the past 17 years. She currently works with the Association of Public Health

Laboratories, Expecting Health, RTI International, and several other rare disease and genomic organizations, as well as the CDC.

Amy also serves as the Chair of the NBS Expert Panel for Clinical and Laboratory Standards Institute, and is currently the Chair of Minnesota's Rare Disease Advisory Council, and is joining us as a new Organizational Rep for the National Society of Genetic Counselors. Any comments you'd like to make, Amy?

DR. GAVIGLIO: No. Just to say thank you, and I'm honored to be in this role, so thank you.

DR. CALONGE: And again, thanks for making the trip and joining us, and we look forward to your participation. That means we are saying goodbye to Cate Walsh Vockley, who is yeah, she's --- there she is, hi Cate. She has served as the National Society of Genetic Counselors, Organization Representative for I think more than a decade, and I think she's moving on off the

Committee to see what in my note says, "some more enjoyable things." It's just hard to believe what that may be. -Cate, do you have any comments for us today?

DR. VOCKLEY: My more enjoyable things is I'm planning to retire at the end of the year, so I thought it was time to pass the torch. I have really enjoyed my work with the Committee. I especially enjoyed working on the Education Subcommittee when that existed. I'm really enthusiastic about the work currently being done to include lived experiences in the deliberations about additional conditions, and I wholeheartedly support Amy's addition to the Committee.

She's done so much work in newborn screening, and I think will really be a terrific addition, so thank you all. It's been a wonderful experience.

DR. CALONGE: Thanks Cate. That's all my introductory comments. I'd like to call Leticia Manning to the podium to do a roll call and go over some logistics, and point out where everything is.

COMMANDER MANNING: Thank you, Ned. Welcome everyone to rainy D.C. in August. It's a lovely time. So, we're going to start off with the roll call, and just acknowledge that you're here when I say your name. Michele Caggana?

DR. CAGGANA: Good morning, I'm here.

COMMANDER MANNING: Ned Calonge?

DR. CALONGE: I am here.

COMMANDER MANNING: From the Centers for Disease Control and Prevention Carla Cuthbert?

DR. CUTHBERT: I'm here.

COMMANDER MANNING: From the Agency for Healthcare Research and Quality, Robyn Sagatov?

DR. SAGATOV: Here, thank you.

COMMANDER MANNING: Janine Cody?

DR. CODY: Here.

COMMANDER MANNING: Christine Dorley?

DR. DORLEY: Here.

COMMANDER MANNING: From the Food and Drug

Administration Paula Caposino?

DR. CAPOSINO: Good morning. I am here, I'm virtual today.

COMMANDER MANNING: From the Health Resources and Services Administration, Jeff Brosco?

DR. BROSCO: Present.

COMMANDER MANNING: Jennifer Kwon?

DR. KWON: Hi, I'm looking at the blank spot where I should be sitting. I am here, and I'll be really present in the afternoon.

COMMANDER MANNING: Thank you. Ash Lal?

DR. LAL: Here.

COMMANDER MANNING: From the National Institute of Health, Melissa Parisi?

DR. PARISI: Here.

COMMANDER MANNING: And Chanika Phornphutkul?

DR. PHORNPHUTKUL: Here.

COMMANDER MANNING: Okay. And now, I'll do a

roll call for the Organizational Representatives. From the American Academy of Family Physicians, Robert Ostrander?

DR. OSTRANDER: Here.

COMMANDER MANNING: From the American Academy of Pediatrics, Debra Freedenberg?

DR. FREEDENBERG: Here.

COMMANDER MANNING: From the American College of Medical Genetics, Mira Irons?

DR. IRONS: Here.

COMMANDER MANNING: From the American College of Obstetricians and Gynecologist, Mara Black? Okay. From the Association of Maternal and Child Health Programs, Sabra Anckner.

DR. ANCKNER: Here.

COMMANDER MANNING: From the Association of Public Health Laboratories, Susan Tanksley?

DR. TANKSLEY: Here.

COMMANDER MANNING: From the Association of State and Territorial Health, Scott Shone?

DR. SHONE: Here.

COMMANDER MANNING: From the Association of Women's Health Obstetric and Neonatal Nurses, Katie Swinyer?

MS. SWINYER: Good morning, I'm present, it's Katie Swinyer.

COMMANDER MANNING: Swinyer, thank you.

MS. SWINYER: Thank you.

COMMANDER MANNING: From the Child Neurology Society, Margie Ream?

DR. REAM: Here.

COMMANDER MANNING: From the Department of Defense, Jacob Hogue?

MR. HOGUE: Here.

COMMANDER MANNING: From the Genetic Alliance, Natasha Bonhomme?

MS. BONHOMME: Here.

COMMANDER MANNING: From the March of Dimes, KJ Hertz? From the National Society of Genetic Counselors, Amy Gaviglio?

DR. GAVIGLIO: Here.

COMMANDER MANNING: And from the Society for Inherited Metabolic Disorders, Sue Berry.

DR. BERRY: Here.

COMMANDER MANNING: Okay, thank you. That is roll call. Now, I'm just going to go over a few housekeeping items. So, according to FACA, which is the Federal Advisory Committee Act, all Committee Meetings are open to the public. If the public wish to participate in the discussion, the procedures for doing so are published in the Federal Register, and/or are announced at the opening of a meeting.

And so for this meeting it was published in the Federal Register. Only with advance approval of the Chair, or the Designated Federal Official, which is myself, may public participants question Committee

Members or other presenters. Public participants may submit written statements, and we did receive several written comments that were provided to the Committee in advance.

As a reminder, it is stated in the Federal Register Notice, as well as the registration website, that all written, public comments are part of the official meeting record and are shared with Committee members. Any further public participation will be solely at the discretion of the Chair, and the DFO.

In regards to ethics and conflicts of interest, I must remind Committee Members that you must recuse yourself from participation in all particular matters likely to affect the financial interest of any organization, with which you serve as an officer, director, trustee, or general partner, unless you are also an employee of the organization, or unless you have received a waiver from the Health and Human Services authorizing you to participate.

As is the case today when a vote is scheduled, or an activity is proposed, and you have a question about a potential conflict of interest, please notify me immediately. So today we are all here in 5600 Fishers Lane. Visitors only have access to the fifth floor, and even though we entered on this floor, it is considered to be the fifth floor.

There is a cafeteria across the way here. There are restrooms behind us on both sides, and in front of us on both sides of the building. Visitors are not allowed to take videos or photographs in the building. If you need to leave and re-enter, you will be required to go through security screening again, so we really encourage folks not to leave.

But if you need to leave, please notify HRSA staff, we're located all around here, and someone could escort you in and out of the building. During an evacuation, please exit the conference room, and exit out the way you entered through that way there. You'll

see people headed to a parking lot kind of across the way, and that's where we'll wait until we're informed that we can enter -- reenter the building.

Okay. For those of you that are joining us virtually, audio will come through your computer. You're able to speak through your computer microphone. If you are unable to access the audio, or microphone through your computer or conference line, I mean please use the conference line that was sent to you via email. Also, in order to aid the logistics part of the meeting, when you are speaking virtually please turn your camera on and use the raised hand feature.

If you're having technical difficulties, try reopening the webinar using a different browser, and if you still have technical issues, please refer to the contact information provided in the registration confirmation email that you received previously. Okay. And this is just a screenshot of how to access the closed captions icon through Zoom.

And the last thing that I want to go over is many of you are aware that we recently funded a new grant program titled the Cooperative Newborn Screening System Priorities Program, or NBS Co-Propel. We've provided over three million dollars, where it was awarded to states, and this program builds on the Newborn Screening Propel Program to ensure all babies receive better screening and care, and it shares the same goals as the NBS Propel Program, but it allows states to partner as a region to apply for funding.

So, this is a map displaying the Propel states as well as the Co-Propel states. And the striped states that you see on the map are states that are consortium states, so they receive funding, even if it's not direct funding through the consortium. And so, we are very excited about this newly awarded grant opportunity. Thank you, Jeff?

DR. BROSCO: Yeah, this is Jeff Brosco.

COMMANDER MANNING: Just grab another mic.

DR. BROSCO: All right. So this is Jeff Brosco. I just wanted to reiterate that the whole idea with the Propel and Co-Propel grants is to make sure that we are fulfilling the promise of newborn screening, and the three objectives of these are to help states with taking on new conditions that we add to the RUSP there to help states with the quality indicators for timeliness, and help states start looking at long-term follow-up more generally, so something this Committee has been talking about for over a decade.

So, we are really thrilled to be working with states and other partners to be trying to make sure that all the things that happened when screening continued through that child's lifespan. Thank you.

COMMANDER MANNING: Thank you. And now I'm going to turn it back over to Ned.

DR. CALONGE: Thanks Leticia. And so, I think we've talked about in previous meetings, I wanted to remind you that the National Academies of Sciences,

Engineering and Medicine is conducting a study examining the current landscape of newborn screening systems and processes. The research will also consider sustainable adoption of screening for new conditions, using new technologies.

The last open meeting was on May 16, 2024, and the proceedings of that meeting are accessible online, as well as other past open events. To stay up to date with the study please use the QR code, which I think is on a slide -- two slides from now. There it is. And using that you can go to the website and keep up with it.

The other things I would say is the NASEM website, I'm active with NASEM, it's a wonderful website. You can just put in NASEM, and then what you're interested in, and it will come right up. Next slide please.

I'll just say that the Health Resources and Service Administration's Maternal and Child Health

Bureau maintains the Newborn Screening Information Center website. In a future meeting we'll have a presentation that will provide more details about the NBSIC, and you can use this QR code to find out more as well.

But you can see things that we have for both parents and providers, why screening is important, where and how it happens, what happens during the screening process, and then information on how to understand screening results.

A lot of people I think in this room have contributed information that is summarized in this information, and I want to appreciate those other efforts, those other websites, and those other nonprofit organization that have been doing this work for so long. There will be ongoing updates to the website, and I encourage you to check it out periodically.

ACHDNC Nomination and Evidence Review Process

DR. CALONGE: I want to pause and just give an update on some condition nominations. Between May and June we received two condition nominations, using our new nomination process, which I'm going to discuss in the next presentation. Metachromatic Leukodystrophy completed the preliminary nomination in May, and the full nomination package in June.

That's been reviewed, and we will discuss the MLD nomination in-depth tomorrow, and include a vote. In June we received a preliminary nomination for Biliary Atresia. In September we received a nomination package for Biliary Atresia, with the lead nominator for the application, BARE, or BARE, Inc., which is the national nonprofit organization that supports Biliary Atresia research and education.

You are aware that Biliary Atresia is a congenital liver disease characterized by the obstruction of the extra hepatic bile ducts, and

impaired bile flow out of the liver. The Nomination and Prioritization Workgroup reviewed the preliminary nomination form and determined that it does not meet the full requirements to move on to step two, which is completion of a full nomination package.

Last week Leticia and I met with the Biliary Atresia nominators to discuss their nomination, provide some guidance on what we felt was needed to help move it forward, and will be available in an ongoing method -- ongoing manner to provide technical assistance as requested.

And then during the last meeting I would remind you at the request of the nominators the Committee paused the evidence review for Duchenne's Muscular Dystrophy. Moving on to the May 2024 meeting summary. I want to thank the Committee members who reviewed the summary and provided additional edits, so we have those comments, we're going to revise those, distribute them tonight, and vote on them to adopt them

tomorrow.

To kind of give you a roadmap of today, we have presentations on the revised nomination process, and the revised decision matrix tool. Then I'm going to summarize our prior presentations the Committee has had to highlight research that is focused on lived experiences.

We will have a brief presentation and discussion on a method for a standardized reporting of newborn outcomes, and after lunch we'll have our last presentation today related to population-based screenings for newborns and children. Tomorrow, we're going to start the morning with public comments, then we'll have a presentation from the Nomination and Prioritization Workgroup on Metachromatic Leukodystrophy, and we'll end the meeting with updates from the Naming and Counting Conditions Ad Hoc topic group.

So, that's a roadmap of what we're going to

try to get through in the next couple of days, and again, I appreciate you being here and your participation. So, if we could start by getting up the first set of slides for the nomination and evidence review process.

You remember that in November of 2023, we paused the acceptance of condition nominations while we made revisions to the process. We received feedback from various stakeholder groups during small group listening sessions in November of 2023, and from the rest of the public through a Federal Registry notice that closed in April of 2024.

We had a Committee discussion about the process during our May 2024 meeting, and I wanted to take time today to summarize the new nomination and evidence review process. So, to give you some background on how we got to where we are, we know that nominations from different groups, and for consideration for addition to the RUSP are critical to our work.

But we recognized in talking with the nominators that there's challenges. They have a burden in making compelling and comprehensive cases for adding a condition to the RUSP, which requires a tremendous amount of time and effort and resources.

We also know that we use a language that's not normally totally accessible to all members of the public, and so trying to figure out to translate how we talk about evidence and newborn screening in a way that's more approachable was another important issue.

So, our goal was to simplify the process for nominators, and maintain a central role that nominations have for evidence review, and our recommendation process. The next slide please. So, we have feedback from groups of five recent and current nominations. We've discussed these at two previous meetings, a small group listening sessions in November of last year, and a large group discussion in January this year.

We had input from our former standing

workgroups, Follow-Up and Treatment, Education and Training, and Laboratory Standards and Procedures. And then we had public comment as I said, in respect to the Federal Registry request for information between March and April of this year. Next slide.

So, what we tried to do, and what we have done in terms of making the process simple is to start with a pre-nomination process. So the condition nomination group would complete the preliminary nomination form, which there's a link to on the slide set, and can even be found on the Advisory Committee's website, consists of the following four questions: Is there a newborn screening test available? Is there agreement about the case definition of the targeted condition and diagnostic confirmation after a positive newborn screen? Is there a prospective population-based newborn screening project that has identified at least one infant with the condition? And then lastly, can identification of the target condition before clinical

presentation allow provision of effective therapy, and improve outcomes for screen infants? So, those are the four questions.

If there is a yes to each question, and on review by the Nomination and Prioritization Workgroup, there's agreement that yes is the correct answer, the nominators are asked to submit --- oh, I'm sorry. In addition to that they are to submit- one to three peer reviewed references for each question with a brief explanation.

This helps us understand whether there's enough evidence to move to a full evidence review, but I want to point out it doesn't replace a full nomination package, or a full nomination review. So the idea is that can we simplify the front end, and then provide technical assistance in guidance to the nominators, and then all with the intent of moving them closer to having a packet that might be forwarded to full evidence review.

I always like to pause and say full evidence review doesn't mean the condition will be added to the RUSP, it means there will be a full evidence review that the Committee will determine in making its decision. Next slide.

So, the N&P Workgroup is selected by the Committee Chair, and consists of selected Committee members. The Workgroup reviews a preliminary nomination form, verifies it meets the four requirements to be considered for review, and then the Designated Federal Officer, Colonel Manning communicates the N&P's findings to the nominators.

Nominators are encouraged --- Commander, not Colonel, I'm sorry. Commander Manning. I just love saying that, Commander Manning. Nominators are encouraged to meet with the Committee Chair and DFO to discuss next steps which may or- may not include the completion of the full nomination package. Next slide please.

Once the form is verified by the N&P Workgroup, we then ask for the full package. Those sections include the condition screening, impact of screening, other considerations not captured in previous categories, and a more extensive set of references. Next slide.

The N&P Workgroup then reviews the full nomination package, and creates a summary for the Committee's assessment, shared with the Committee at a Committee meeting, and then the Committee votes on whether or not to move the condition forward to a full evidence review.

So, let me just pause, and sorry -- I'll- use MLD as an example. First of all,- I appreciate the work with MLD in piloting this new process. We learned a lot. There was a good dialogue back and forth with the nominators that helped us do this. So, we got the preliminary form. We reviewed it, we chose to move it on to full evidence review.

We got the complete package prior to this meeting. The N&P Workgroup has looked through it. We'll do a presentation tomorrow, which we're looking forward to hearing, and at that point the Committee will vote for the next step in the process, which would be to move or not move MLD on to a full evidence review.

At that point the topic goes into full evidence review with our contracted evidence review group, which puts together a Technical Advisory Committee that includes members of the public, and advocates for the condition, as well as Committee members and other potential experts.

We go through a full review that's been presented to this Committee where we make the decision about whether or not to add it to the Recommended Uniform Screening Panel. We'll talk a little bit about that, the decision-making step today as well. Next slide.

These are just the criteria for a full

evidence review, so these are the questions that are included, and these are available to folks, and I don't think I'm going to read through it today. Next slide.

Committee Discussion

DR. CALONGE: So, I'm going to pause, and just open the floor for discussion from other Committee members, other questions and other comments. We'll also take comments from our organizational reps, but I want to start with Committee members. Jeff?

DR. BROSCO: Just --- this is Jeff Brosco, just one quick comment. As Ned described, we heard from the five previous nominating groups, a huge burden for filling out the long nomination form. So- the idea of the two steps was it's relatively easy to do a quick nomination if you just have the evidence, and get back to you quickly, so you don't have to do the whole thing if there's something that's not going to let you move forward.

The concern was well, if we had a two-step process is that going to make it so long that nomination has to go through a lot more work. And I think in the case of MLD, it didn't slow things down. And in fact we were able from between May and tomorrow, to be able to vote on that, so I think this worked about as well as we can hope, but there's always this balance between how much information up front.

And just for folks to know that for the last decade, the N&P Workgroup, the N&P Advisory Group that the Chair chooses, there's a lot of back and forth with the nominators, and so this just makes it much simpler, and gets to the key points sooner. So far it's working well, but we're open to change I'm sure.

DR. CALONGE: I like the concept of continual quality improvement. Thanks, Jeff. Ash?

DR. LAL: Thank you, and I do appreciate, and I support the change in having a separate nominating vote. I think to me, apart from the downside of

prolonging the process, but the main up side to me is the preliminary review may identify certain areas that require more focus for the full evidence review package, and that could be tremendously helpful in eventually keeping things in a reasonable timeframe of the back and forth that may happen after the evidence review is being done. Thank you.

DR. CALONGE: Thanks, Ash. Christine?

DR. DORLEY: Yes. So, it would be great to hear from the MLD people regarding the use of the form, how they found it to be user-friendly, or not user-friendly, and what would be even more beneficial is if you had someone who nominated a condition before with the old process, and then they nominated with the new process, what the difference is, and if they found it to be any easier, just curious.

DR. CALONGE: So, great questions, and we have actually, and we've talked with MLD a lot, Christine, and everyone who participated in those calls

about the process, and how we can make it better. There was a little back and forth about the issue about explaining what the evidence is telling us, adding a little bit more comments to help guide the N&P, the preliminary review group.

I think MLD is the one condition who had an almost completed nomination package ready to go, so I think that was really good feedback to have, so that's our one group that had both, an old process, nomination ready to go, and the new one. And other than that little, I think the pause, plus filling out the form, they were ready to do it because they had all the information on the four questions, and we'll have to kind of keep asking people as we go forward.

I would say we pilot the process, continue using the process for one or two more nominations, and then go back and look at the process, see what works, what didn't work, are we asking the right questions, and then do revisions as we go forward.

Let me turn to the Organizational Reps, and I think I have Natasha first.

MS. BONHOMME: Thank you, Natasha Bonhomme, Genetic Alliance. For on the slide that talked about the four questions, the third one basically being about finding one child through newborn screening. Is that U.S.-based? In the U.S.-based newborn screening program, or can it be international?

DR. CALONGE: Thanks for the question, Natasha, and it's not specified, so I would think that either would be acceptable. And if I recall right, we have accepted international population-based so, yeah.

M. BONHOMME: Right. I know it's been a question in the past, that's why I bring it up. So when this is put on the website will that be clarified, so people know about that.

DR. CALONGE: We will clarify that. Thanks for that recommendation. Amy?

MS. GAVIGLIO: Yeah, thank you, Amy Gaviglio,

National Society of Genetic Counselors. So, I think there are potentially in the pre-nomination form two areas where further clarification, somewhat akin to what Natasha just mentioned would be helpful. I think the first is the question around whether there's a newborn screening test available.

Will the Committee examine tests that are either in a non-dry blood spot matrix, or a point of care, and if so, are there any additional components that need to be addressed by nominators? And then the second is also on the third requirement, and I think given that the achievement of a perspective pilot detection is likely to be one of the limiting factors for most upcoming conditions, it would be good to be much more clear on what exactly this requirement is providing the Committee in terms of evidence.

And I think saying that it tests the system is just simply not concrete enough, especially understanding that to achieve this requirement we have

historically had to rely on data that has come about from actually circumventing the RUSP process. I think we should also acknowledge that the detection of a single case in a single environment on its own really doesn't test the system, as we know that each family's experience with the system is really dependent upon their own individual environment.

And so, I think if a single detection through a prospective pilot is going to continue to be a foundational requirement for a nomination, I would ask the Committee to take the time to reflect on what information that truly provides, and really be abundantly clear about that to the public.

DR. CALONGE: Thanks, Amy. And we have in the last two meetings extensively discussed this issue, so I think adding a little bit more information about the importance of it could be beneficial to the form. And your other point was -- sorry, what was the first?

MS. GAVIGLIO: Just clarifying whether tests

that occur in a non-dry blood spot matrix or point of care, those would be examined, or if anything further would be needed from nominators nominating a condition using something other than a dry blood spot matrix.

DR. CALONGE: So, this is another area of ongoing discussion because we're looking at charging states and newborn screening programs, usually laboratories to do testing, and they don't have strategies for point of care testing, and so trying to decide a route for recommending universal screening for something that doesn't involve a state health department or state laboratory, is something that we're actively discussing.

We have experience, you know, from that first one from 2011, which I remember very well, which was congenital ---- cyanotic heart disease, which requires an onsite pulse oxy. And states have managed to implement that in ways that don't require the laboratory because the laboratories aren't onsite.

Hearing, of course, started that as well. I think charging the state public health system with figuring that out gives you 50 unique challenges, and so we have started discussions, myself and staff, about thinking about other approaches, especially the point of care studies because the state laboratories do well, very well, extremely well when they can test with the dry blood spot. Thanks. Other questions? Yeah, Michele?

DR. CAGGANA: Hi, Michele Caggana, Committee Member. Yeah, following-up on that I think it's really incumbent on the Committee and the community as well to come up with a mechanism in order to also influence pediatric care because the Committee is Heritable Disorders in Newborns and Children, and so that was used as the argument for some of the other conditions that were a point of care, but I think we need to think broader on how to make these recommendations outside of newborn screening as well, and more on the pediatric

setting.

DR. CALONGE: I actually know what you're going to say, Jeff, but I'm going to let you say it.

DR. BROSCO: I think what we're both going to say is that it's part of what this afternoon's discussion is about, to talk about what are some of the other mechanisms for setting the standard of care besides the public health laboratory being responsible.

DR. CALONGE: I'm sorry, Sue?

DR. BERRY: Thank you, Sue Berry for the Society for Heritable Metabolic Disorders. We didn't talk about this, and it's not included in this, but one element in this that I think has major impact on public health, and on the health of the children is access to care for treatment for a screened disorder.

So that for example, if only six centers in the U.S. are available to do a specific gene therapy, and that's not going to be widely available in every state, how are children who are on Medicaid in one state

going to be accepted for care in another state? And that's a tremendous barrier, a huge source of injustice, and lack of equity that we're going to have to address somehow.

I don't know if the Committee is really the venue for that, but it's a point of real sadness for me to see that happen.

DR. CALONGE: Jeff, I don't know if you want to make a comment?

DR. BROSCO: I think my comment is that this might be a really good topic for a future discussion, and we can think about who might be good presenters to talk about how it's worked at other place because it surely is not the first time that a child has needed out-of-state treatment of some sort.

And so, learning what states have done, what's been successful might be a good thing for this group to think about.

DR. CALONGE: Scott Shone online?

DR. SHONE: Thank you. I wanted to go back to Natasha's comment for clarification on the U.S. population. So, historically when the recommendation was originally made, I believe that it was perspective data from a population similar to U.S., and I can remember a conversation with Dieter Matern where he acknowledged that he wasn't a demographer but was pontificating on the proposed population that was being discussed under the nomination. That's why this is sort of engrained in my memory.

And so, I do --- so, what I want to say is that I agree with Natasha that if that position is going to change, that should be clarified quite clearly in where -- on the Committee's notification on this, and so it felt like when you said that no, we'll accept international, that's a little different, and not as nuanced as I think the Committee has said previously, so I just- ---- I'm not asking you to articulate that now, but I do think it needs to be clarified if the historic

language is being maintained, then that should be clarified if it's going to be changed a bit. I would appreciate that as well.

DR. CALONGE: Yeah, I appreciate that Scott, and I think it actually gets to Amy's point as well, that the information that we get from finding a single case is that kind of tests the feasibility and approachability of the system. And so, the setting in which it occurs has to provide us with that information.

And so that has those nuances about what was the setting. From my standpoint, from the population issue, the other things that could change would be the prevalence, or incidents of the condition, which we take into account in other ways, and so I think the issue about understanding how it can be done, and is going to be done through a newborn screening system similar to that in the United States is the information that's important, and I think we can clarify that. Scott, I'm sorry Jeff?

DR. BROSCO: Jeff Brosco, and just to clarify more generally that the moving to a two-step nomination process and changing the questions a little bit was not meant to change in any way, shape or form the criteria, right, it's still the same that we've been doing, but trying to clarify.

So, it's not a change in the population, or in anything else as far as I can tell.

DR. CALONGE: Debra?

DR. FREEDENBERG: So, in considering treatment of the conditions that are detected, and kind of expanding the thought process about that, I think there needs to be some consideration of the unique conditions that are being identified, but also the extraordinary cost of treatment of these conditions, and you know, Sue brought up the question of equity, is rather large.

And, you know, part of what I'm referring to is the cost of gene therapy, which you know, who bears

that burden? Where is that responsibility to make certain that it's equitable and available to all? And also, from the pediatrician standpoint, you know, what is going to be their role in expanding the full-scale care of children with these conditions?

DR. CALONGE: Thanks, Debra. Melissa?

DR. PARISI: Melissa Parisi, NICHHD. I just had a comment about the recent discussion around ensuring that the one identified individual, newborn, is actually from a country or a setting that is similar to the U.S. While I agree that having it be a similar newborn screening setting, I would certainly not expect that the diversity in the United States needs to be replicated in another pilot program in another country.

For example, if a condition is more prevalent because these are usually recessive disorders, in a Scandinavian country, or an Asian country, I mean it would be ideal for those pilots to be done in those countries where they're more likely to pick up an

affected individual given that our bar is so high of expecting at least one identified newborn, so I just wanted to make that point, thank you.

DR. CALONGE: Thanks, Natasha?

MS. BONHOMME: Great, thank you. Natasha Bonhomme, Genetic Alliance. Kind of building on some of the comments that have been said. When we've spoken to groups who have gone through the nomination process, so often it hasn't necessarily been just the form that has been a lot, but really getting to that point, to really building that evidence as Amy said.

That that's really what's been burdensome, and some could say not equitable, because different groups have different resources and things like that. So, I guess I'm just wondering thinking of the next phase of this broader conversation of making the nomination, I want to say process, because I don't want it just to be the forms, but you know, the activity of nominating a condition as accessible as possible.

You know, what is the Committee thinking in terms of helping, which can means lots of different things, organizations and groups who want to be able to develop that data, and to develop that evidence base. It is more conversations with NIH, who has oftentimes supported pilots? Or is it not seen as within the purview of the Committee to help because I can't think of another word, organizations before they get to the point of being able to fill out that form?

Just trying to get a better sense of that, that bigger picture.

DR. CALONGE: Well, I can speak as a Chair, and less as a Committee for this particular issue. I think the Committee has the resources it has, and then we have the time to commit to the process we have. And we have a defined purview. I think moving from our position of evidence receivers, nomination receivers, to evidence creation, I don't currently see within the purview of the Committee.

We do work actually well with both our partners at NIH and CDC. I just want to make sure I put CDC in there because they've been a good funder and a good partner in the area as well. And they listen, and they make contacts as well. We would need to talk I think extensively with HRSA and leadership about whether or not we wanted to extend into being more purposeful, or a bigger part in that process of evidence creation.

MS. BONHOMME: Yeah, and just to add to that, I guess I wouldn't even say necessarily the creation of, but just the support of, which can come in lots of different ways, which I do think the Committee has done, and yeah.

DR. CALONGE: I think we can do that, yes. Yeah. Appreciate the conversation. We'll take these comments back. We've had some good suggestions about clarification on the form, clarification on the process, and we'll move forward. Appreciate that. And again, it will be in the meeting notes, but the idea that we might

take two or three conditions through the process and then re-examine it for continued improvement.

Not that we won't make changes as we go along because we learn with every nomination, but make sure that we take an appropriate look after we've done it a couple times.

ACHDNC Decision Matrix Tool: Public Health System Assessment

DR. CALONGE: So, at this point I'd like to move on again to the decision matrix and the next slide set.

Hopefully, a lot of this you will have seen before. Next slide. Remember that the matrix tool is to support decision making. It doesn't make decisions, so it's not rote, it is not formulated, it's supposed to help the Committee think through the evidence and support our decision and voting on whether or not to add, or not to add a condition to the RUSP.

Next slide. Here is a draft that we would like to vote on today, and you've seen it at least twice. There's a top part, which is just a description of the letter grades. There's a letter grade description and action in the middle piece, and then a public health impact assessment at the bottom.

The public health impact assessment is required by statute, which is why it appears on the matrix. Next slide. To review the top piece, conditions with eight designations will be forwarded to the Secretary with the recommendation to add to the RUSP. Conditions with the B designation may be forwarded to the Secretary with the recommendation to add to the RUSP after discussion and a separate vote.

Conditions with a C designation will not be forwarded to the Secretary, but evidence gaps will be identified and shared with the nominators, and conditions with an I designation will not be forwarded to the Secretary, but, again, gaps will be identified

and shared with the nominators.

Let me just pause and say if you are a B designation, and isn't forwarded, those also will be discussed in terms of evidence gaps with the nominators. Next slide. So, turning to the B designation, which is probably the most substantive change to the matrix for the top part, based on assessment of the magnitude of net benefit, and the certainty of net benefit, the Committee will vote to assign a B designation.

There will then be additional discussion of the evidence and assessment of the anticipated impact of adding the condition in terms of the individual family and public health benefit, so then the Committee would take a separate vote on whether to recommend adding the condition to the RUSP.

This separates agreement on the evidence from agreement that the condition should be added to the RUSP, and I think will be the source of very vigorous conversations. I want to just review that B rating

talks about moderate certainty, and in the certainty world as you look at grade, and you look at the USPSTF and the AHRQ's process, moderate evidence means that we're --- there is a chance that future evidence could come up with- a different decision.

There's a change that future evidence will just confirm the certainty, and so that moderate certainty means it's in that kind of gray area where we can't move it into an A recommendation based on some kind of gaps in the evidence, and uncertainty that future research could fill in in one way, moving up to an A, or another moving it down to a C. Next slide.

So, we have two areas of judgment, certainty of net benefit, and magnitude of net benefit. Again, certainty of net benefit has well-established approaches. When you look at those sources I talked about they actually talk about the certainty of the evidence in terms of risk of bias, precision, size of the effect, coherence, a lot of criteria that go into

the kind of evaluation of clinical trials evidence, and definitely have been used in the screening world by the USPSTF and the Canadian Task Force on Preventative Services for a number of years.

The magnitude of net benefit is more complex, especially in setting the levels of new benefit, substantial net benefit, and what's moderate net benefit. And the net benefit means we have considered the harms and the magnitude of the harms in the context of the benefits and the magnitude of the benefits, and it's like a virtual subtraction of the two trying to say that overall we think there's a lot of net benefit, or a moderate amount of net benefit.

And, that is an experiential discussion for the Committee as we go forward, and that's why you have votes that are not all or that are not unanimous in one direction or another, and it's one of the important reasons why the varying experience of the people on the Advisory Committee is so important in decision making.

Next slide please.

So, we've agreed on that matrix, that part, the top part, and now we've been working for the last, oh three or four meetings on the public health impact assessment. Next slide. So, this is what we're proposing today from a process standpoint. I want to point out that we're --- we- want to gain experience with doing this, and so while I'll outline a way to do it as we actually implement it, we may make some tweaks to it going forward.

But we would, as an Advisory Committee, initiate the assessment process when we vote to move a topic to the evidence review group. We would then survey pilot states and take those results to distribute to all other states. The survey should represent the diversity of state population size and overall newborn screening resources, so that we have an accurate look at the impact. Next slide.

The pilot state survey, next slide, would

include current ERG and APHL methods, so we already do this as part of evidence review, APHL has done it for a number of years, and we're going to kind of piggyback on those methods.

They will include questions regarding screening testing first in higher tier, confirmatory testing, diagnosis and first year treatment. Next slide. For every area the questions will cover whether -- what new equipment, staff, and medical expertise was required with estimates of costs involved focusing on what we call reasonable ranges.

Next slide. So, the most important metric is the ease of implementation, and we've had really good discussions that that isn't covered by estimating costs. Costs will vary by state, costs will vary by existing relationships, and contracts, and that the most important thing is how hard was it to implement.

But costs will be useful for other states contemplating screening implementation. What will they

need? More than how much it will cost. What access exists to treatment, and how it's worked in other states? We still feel cost estimates and opportunity costs are likely to provide useful information as we look at the required level of effort, and we also know that the ERG does use cost estimates in their evidence review and presentation. Next slide.

So here's an example of a pilot test report. You see on one side just the testing issues, what equipment, staff and expertise was needed for first tier and higher tier testing, what expertise and availability was available for diagnosis required for treatment in the first year.

Then an estimate of costs for implementation and ranges, caveats, including comments on opportunity costs, and then pilot results, the total tests, positive tests, and confirmed cases. And then finally I expect there to be a long dialogue about issues in implementation that might be useful for other state

laboratories to look at in the next survey.

Next slide please. So, the state's survey, next slide, asks a series of questions. If the condition is added to the RUSP, what resources or additional support would you need to implement within two years, like external support for start-up, regionalization agreements and others. I have a lot of comments that these will be the same supports and issues as will the next slide, that we already know, however, we think this information will be useful to the Committee, and useful to the Secretary as we think about implementation.

If you could not implement within two years, what would be the barriers? Are there competing priorities, such as implementing other RUSP additions? Are there other state laboratory priorities? Are there funding, staffing and policy challenges, and other things that states might identify as being barriers in the first couple of years, next slide.

And then question three is, what is your estimate of the effort required for implementation within three years? So, here's an area where we really want to get experience, and we want to talk to state laboratories, and flush out the anchors for making these judgments. So, we estimate the required effort will be low, so it could be that low means minimal costs, little or no new equipment or staff or expertise, and the treatment is readily available.

We have had a comment from one of our ad hoc topic group members that there will be no easy additions, but we want to put that on the list. We estimate the effort will be moderate, that is there will be significant costs, or new expertise for testing, or new equipment, or new resources for referrals that will be required. And number three was effort will be high, substantial new investment necessary, and staff expertise, and referral resources.

And these are unlikely to be available within

two to three years, next slide. So, that's the end of the presentation.

Committee Discussion

DR. CALONGE: This is the complete decision matrix draft that I would like to open for discussion first with Committee members, then with the nomination -- with our Org Rep individuals, and then at the then of that discussion, hopefully move to a vote for adoption, starting with Committee members. Christine?

DR. DORLEY: I'll make a comment as far as laboratory is concerned. I think in adding any new RUSP conditions if they're not FDA-approved assays to go along with that, then everyone is going to report from the public health impact assessment that the ability to add will be high from the standpoint of the new FDA regulations, and the costs that would be associated with just bringing on a laboratory developed test.

So, just throwing that out there, when we

make these decisions to add a disorder, that there would be some type of consideration to if the test is FDA-approved, that can be readily adopted in the laboratory.

DR. CALONGE: I appreciate that, Christine, and if you have the opportunity to go back and look at the full nomination package, that's one of the questions asked. Is there an FDA-approved test? Is there an FDA-approved treatment? So, those are two issues, and I'm glad you brought that up because as we've learned about the implementation of the laboratory developed tests, that there are new challenges and new barriers that will come from that, thank you. Ash?

DR. LAL: I have two comments or questions. So for the B grade, I think that's -- I'm sure is on everybody's mind how that would be adjudicated eventually. So, one of the things that could be more than one factor why a vote is a B, or assignment is a B, if it is so, is there a subset of conditions that get assigned a B to qualify for an expedited review, that's

one consideration?

There is some circumstance, or some information that is likely to become available, or so could that be a recommendation instead of having to have a vote on whether or not to recommend this to that? That's one comment.

And the second, which is maybe more of a concern because we haven't gone through the process, and this potential is that the overlap between B and I. When you say that there's insufficient evidence, or there is moderate evidence of benefit, I think that the distinction, I'm not totally clear between the two when because between the low certainty and moderate certainty.

And that's the area where --- but getting assigned --- I seem to have more severe percussions to the package, compared to getting a B. And we would probably have to be very careful as to where in the spectrum we place the certainty level at, that to me is

a potential concern, maybe not having gone through the process.

DR. CALONGE: Thanks for your comment. I actually think they're related, so the idea is that if you're --- the judgement is, these are judgements, so you're at that B level, and the judgement is uncertain. Uncertainty comes from having an evidence gap, and so if it's an evidence gap that could be filled in by --- within a year, by researchers or the nominators, then that would be a candidate for an expedited review, which is a decision that the Committee could make.

So, I think those are --- we don't specify that in the matrix, and maybe we could include that in the kind of notes that if you get a B, that would be a candidate. Because if you're a B and you move to a C, that's different. That means pretty sure that, you know, that this isn't going to come up, so that actually is a little bit worse. If you go down to an I- it means there's an evidence gap and we're just uncertain.

So, I think we can make that, and then perhaps what I should do is provide at least the reading list, and then maybe even a presentation on the assessment of certainty, and we can do that because there's a lot written about it. I can't, it's -- remember that word judgement, and I always come back to this. People can look at the same body of evidence and make a different decision on certainty.

And that's why as I said, votes are rarely unanimous, but not never. And it really has that, you know, do you feel that the evidence meets all of these criteria in a satisfactory way? I think the task force's levels are convincing, satisfactory, and unsatisfactory, so there's a whole process for that certainty, but it ends up with a judgement looking at the evidence.

So, we'll provide that information, and we'll do a presentation if that's okay at our next meeting. Melissa, I think you're next.

DR. PARISI: Melissa Parisi, NIH. So I guess I'm a little bit uncertain, and I think I might have raised this at a prior meeting as well, who is making the determination of these B and C, A, B and C, and I? This is the ERG?

DR. CALONGE: No. This is us. This is our discussion.

DR. PARISI: But it's --- so, does that mean then that, I mean you said that all B's would be discussed, but it sounds like it implied that there was not going to be discussion of a C designation. I guess the process- is unclear.

DR. CALONGE: No. If we say a C, that's at least moderate certainty of zero, small or net benefit. That's a decision we would make. We would assign a C.

DR. BROSCO: May I jump in?

DR. PARISI: Yeah, please go ahead.

DR. BROSCO: Part of the confusion I think is that if you look at our current decision matrix, a B

does not go to the RUSP, does not get recommended, and that has not been our --- what we've been doing, because that's- been our practice for the last ten years.

So, this idea is there is discussion about all of them, we discuss all of these, but a B or A grade is yes, we're commending A equals, we recommend to the Secretary. In the past, what our decision matrix said was a B or C we don't, and yet this Committee has fairly often said a B, yes or no. So what we've done, we haven't changed the criteria per se, we just update it to match what we've been doing the last ten years. There's a discussion about all of these, this is graded by this group, but a B may or may not be recommended to the Secretary for inclusion in the RUSP.

DR. PARISI: Okay. And I guess kind of as a follow-up to that, I think it might be worth clarifying that because when you just read through the slides, it's sort of that did not come through that there was actually discussion around A, B, C and I. And then

just, you know, a final thought, which I know I've made this point before.

I think there's a big difference between a negative magnitude of net benefit, which is actually a harm, and zero or small. And small, of course, as you just said, Dr. Calonge, it's, you know, very much a judgement call in terms of, you know, the survival of a child for some individuals is a significant net benefit.

Some other people might think of it as small, and so the lumping of zero, small or negative into that C category is still somewhat problematic for me at least, thank you.

DR. CALONGE: Yeah. There is another category called a D, and for simplicity sake I figured that we should drop it off because if it's so small, if it's not --- if it's more than small, then we're going to put it in a B, and that will be a judgement call. -And trying to figure out that cut-off is difficult, so I wanted to have a B discussion.

So, I mean we could expand it, and I guess my recommendation is we not, unless it becomes a problem. And I'm uncertain it will become a problem, but I understand your issue. I thought about it a long time. I think currently the USPSTF gives those C's as well, but a D goes to the absolute harms, and so we just kind of collapse it. Michele?

DR. CAGGANA: Michele Caggana. Just a couple comments. So, I feel that in the past after the evidence review makes their presentation, that they do put up this matrix with a suggestion, so that process will continue, and then we will discuss to come up with sort of the final designation. Is that what you're seeing as the process?

DR. CALONGE: Yes.

DR. CAGGANA: Okay. I just wanted to clarify, sorry.

DR. BROSCO: Can I just clarify that for a second?

DR. CAGGANA: Yes.

DR. BROSCO: So the ERG makes a presentation of the evidence. The Committee Members who are liaisons to the ERG, they're the ones that make the recommendation about A, B, or C or I. So, the ERG is not making recommendations about this, it's the Committee members, the liaisons that make the recommendation.

DR. CAGGANA: Yeah.

DR. BROSCO: And it's their recommendation, but then the Committee votes on it.

DR. CAGGANA: Yeah, okay. Because in the past I thought that they did show the matrix at the end of their presentation.

DR. BROSCO: No. They do show the matrix, but I just want to be clear that the recommendation is not coming from the ERG.

DR. CAGGANA: Right, right. Yes.

DR. BROSCO: That's all.

DR. CAGGANA: Okay. And then the --- so, I

think the D is just, we're just going to have to try it out and see how it works, and how we discuss it. And then the last clarification was going back to Dr. Dorley, on the nomination package, the issue about an FDA approved test is really talking about the confirmatory and diagnostic, and not necessarily the screening test, which is what the newborn screening programs will be ---- will- have to, you know, answer to.

And so, I think it is kind of important that we make sure we make that distinction during the nomination, and understand that that's going to be a tough piece of this as we go forward for the public health assessment as well.

DR. CALONGE: Thanks, Michele. Ash?

DR. LAL: I just wanted to follow up on the -- so looking at the distinction between the C and I, is whether it's a question of certainty, or whether it's a question of magnitude of benefit, if I get the

sense of the categories here.

So, following up on the comment that if you want to avoid negative language, the C designation gives moderate certainty of less than moderate benefit. It could be reframed in some way. But that's probably what they're trying to say that it be moderately certain that the benefit is not even moderate, it's less than moderate.

Because we don't --- so that could be either a small, or it could be zero, it could be negative, but one could consider changing the language to ensure it doesn't come across like that. And then the I is then not the magnitude, but it's- on certainty.

DR. CALONGE: Yeah. I understand what you're saying. I get it. Chanika?

DR. PHORNPHUTKUL: So, for the public health impact assessment, the lower table, I think it's great that we put it up there. From what I recall from Dr. Talalay presentation that that number is very high, that

most states can't implement it in two years, and perhaps that would be something that you know, people can use that as, what can we do to make sure that they can have enough resources for them to help?

Because I feel that, you know, two years is a very short time for most laboratories to implement anything that's recommended, but I'm not in the lab, so I don't know how you feel about it.

DR. CALONGE: So, I appreciate that comment. If you go back and look I think at the second question it's like, you know, the first and second questions are, you know, what are you going to need, and what are the barriers to get there? The two years we went back and for in, and it was actually based on the median in states that have – what is it, requirement loss? Alignment loss, so that's where we got the two years from.

So, for those states, we were trying to make sure those states had a voice in saying can we do this

in our alignment law issue because I thought that would be important. And actually, I like your suggestion. I have no issues, unless the Committee does, in changing that to at least moderate certainty of less than moderate net benefit. Okay. Melissa?

DR. PARISI: So, I have a question about the public health impact assessment. It feels to me like just having those three categories does not capture the nuance of what may exist for many of the states, and so also like Chanika, I was concerned about the two years. I'm wondering if there is also the option of asking five years, two years and five years?

I know that's a little bit of trying to, you know, anticipate the crystal ball, but it feels to me like that's a little more realistic in terms of what some states are capable of. Oh, I'm sure Jeff will have something to say about that. But then, really my question is it seems like the effort required is going to vary depending on whether a state has received

funding to support the addition of new conditions, either through some of the HRSA funded Propel, and Co-Propel grants, or some of our NIH-funded pilot studies.

And that's not captured in this kind of simplified chart, and in addition, you know, it just seems like there's so much more nuance around whether or not a state also has RUSP alignment legislation that is dictating that when something gets added to the RUSP they are required to bring it on within a certain period of time.

So, I just wonder whether having these gross percentages is really going to be meaningful, given the fact that there are so many nuances that underlie a state's ability to make a public health impact assessment, those are my thoughts.

DR. CALONGE: Pretty much putting anything on the matrix is tough, and clearly B-1, B-2, A-1, A-2, didn't work, and so we are trying to think of something to meet the statute that might actually be something

that the Committee could look at. Not that we would say, or we might, if 48 states say there's no way we can do this within two years, that may be something that we would want to consider before we vote on starting the clock, especially for states with alignment.

And it won't be the only information that we have. We'll have the answers to the other questions, but in terms of putting it on one page, and having a matrix that meets the requirement of the statute, this is what we -- after three meetings of trying to figure out what we could put on the matrix, this is what we thought would be best. Jeff, I'm sorry?

DR. BROSCO: Just to say that you're absolutely right, Melissa. And as Ned said, we've had multiple workgroup meetings with laboratorians, and followed folks, and there's just -- there's not a way to do this easily, but it needs to be there, and you have noticed a switch before it said how many years will it take, and the response was well, it often depends on how

much resources I have.

And so, given the RUSP alignment legislation and saying you know, this needs to be done in 18 months, two years, three years, we chose two for the reasons Ned said. And I would just give you an example. Imagine it's 2019, and I said to you how many years will it take to develop messenger RNA vaccine, get it to every single person in the United States?

You'd say ten years, 15 years, if you said nine months, you'd say that was absurd. There's no way you can do that in nine months, and yet if you put enough resources into something you can. So, the idea was to sort of flip the question around and say well, if we had to do this in two years, what would it take?

And what we learned from our friends is that there are 50 different answers, and this is not meant to be the --- you're not meant to remove information. The Committee would still have a lot of information about stuff, and a lot of discussion, how much it helps the

Committee make a decision about something, you're right, it's probably not- the most important thing.

DR. PARISI: Could I just suggest then adding the number of states that were part of the survey process, so that we understand what the denominator was?

DR. CALONGE: You bet. Let me get back to that issue. We want 100%, that's our goal, and at least be representative of the spectrum of states from a resources and capability standpoint, yeah. Jannine?

DR. CODY: Jannine Cody, Committee Member. For back to the resources thought, now that you've been through this new multi-step process, is there a capacity among the staff here to do this on an ongoing basis, or have we slowed down the process because there's not enough capacity on the HRSA staff side to really accomplish these goals?

DR. BROSCO: So, I think it's important to point out that Ned presented a way of doing this. You know, serving the pilot states, and then serving all the

other states. Right, so just to say that how that actually happens, you're right, is going to depend some degree on HRSA resources, and a whole bunch of other things.

You know when people say you can't survey more than nine people without, you know, in the requirements, so a lot of things have to be figured out in the process. The key thing for I think the Committee is to vote on whether this overall concept, you know, how much is required, what are the resources necessary to implement in two years? That's what the Committee needs to sort of focus on.

DR. CODY: Well, that was part of the question, but the other part was this whole thing. Now that we've been through this multistep process with MLD, I mean did that put a huge burden on the staff here that if there's multiple conditions coming through does the process slow it down for the groups?

DR. BROSCO: The rate and extent for that is

really the evidence review, and what the research that is available for the evidence review group, so I think our team is strong. We're good.

DR. CALONGE: It put additional strain on the Chair.

DR. CODY: That's apparent, actually.

DR. CALONGE: That's why I get the big bucks. I think the other thing I would have to say, Melissa, is that we reached the bottom part of the matrix that was the least objectionable to all of our stakeholders from the state laboratories, so that it was interesting.

We did not come up with what's perfect, but we came up with something that we could say, this might be useful, and we think we can get this information, and now we'll see. Let me turn to our Organizational Reps, oh, Michele, I'm sorry.

DR. CAGGANA: That's okay. I think commenting on what Dr. Parisi said, I think another thing that might be helpful in the discussion, not

necessarily in the matrix, but when we're thinking about this is not only the N of states that responded, but the number of babies that will be covered by those responding states as well, so you can an assessment on the impact across the entire country, so maybe as part of this we can capture that as well.

DR. CALONGE: Great. I like that. I just want to make sure Jennifer Kwon didn't have any comments. Thanks. All right. I apologize, I don't have the order, but I'm just going to go. Let's start with Amy.

MS. GAVIGLIO: Thank you, Amy Gaviglio, National Society of Genetic Counselors. So, the public health public impact assessment process seems to hinge on there being a universal pilot state within the U.S., and I wonder what the plan will be in the absence of such a U.S.-based pilot.

And then, I also wanted to affirm what Dr. Caggana said with the new nomination. There are

actually no questions that are explicit around FDA-approved kits for screening, diagnostic tests or treatment, and so if that's going to be something that's taken into account, that should be added.

DR. CALONGE: Sorry, Jeff?

DR. BROSCO: Oh. Yeah, I think what we are going to do is add that to the notes for the second step of the nomination process. I think it's going back to our previous discussion.

DR. CALONGE: Great question about our ability to serve international programs, and we're just going to have to try it, thanks. Natasha?

MS. BONHOMME: Natasha Bonhomme, Genetic Alliance. I have a couple of comments, or questions. So first in regard to the public health impact assessment, I would encourage a re-naming of that to public health lab, or public health lab and program assessment because that is where the deep dive is done, and not on all the other components of public health

around newborn screening.

In terms of, you know, we're not screening just to screen, but really looking at that, you know, the impact on the child and family, which I know we will talk about later on. You know, there's no inquiry into the cost of from the maternal and child health system beyond the program, which I'm not saying we should. I'm just kind of highlight that it's not public health, it's really --- Jeff you are looking at me super confused, so hopefully I'm- making sense to someone in here.

So, it's just clarifying that labeling of it, that I just encourage someone who likes to get as much clarity as possible. Next is really building on what Dr. Parisi and Dr. Caggana mentioned, you know, we always know different states have different means, but you know, I think it's over 20% of states have some type of RUSP alignment legislation that does come with various form of fee structures and things like that.

And I also believe that that actually covers 50% of the babies born, so it is a large portion, and so I think having the denominators when we are having the discussion would be really helpful in the survey. And lastly, I also appreciated Dr. Parisi's comments about splitting C.

You know, when this information goes back to patient advocacy organizations, and the researcher doing this work, they really do take the words of this Committee seriously and strongly, so having that sense of the difference between, you know, least moderate to negative net benefit I think could have a real impact on those groups, thank you.

DR. CALONGE: Thanks Natasha, Sue?

DR. BERRY: Sue Berry for the SIMD. I'm coming back to the public health impact, which is sort of down at the bottom, and sort of --- I understand why it fits the way it does, but one of the things you mentioned in there was to have states assess the impact

of follow-up and treatment. And I'm uncertain that states really have a great handle on the impact of long-term follow-up, and that they really have access to the complexity and details that are going to be involved in the treatment.

I know that when we've gotten sort of this kind of --- we've had surveys like this, and in my state they always turn to me and say well, what do you think? And I go well, who is going to pay for the transplant, you know, things like that. And you know, it's- going to be difficult for states, particularly larger states, to be able to get a fair assessment of that, and for smaller states to even know if the resources exist.

And so, I'm not sure how that impacts your decision, your overall decision, which I think we should pay more attention to, so dropping the same question out to you again. Thanks.

DR. CALONGE: Yeah. It's a great point. I only know how we do it in Colorado. We have close links

between our state laboratory newborn screening program and the Children's Hospital, so when we are looking at adding Krabbe, which even though I'm in the State Health Department, the lab never asked me about it.

They just asked Children's. It was independent. They were watching the Committee's work going forward and starting to explore already what we would need to do. They did the same thing with Psychosine. We can’t do Psychosine, we're going to have to figure out how to do that regionally before we implement it, and those are things we have to work through.

So, they're already thinking, but they think, at least our folks think all the way through the process and capitalize on existing relationships. In a large state where there are multiple centers, I think there will be other challenges, but Michele, you worked through this in what I think is a not large geographically, but huge from a population standpoint,

and I have to wonder if you think these are questions that your colleagues in other large states can answer?

DR. CAGGANA: I think a lot of it depends on what their experience is, and how they've actually carried it out. Different states have different mechanisms for funding, and whether there's a fee structure or not, whenever we want to add a new condition to our panel we reach out to our specialists and say what do you think about this?

And make sure that we have their input and buy-in before we actually do move forward. But I think the questions that are on the pilot survey, they are pretty answerable for the states that have the experience. It might be ---- and- I think if states know, I think we had this discussion, but I think if states sort of know what they might need, they kind of can understand what it's going to take.

I think maybe instead of issues for implementation, it might be considerations for

implementation, that one category, and you know, based on our experience, and how we do things, which we share with people, you can sort of get an idea of what you're going to need in your situation, so I think it's doable.

DR. BERRY: The corollary to all of this is I think it assumes that the -- somebody is going to pay for all of this, and that they will know how that happens. And I would assert that that is a very difficult thing to determine.

DR. CALONGE: All right. I know that's true, and I think one of the issues you already brought up, one of the issues was transplant, and if I'm in a state that doesn't have a transplant center, and my Medicaid program doesn't pay for caregivers in another state, then we're not providing the benefit of newborn screening.

We're providing a lot more challenges, yeah. Michele?

DR. CAGGANA: When we began Krabbe screening,

and I know this was going back aways, but we made --- we put in considerable effort to make sure that our Medicaid folks in DOH knew what the situation was going to be, and that these kids may have to go outside of the state for transplants.

And so, it's necessary for the state, for the program, or their chain of command to figure out how to make that work, and make sure that they have buy-in from their Medicaid providers within the Health Department, so that it's possible, and those kids don't have to wait.

And so, we actually did a considerable effort to make sure everybody was onboard with that, so it is possible, it's a lot of work, but it's possible.

DR. BERRY: And you're in New York, and gene therapies are not going to be done in more than three or four places.

DR. CAGGANA: Right, exactly.

DR. CALONGE: Margie?

DR. REAM: Margie Ream, Child Neurology Society. I think that my question also picks up on the theme that we've had the last few questions. Can you clarify what's meant by referral resources? So, that was on your last slide with kind of detail about the public health impact, and so referral resources, is that just for diagnostic confirmation, or is that for treatment? And if the process maybe, you suggested that maybe the Committee would consider the effort involved before recommending addition to the RUSP.

If a treatment is not readily accessible, whether it's because of geographic location of that treatment or cost, you know, how does that play into kind of what you had said about if there is high effort required, particularly for the rest of the states maybe that would be part of the consideration, the timing of recommendation.

DR. CALONGE: First thing, first part, we were mainly thinking about treatment referrals. There

is a section in there on diagnostic testing, and we can certainly add referral resources for that as well. I think the issue about availability of treatment is an ongoing one that the Committee --- it won't be on the form, but all of- that information should be in the background whenever we look at adding something to the RUSP.

And thinking about timing I think is important, and it's a consideration that I think we need to continue to bring forward into our discussion. Remember, this is a tool to help us make decisions, and there will be --- it's not an easy decision. That's why I try to stress that the matrix doesn't make the decision for you. You make the decision. And the matrix is a tool designed to help us get through that. -

It's the same way I look at negative, like a net harm. You may get a C, but to Natasha's point, the information back to the nominators will be, this looks

like it does more harm than good. It's pretty direct language, and so we won't just --- we won't, the matrix doesn't- define the letter.

It's something to help us make a decision whether to add or not add, and there are nuances that we bring up for every part of it other than it would be nice to have a few more high certainty of substantial net benefits, because those are a little bit easier, oh that could be easy to implement.

So, the homerun of newborn screening probably is rare, so I appreciate the question. Go ahead?

DR. REAM: I think that, you know, access, kind of like what Sue was saying, access to care, whether it's financial or logistical, access to care is identified as a big barrier. You know, what can the Committee do to advocate through other avenues to reduce that barrier?

DR. BROSCO: I'm putting on my hat as the Director of Children with Special Healthcare Needs

section. So that is something that we are actively working on, and we can either do, you'll remember two years ago we had a presentation, the Blueprint for Change, with children with special healthcare needs, so clearly the population of kids identified in newborn screening fits into that.

So, HRSA is working with all of our federal partners to try to make sure that if a treatment is necessary, that it is available to every child.

DR. CALONGE: All great questions. I think it gets to the equity issue as well.

DR. KWON: Do you mind if I ask a question?

DR. CALONGE: Yes, Jennifer, please.

DR. KWON: So I think this conversation about the availability of treatment is really terrific, and not that I think it necessarily belongs on the matrix, but I think what I'm hearing from a variety of speakers is that it belongs somewhere, right? So, we have the evidence review, we have you know, a comment from APHL

about the lab's capacity, estimated capacity, but we don't really have a discussion about treatment and the availability of treatment.

And I didn't know if what I'm hearing from people is a desire to have a more robust discussion and review of that? What do you think?

DR. CALONGE: I think that is what you're hearing, and again, I think there's a question in the full nomination package that addresses that, but it may be that it's something we need to address more specifically, and make sure that when we're looking at a nomination package, and maybe even -- I don't have the ability to say what should be in a contract with ERG, but you know, it may be that we can look at our partners who do evidence reviews and assessments, and figure out a way to make sure we have a complete set of ---- sorry, an assessment of the availability of what's going to be needed to provide services for the kids identified is really important.

If you remember, if you remember the Wilson Young criteria, which of course I know very well. One of the criteria is that adequate resources, exist and provide treatment to those identified with the screening test. And if you fail that, Wilson and Young would say don't screen for it.

That's a hard concept for a lot of folks, especially advocates to grasp. But as a public health care system, it's like what have I done that's beneficial to identify someone who then cannot get treatment? And there may be benefits that many people adhere to, and feel are important, but it's just part of the screening test criteria, and I think it's an important point.

DR. KWON: And did I not hear Jeff Brosco volunteer HRSA as maybe the group that could provide evidence of treatment availability?

DR. BROSCO: Can we go back a few slides because I think we missed this in the discussion. If

you go back to the slide that says, go back again, the other way, oops, the other direction. The one that's -- what's the title, go back another one please, one more? -Stop there.

So, look in the bottom left-hand corner. Follow-up treatment expertise availability. So in the example that we've given of what the kinds of information that would be asked, this is clearly included. Can you go forward two more slides again to the anchors? One more. And it's not as explicit here, but and Margie, you asked this question, so treatment readily available is for low.

The other is referrals, referral includes treatment, so I think we tried to put this into both the anchors and the overall survey, that's why I was frowning when you made your comment before Natasha, because I thought we tried to include this as really a public health assessment, and not a narrow laboratory or follow-up program.

Getting information is hard. It varies across states. There's all sort of issues, but to agree that the Committee can gather the information, and have it at their disposal, it can be part of the decision making process.

DR. CALONGE: Sabra?

MS. ANCKNER: Thanks. Sabra Anckner from the Association for Maternal and Child Health Programs. So, kind of coalescing with what I think a lot of folks here have said, but I do want to say from the start we're specifically talking about readiness of state programs, there's really got to be a, do you have a lab or not?

I think that's been a problem for a while that they're, you know, asking a state that doesn't have their own lab about their readiness is just profoundly different than asking a state with a lab. The way, you know, they -- first I need the lab I contract with to be able to do this test.

Then, right, and so that has, you know, I

used to fill out that survey, and that was the problem that I ---- I don't know, I'm not in charge of that part. I can tell you about our specialist availability. I could tell you about the other things, but I'm not actually in control of the lab piece, and so I think really having a way to for folks to delineate that.

It's not the biggest percentage of the population, right? If we're basing it on that, that are going to be those jurisdictions, but it is often the jurisdictions that are going to have the biggest barriers in basically every other piece. So, I think that part is really important.

The thing is I agree with these guys that have said this already, what is being listed here as a public health impact assessment is not. It is a public health lab and program assessment, you know, I pulled up CDC's definition of health impact assessment, which is helps evaluate the potential effects of a plan, project or policy before it is built or implemented, and can

provide recommendations to increase positive health outcomes, and minimize adverse outcomes.

In that context this whole thing is the public health impact assessment, right, so I feel like we're getting stuck on the term that is in the statute, which again just says, included in the evaluation the potential public health impact, including the cost of such expansion.

Which again, it doesn't say anywhere in there, just at the state lab, right? It's broader than that. I think that this is, you know, even just if you're talking about the public health state agencies, this -- newborn screening is a small part of what public health state agencies do, and what they have to account for, and what they have to go to their legislatures and ask for funding for, and -- including in the maternal child health space.

And so, I really think that really trying to better ascertain if that's what we're doing, if we're

really including this percentage of states reporting and their effort because we feel like that's what makes it compliant with the statute, I don't know that that's again, I think this whole thing is a public health public impact assessment.

But I think that also really thinking about what the costs of treatment are, the availability of treatment of diagnostic testing, and the harms of all of these things because they do exist, is really crucial. And what the reality is that if we are paying for one thing, we are not paying for something else.

Do we wish that those decisions were made differently? Yeah. But they aren't, right, and so we are working from one pot of money, and that really is the reality for public health agencies, and I think that it would do us well to have a better understanding and appreciation of that.

DR. CALONGE: So, I appreciate the comments. Part of the understanding of the use of the word comes

from where this came from, which was congenital cyanotic heart disease, which is a point of service test that state labs couldn't do. And because the recommendation came to add it to the RUSP, it ended up in a lot of activity. And one of the activities says we should be able to talk about whether or not states are ready, or able, or is it feasible for them to do this testing.

So, given that's where it came from, that's why it's restricted to kind of state screening programs, as terms of the assessment. But as Jeff said, we're trying to be inclusive of those other elements of treatment and diagnoses, so given where it came from, I think and that we have to do some assessment about – sorry,-- the other piece is the understanding that not all states have implemented all conditions.

And for a lot of the reasons people have talked about, trying to bring that into consideration and better identify matching of resources with intent, which I came in as Chair hoping to further, and I've had

a little if any success, is that all 50 states should screen for all of the conditions that are approved by this Committee.

And we're not there. And so, thinking about the assessment, and how that can be used to argue and promote, and advocate, for resources to meet that need, shouldn't we do the ones we've already approved in all 50 states? Shouldn't that be a priority? I think that's kind of where I'm at with the assessment issues, and how could we get people, how can we help states to get there? What is the role of HRSA and other federal funding to get us to at least that point?

There will be new conditions. We're in the middle of considering new conditions now that will add to the list of things like a small, or a less resources state isn't doing. And have we helped the children being born in that state? Have we helped people in that state? I'm uncertain.

So, I understand that this is looking at the

benefits to the children, and the potential harms, all of the other issues as an entire impact. This section is just, are we ready, are we able? And we could have used those words, feasibility and readiness, I think those were the terms in the original set.

And we wanted to kind of meet with the statutory wording was.

MS. ANCKNER: And I think it would also behoove us to look at not just is everybody screening, but are they screening well, and are the outcomes improved? Because we, you know, even if every jurisdiction is screening for every RUSP condition, but there are some kids who are still never getting treatment, never getting care, never getting appropriate care, which we know is the case already for the conditions that are universally screened for in theory, right?

And you know, so what are we, you know, what are we asking folks to do? Because we're not doing the

things we say we're doing well yet.

DR. CALONGE: Yep. Yep. Thanks. Debra?

DR. FREEDENBERG: Debra Freedenberg, AAP. And I think there's kind of been a little bit of diversity, you know, there's been a theme in terms of follow-up and treatment, and the readiness within states, versus the laboratory's ability to actually perform things. And one of the things that you know, as I was listening to this, and I was thinking about is that it's very hard for treatment to follow up for a state to really get a good handle on that, as hard as they try.

And even in states that think they have good relationships, you know, when you have not one particular specialty center, but you're dealing with eight or nine of them across a large state, that sometimes there's going to be a diversity of opinion in those states, you may never come to consensus on what people think would be the best way to approach it, and I

just think that should be part of our consciousness in thinking about this.

DR. CALONGE: Thanks Debra. Michele?

DR. CAGGANA: Just a couple comments. I think when we're talking about help with implementation, I think we should remember that we have advocates that can help us with some of this work and getting things onboard. The other thing I would mention is that the community itself is working through CDC and others to create centers of excellence to help with some of the efforts of states that may not be able to bring onboard either the initial, or higher tiered testing, and so there is activity to help us within the newborn screening, at least lab community.

And the last thing is this whole discussion about follow-up and availability and expertise- from the pilot states, and I don't want to say it, but I will, stems on the N-of-1 rule, right? Because we're not going to be able to do any kind of assessment unless we

have a pilot study within the state that you're surveying, who finds a baby, and then sees whether or not they're available for treatment -- whether treatment is available to them.

And I think that's important to kind of keep in mind. The last thing we want to do is identify a child, and then say sorry, we have no --- nothing- for you, so that's probably just as bad as having a diagnosis when you're not screened, to say we know what you have, and we can't do anything for you, so thanks.

DR. CALONGE: Susan?

DR. TANKSLEY: Susan Tanksley, Association of Public Health Laboratories. So, I wanted to follow up on a few of the comments that have been made, and I appreciate so many of the comments that have been made today. Regarding the how do you gather the information on treatment availability, and expertise in states.

And Dr. Freedenberg just mentioned that there might be differing opinion across a state, and we found

that when we did the public health system impact assessments, and tried to gather information from specialists within our own state, and would literally get complete opposite ends of the spectrum. And then as a program, how do you respond to that A, B, C, response in the survey, and they average each other out.

And so, I'm wondering if there's a way to gather information, and Alex will love me for this, I'm sure. During the evidence review process where so, we have a technical expert panel, but typically that's people who are on the nominating, you know, part of the nomination packet, the experts who have helped put together the information for the nomination, but it really doesn't represent specialists in the field from a more diverse perspective.

And so, I'm just wondering if that might be a way to gather some of that information from throughout the nation, so that's one comment I have. And then the other piece is that we know from history that the public

health impact assessment has really not been taken into, as a factor in the vote, and so feeling that that will probably still be the way forward.

Will the information gathered from the public health impact assessment -- how will it be used? Will it be used to try to develop funding, to develop ways to fill those gaps, those sorts of things from a national perspective versus each state trying to figure out how to fill those gaps, thank you.

DR. CALONGE: Thank you, Susan, and that is certainly the intent. I think also with this discussion while I talked about the assessment being separate from the decision, I think thinking about the timing of implementation and voting might be something that's within the purview of the Committee to think about when we have a condition that's -- implementation seems far out of reach without additional resources, appreciate that. Scott Shone?

DR. SHONE: I'm good.

DR. CALONGE: Hard to believe. Carla?

DR. CUTHBERT: I can't follow that one. Carla Cuthbert, CDC. So, Susan, thank you for your comments there. When we were reviewing, we were reviewing the slide deck, you know, we wrestled with the idea and the thought again that yes, there are some things that we don't factor in necessarily, when we're thinking about the vote, and the public health impact seems to be one of them.

And we recognize that it takes a considerable amount of effort for all of the states to fill this out, and it may even feel a little disheartening when you go through this entire process, you pour your heart out, and you try to resolve this, put it down there and it feels like there's nothing.

But, you know, I think that what we understand, again, apart from it being required, is that it does provide us as feds, and I speak for ourselves, it provides us with a bit of information as to what can

we do to position ourselves to help. And being able to understand what some of the barriers are, they're going to be different for each state, and Melissa brought this up as well earlier.

It's that everything is so nuanced. You know, you may have a condition for, well, we don't have another set of instruments, we would need more space, we would need all of these other things. But being able to have this information available, even if it's not factored into the vote itself helps the feds to be able to consider how to mobilize to be able to address it. And it may not be an immediate flick of the switch, but hey, you need money, we got money.

But it does get us geared to try to figure out how can we really help. And this is something that has sort of motivated us to the center of excellence idea. This was something that again we thought about for several years, and provides us with an opportunity to evaluate this particular idea.

I know that the states have thought through this as well as a possible solution. Our program at CDC is really are moving forward with technical assists as well, where we have a group of laboratorians. Again, this is from a laboratory perspective, I recognize that this doesn't solve all the problems, to be able to just send our staff out there to be able to work through issues, help with the implementation, and be able to get over that hurdle.

So, it does allow us to try to figure out how are we going to do this, and how can we help? So, I hope that's helpful. We do, like I said, we do recognize that it takes a lot of effort, but it's not for naught. I just want the states to hear that specifically.

DR. CALONGE: Thanks, Carla. So, moving on. I --- before we entertain a motion I want to tell you what you're voting on. So, you'll be voting on the adoption of the matrix. -Oh, let me just pause and say

we've used one slide to discuss almost all of the challenges of newborn screening, which cannot be fixed with a single slide, so I appreciate all the comments, and a lot of rich discussion, and things that we will continue to talk about and work with our federal partners, our clinical partners and our state partners, and other advocates.

The revisions that I think that we agreed on was that C will say at least moderate certainty of less than not moderate net benefit. That's one change. The second, will the public health assessment for implementation in two years will include the number of states that completed the survey question. There are other caveats that we will add to notes in supporting the matrix, and we will keep in mind we may need to modify and add another category in the future, depending on experience.

But with those two caveats, I'd like to make a motion if it could come up with the next slide, is

there a slide, a motion slide?

DR. PHORNPHUTKUL: I'll move.

DR. CALONGE: Okay. Chanika. Go ahead.

DR. PHORNPHUTKUL: I'll move to move forward.

DR. CALONGE: Adopt the decision matrix with --

DR. PHORNPHUTKUL: Adopt the decision matrix.

DR. CALONGE: With- the- changes discussed.

DR. PHORNPHUTKUL: Okay. With the decision, sorry, yeah. Okay.

DR. CALONGE: Just maybe the next slide. We'll fix it. You understand where that goes, yeah. Is there a second?

DR. LAL: I would. I'll second.

DR. CALONGE: Thank you, Ash. Could I have a roll call vote please, Leticia?

COMMANDER MANNING: Okay. Just say yes if you agree with the motion. Michelle Caggana?

DR. CAGGANA: Yes.

COMMANDER MANNING: Carla Cuthbert?

DR. CUTHBERT: Yes.

COMMANDER MANNING: Jannine Cody?

DR. CODY: Yes.

COMMANDER MANNING: Robyn Sagatov?

DR. SAGATOV: Yes.

COMMANDER MANNING: Christine Dorley?

DR. DORLEY: Yes.

COMMANDER MANNING: Paula Caposino?

DR. CAPOSINO: Yes.

COMMANDER MANNING: Jeff Brosco?

DR. BROSCO: Yes.

COMMANDER MANNING: Jennifer Kwon?

DR. KWON: Yes.

COMMANDER MANNING: Chanika Phornphutkul?

DR. PHORNPHUTKUL: Yes.

COMMANDER MANNING: Ash Lal?

DR. LAL: Yes.

COMMANDER MANNING: And Ned Calonge?

DR. CALONGE: Yes.

COMMANDER MANNING: Thank you.

DR. CALONGE: The motion passes. I appreciate all the work, all the comments, and Melissa?

DR. PARISI: You didn't call on me, so I'll say yes.

DR. CALONGE: Oh.

COMMANDER MANNING: I'm so sorry, Melissa.

DR. CALONGE: Thanks, Melissa. We're going to take a ten minute break. We are behind schedule, but it's okay, we'll shorten lunch a little bit, and it will be marvelous. So, please get up and stretch if you do nothing else, and we'll see you back promptly at 10 after noon for Alex's presentation on outcomes, standardized outcome reporting.

(Break 12:02 p.m. - 12:15 p.m.)

Standardized Reporting of Newborn Screening Outcomes (STAR-NBS)

DR. CALONGE: All right. So our next presentation is on the standardized reporting of newborn screening outcomes (STAR-NBS) presented by Dr. Alex Kemper. You remember that Alex is Division Chief of Primary Care Pediatrics at Nationwide Children's Hospital, and Professor of Pediatrics at the Ohio State University College of Medicine, also the Deputy Director of Pediatrics.

He also is the lead for the evidence review group. Dr. Kemper?

DR. KEMPER: Thank you very much. I'm also going to make the world's fastest presentation, and try to get us back on time. I just wanted to inform everyone about this small ongoing project that we affectionately refer to as STAR-NBS. And this grew out of work that the evidence review group has been doing around evaluations of newborn screening tests, and one

of the challenges that we have when we look at publications is that there's just a ton of variation in how data are reported, which creates confusion and makes it really difficult to synthesize data.

And there are a wide number of areas that often need clarity, so things like the clinical case definition, of the screening, what the reference standard is, how the test characteristics are assessed by that. I mean things like sensitivity and specificity, your positive predictive value, and negative predictive value.

Because sometimes it can be unclear how, when samples are submitted that are inadequate are taken into account, when the test characteristics are calculated, what happens with lost to follow-up or when there are indeterminate diagnostic test results, there's also a variation in how nontargeted conditions are reported, and how that plays into the test characteristics.

So, things like carrier status, if there are

other nontargeted phenotypes, like late onset disease that are identified, or just other conditions completely different conditions that may or may not be beneficial to identify. And it makes the job of synthesizing the data really quite difficult.

There are often other areas that need clarity, so the unit of analysis, so we are particularly interested in looking at the newborn as is the unit of analysis, but sometimes reports talk about the screening test is the unit of analysis, and that can be complicated if there's more than one screening test done per newborn.

As you would expect, there's evolution of the screening algorithm over the course of a study period, and it can be hard to figure out in some reports. When you look at the characteristics, how does it play out with the final screening algorithm, versus one that might have been in progress. Sometimes there's components of cost analysis that are reported or not

reported, and it can be hard to understand that.

And then oftentimes the plans for follow-up are reported differently, in terms of what happens after diagnosis, or if there's diagnostic uncertainty. So, we are interested in coming up with the standardized report guideline that journals could use. And something like this already exists, so there's something called the STARD, which are reporting guidelines for diagnostic accuracy studies in general.

And there are 30 items, and you'll be happy to know I'm not going to read all 30, that cover most of the points needed to fully understand newborn screening. So, if reports followed the STARD guidelines, a lot of the issues I talked about would be covered, but there are some aspects that often that we are interested in, that need clarity that don't fit into the STARD reporting guidelines.

And so, we proposed an extension to the existing reporting guideline, and that includes the

clinical case definition of the targeted screening, the reference standard, and there's other things that are in bold that I talked about before. I'm just going to skip over -- so, where are we now in this process?

So the STARD guideline is part of a network of reporting guidelines that are maintained by something called the EQUATOR Group, and it's maintained on their website, and a lot of journals will look --- tell authors to look at the EQUATOR Guidelines when they submit- studies related to particular topics.

So, we want to expand the STARD to make it relevant for newborn screening, and we have gone to the EQUATOR mountain, so to speak, and gotten permission to extend the STARD. I've spoken to some experts in the newborn screening world, including sending some surveys, and that kind of thing. We've gotten preliminary feedback in terms of the things that we thought that might be good to add that maybe we do need, and some that we maybe don't need.

And we put it all together, and at that point, at this point we may reach out to those that are doing newborn screening studies, just to see how this would play in the kind of reporting that they do. And once we do some pilot testing, and are happy with how things are, then we can go back to Equator and ask them to make it an officially recognized thing, and it's just a matter of going back to the journals and getting them to recognize that this is out there, as well as promoting this within the newborn screening community.

It's, I think personally, a simple, small request for those that are interested in publishing their work, that at the end of the day would facilitate better outcomes in terms of being able to understand findings from studies, and being able to synthesize across them, and ultimately help with the complex decision making that this body has to make.

Committee Discussion

DR. CALONGE: So, thanks Dr. Kemper. I wonder if there are any questions or comments from members of the Committee? Jeff? Jeff Brosco?

DR. BROSCO: Jeff Brosco. So, Alex, I understand why this is so important for the Committee, and an example of how the federal government is trying to support folks who want to nominate additions. Very often in the evidence review process we'll hear that you've looked at lots of studies, but it's hard to put them together, make much sense of them, and be able to say this is what the evidence shows.

And this is routinely done in the research world. Now, if there are standard, and you want to do a qualitative study you follow this. If you want to do randomized control trial, you follow this, and journals will ask you to do that. So, in some ways what you're talking about is a guide for people who want to do newborn screening research, that will allow their

research to easily be used in the evidence review process, if that informs this Committee. Did I get that right?

DR. KEMPER: 100%. I should have had you do the presentation.

DR. CALONGE: From my standpoint I'm fully supportive.

DR. KEMPER: Excellent, all right. Well, then I'm going to hurry up and sit down then before somebody can say something different.

DR. CALONGE: Any Organizational Representatives, comments or questions?

DR. KEMPER: Thank you.

ACHDNC Review of Research Focusing on Lived Experience Perspectives

DR. CALONGE: Yeah. Well, it's hard to let him off without some grief, but all right. You know, we talked, staff and I, talked after the last meeting when

we had Dr. Noyes join us from Bangor, Maine. Wales, different than Bangor, to talk about qualitative data synthesis, and people saying we're trying to put that within context. So, we've been trying to systematically learn and understand ways in which data on information, other than what the Committee usually looks at in evidence reviews, might be lifted up and valued, and be part of decision making for the Committee.

Especially in terms of the lived experience of families with children with the conditions for which screening is being recommended or examined. And so, what we decided to do with this hopefully brief presentation, is to try to go over and remind you what we've looked at as we're building the information that we think could help us move into that part of net benefit considerations that includes kind of lived experience, and additional information from families, specifically.

So, what we've done is put together a slide

set that just reminds you of what we've been through, and suggests what we would like to do next. Next slide please. So, in starting --- here's- the background, our stakeholders expressed the need for patients, lived experience to be taken into consideration in our processes.

Those expressed by public comments during our meetings are able to be translated into evidence, and therefore considered by the Committee. So, both the Committee Members and HRSA staff, we agree with our stakeholders, and then have identified the speakers that started since May of 2023. Next slide.

The first of those was in 2023 we had Beth Tarini from the Children's National Research Institute present on mining the gap. This was a project that describes data gaps for the impact of false positives, and uncertain prognoses with newborn screening. Beth summarized active NIH funding research projects looking at the impact of false positives, and prognoses.

And they used mixed method approach, including qualitative research, and we're looking forward to follow-up results to be presented at a future Advisory Committee meeting. Next slide. Then in January of this year, Don Bailey and Elizabeth Reynolds from RTI, sorry, and Melissa Raspa, all from RTI International presented on a project family outcomes of newborn screening.

This project describes previous research, and is using it to develop a tool to measure family outcomes of early intervention, recognizing that there are outcomes that we don't traditionally capture, or necessarily consider in our decision-making process. These are HRSA-funded, this current study to adapt the tool to family outcomes, specifically for newborn screening, and the project is continuing to work with families to develop key concepts around issues such as quality of life. Next slide please.

Also, in January of 2024, we had a project

described the family's search for meaning and value in rare genetic diagnoses. Here, Dr. Ackerman from the University of California talked about her project from the Program in Prenatal and Pediatric Genomic Sequencing, performed 2017 to 2022, looking specifically at the utility of genomic information from families, exploring the ethical and social issues of exome sequencing, and then presenting data collected through clinical observations and in-depth interviews with parents.

Next slide please. And finally also in January, we had The Value of Values, Expanding Assessment of Net Benefit and Harms through Social Science Data. Aaron Goldenberg, from Case Western Reserve, presented on the project that describes the need for more data from the family perspective on newborn screening, in order to expand our notions of benefits and harms for newborns, family, and for society.

He provided an example of ScreenPlus NBS study in New York. This is a consented pilot newborn screening program, which is gathering key stakeholder opinions to guide ethically sensitive decision making about newborn screening expansion. Next slide.

In May of 2024, we streamed in Jane Noyes, Dr. Jane Noyes, Professor in Health and Social Services, Research and Child Health from Bangor University in Wales. She is talking about qualitative evidence synthesis, specifically the GRADE--CERQual approach for assessing confidence in synthesized fundings from qualitative studies.

She talked about how qualitative research can be brought together and synthesized in an evidence review that can then be used by decision making groups. She discussed in depth the GRADE--CERQual approach for assessing confidence in qualitative findings.

This word "confidence" is different from the word that we used in the quantitative assessment, which

is certainty, but it's the qualitative synonym, the same concept for qualitative research. And then she provided examples of how GRADE--CERQual has been used in developing and influencing evidence based clinical guidelines, and we just put a link to GRADE--CERQual in the slide. Next slide.

So, here are the projects that we tried to systematically bring forward in front of the Committee to think about how we could move forward, and this is a very important source of evidence, the mind the gap, early intervention in newborn screening, search for meaning and value in rare genetic diagnoses, values of values looking at net benefits and harms, and social science data, and assessing the confidence in evident synthesis of qualitative studies. Next slide.

Oh, and -- sorry, if you go back, if you hit on that QR code it will take you to the presentation and slide sets that we had summarized. Sorry, now next slide, thanks. So, the conclusions that we made is that

there are established methods for translating lived experience into peer-reviewed research.

We also believe that research can be synthesized in the evidence review for a condition nominated for the RUSP, and this is an evidence-based and structured systematic way of including the voices of family in an evidence-based decision process. So the next steps that we are planning on is to bring together a panel on the resources available to fund research, that includes the lived experience perspective.

And I hope at that time, also in part to funders, why we think this is a critical area of need, next slide.

Committee Discussion

DR. KEMPER: With that, I'd like to open the floor to discussion by Committee Members, and then Org Reps, and see if there's any additional comments or suggestions from my colleagues on the Committee. And

that's what happens pre-lunch right, that preprandial drop in glucose levels. All right. Turning to our Organizational Representatives, Bob?

DR. OSTRANDER: Hi. Robert Ostrander, American Academy of Family Physicians. This has been, and I've been an Organizational Rep for quite a long time now. This has been a concern of mine and ours for a long time, as we've been looking at things on the RUSP, and I'm just going to summarize briefly how I crystalized this in my own mind before I kind of make my comment and ask my question.

It seems to me that there are three domains that should be considered when we're looking at net harms and benefits. One of them is I think what's gotten a lot of the focus and attention, which is biological disease specific interventions, and I think that's often been 98% of the decision-making process. I think then between that and the lived experience, is the nondisease specific interventions that early detection

can assist with.

And I mean I've done some work with MBA a few years ago, and it was our sense is that maybe the benefits of that because of the delay is between symptoms and diagnosis of muscular dystrophy is so long that those benefits were potentially being overlooked. And then there are the lived experiences impacts of screening.

So, that's kind of how I put it in my mind, and I want to make sure that middle one doesn't get neglected. Another concern I have is that we've been so, and I don't mean we here, I mean we, as a society, have been so focused on assigning a higher degree of validity and reality to things that we measure, than things that are harder to put a number on, that we just constantly caution ourselves not to say we're going to look at all these, but the stuff that has the numbers is going to carry, you know, is going to something I assign more reality to.

And this has been an issue for a long time, and it's, you know, we run into it in the practice with daily primary care all the time because, you know, we're judged on what we can measure, and not what really matters a lot of times. And then my final comment and concern, really the question is how are we going to gather information about lived experiences from people who are not forthcoming with their lived experience?

I think people who have suffered harm in their minds at least, from not having their children screened come forward. I think those who have had benefit from having their child screened and been treated come forward. I think it's harder to find the folks that where the opposite is true, that have benefitted from that, you know, benefitting from not being screened, or have been harmed because of the result of being screened, or having a diagnosis.

That has come up a fair amount, I think it's been given a lot of weight, and in some of these early

discussions is oh my goodness, a false positive is so horrible we better not consider a test that isn't perfect. But if we're going to do this lived experience research, how are we going to solicit people that have not benefited from, or potentially benefitted from the program, or have been harmed by the lack of it?

And I think that's going to be a challenge to make sure you get a decent dataset that way.

DR. CALONGE: Yeah, I think these are questions that I asked Dr. Noyes when she was here, and she said you just have to do more research. And there are qualitative researchers who, that's what they do. They figure out recruitment methods, survey strategies and other approaches.

But you're right, it's more difficult than – it'd be more difficult than measuring numbers. People who do qualitative research, who have to look through the narrative developed themes, Dr. Noyes gave an example that two different evidence synthesis groups can

look at the same body of evidence and come up with a different set of themes from the same evidence. So it has the challenges that we see in the quantitative research world as well, and things that I'm excited about the progress that folks are making in qualitative data research.

The other thing I'm interested in looking at is that there's a recognition that AI, and ML, and machine learning might give us additional tools that might be a source of greater consistency and extraction of themes, and a qualitative data synthesis moving forward.

I think it may be a little bit --- well, I don't want to predict. AI has moved pretty fast. It has not always moved in positive directions, but the fact that people are thinking about it for data extraction and synthesis from qualitative data synthesis I think is pretty exciting. So, I think those are good admonitions, and I think we're really trying to look for

a way that lived experience can enter the evidence stream that leads to the consideration by this Committee and those in the future about making decisions about adding additions to the RUSP. Oh, Natasha, I'm sorry -- oh, Ash?

DR. LAL: Very briefly. I would second the comments from Robert that, one place where I have difficulty in assessing and making judgements is the impact of false positives, and I don't think we have the --- some presentations that we've had in the past for some comments we've had in the past. I often feel our problem in previous generation of testing and the fact that all we use genetics now, and genetic diagnosis, and how that has impacted the general process of how people receive news about the genetic diagnosis compared to where we stood maybe 20- or 30 years ago, you know.

For potential impact of a genetic diagnosis, which may not be needed versus later, where maybe some uncertainty, but the diagnosis, both the necessity of

the change. So, these --- I felt sometimes that there's- a lack of current impact of uncertainty of false positives on families, and how that could be addressed.

I don't know whether it could just be surveyed during the evidence review group, or if it may perhaps be an invitation in light of presentations. Thank you.

DR. CALONGE: Thanks, Ash. Jeff?

DR. BROSCO: Just a quick follow-up that the NIH funded, you heard, Aaron Goldenberg and the presentation that we had from Beth Tarini, and they just sort of presented it. They were addressing that very question, they should be having results fairly soon, so when they're ready to come back we're certainly going to have them come and talk to this Committee, because you're right, Ash, we need to have updated information on how false positives and other uncertainty really is working nowadays.

DR. CALONGE: Now, Natasha?

MS. BONHOMME: Natasha Bonhomme, Genetic Alliance. Thank you for the presentation of the recent research in this space. I think it's important to note that, you know, there really is kind of a world of dialogue and discussion amongst patients that does not make it into journals, but it is there.

And so, really thinking about how to engage directly with those patient groups to hear from them, not necessarily just an assessment or an analysis of some of those experiences. FDA has really great processes around that in terms of engaging families in - - - and- parents and a whole range of people, in the discussion, in the actual decision making that they do, so that may be something to look at.

And then in speaking to the point of, you know, how do we get the perspectives of people who tend not to share their perspectives? Oftentimes they are sharing their perspectives, they're just not doing it in

the channels that we are tapped into. So, even long, long time ago when we built baby's first test, we didn't just listen to patient advocates, but we also went on to discussion boards, where people were actually being critical of newborn screening, to see what the discussion was there, and really dive deep in terms of the questions that needed to be addressed.

So again, there are those different both academic and non-academic, formal and non-formal ways to really tap into the very perspectives, not just a family perspective, but the range of perspectives out there.

DR. CALONGE: Thanks.

DR. CUTHBERT: Can I just quickly respond to that?

DR. CALONGE: Yes, Carla?

DR. CUTHBERT: So, those are really, really good points, and again I don't presume to be any kind of expert in this, but I do want to point out that with machine learning and AI, things like sentiment analysis,

can really be very helpful in being able to make those --- --- have an appropriate way to be able to make those assessments, and to pull out information as a result of that.

So, I've been thinking about some of those things. Again, just as part of my understanding of what AI can do to really help, and it would be really interesting to be able to chat with you about places that you can actually find --- get feedback on where people are talking about newborn screening, where we may not be looking. -Thanks.

MS. BONHOMME: Yeah, I just want to add to that. I think that it is important to be thinking about AI and how that can be helpful, and at the same time, hold up the same, you know, equal weight. We've all seen when a new technology comes in that's supposed to solve everything, and then three years down the road people are like oh my gosh, it has the same biases that everything else has had, so I think that's important to

think about, but I mean yes.

Every single day there's a new AI technology that can be implemented that's free, that can be pulled in. So I think we need all of it, it's not a one size fits all, not that you were saying that, Dr. Cuthbert, but I think we need as many of the resources and thought partners around that.

DR. CALONGE: Yeah, there's a great NIH project called Aim Ahead, which is specifically looking at AI and ML in the context of making it appropriate across different marginalized populations, looking at specifically those issues about how to undo the bias, or build supported strategies that are inclusive of other ideas and other concepts, other cultures, other ways of thinking.

So, it's a well-identified issue that even NIH is helping us try to sort through. I appreciate the comments. Amy?

DR. GAVIGLIO: Yeah, thank you, Amy Gaviglio,

National Society of Genetic Counselors. I have a question and a comment, so my question is, is the intent of this research to try to obtain lived experiences for each individual disease that is going through a nomination process, or more globally assessing lived experiences of rare disease was my question?

And then my statement is as we think about assessment of experiences, and potential harms around things like false positive results, I think it will be very important for us to glean the context in which the false positive result occurred, and I ask that, or I mention that in terms of teasing apart whether it truly is the result that causes harm, or the way it is communicated, and the lack of support provided to families.

And I can see that being different if say, a family meets with a genetic counselor right away. And so, I want to make sure that we're not just assuming that a result in and of itself causes harm, but we're

really taking the time to understand the context in which that result was conveyed, and the support the family gets as part of that process.

DR. CALONGE: Yeah, I think those are great additional comments, and I think as we thought about it, at least started, it would not necessarily be top-- I mean, the research that's going on now is not topic specific. And the concept is that within some limits, the topic, it should be agnostic to the topic. There may be issues of rarity or severity, or treatment availability, or other issues that make it different, but I think we're thinking kind of high-level summary, at least as we get started.

And then thinking about the evidence review group, there's a category of evidence called evidence by analogy, so it worked in this setting. Is there any reason to expect it wouldn't work in this other setting? The issue about how the information is provided I think is an important contextual issue, thanks. Thank you so

much for input. Stay tuned, and I'll turn things over to Leticia.

COMMANDER MANNING: So, we're going to head into lunch now. Just as a reminder, there's a cafeteria right across the way here. There's also a store back this way, where you can get a hold of snacks if needed. Please let HRSA staff know if you must exit the building. Tina is in the back there, she was waving her hand, but we really encourage folks to stay in the building if possible.

DR. CALONGE: And this slide is incorrect. It should say 1:45. Yeah. So, we're going to give you a full hour for lunch, and this is just a leftover from earlier strategies, so please resume promptly at 1:45, and we'd be exactly on schedule. Thank you.

(Break 12:48 p.m. - 1:50 p.m.)

Approaches to Population-Based Screening in Newborns and Children

DR. CALONGE: As we reconvene, we have been talking, and we've even heard references this morning about issues around what state newborn screening systems and programs and labs can do, and things that are more challenging in terms of implementing. When our intent is to try to look at universal screening for different rare conditions.

So, there are other approaches that have been used successfully in the past. Things like clinical standard of care is an alternate pathway for achieving universal screening in clinical care. Also, clinicians and organizations use continuous quality improvement as a way to do this, just like newborn screening programs do, or organizations or HMOs who are competing in the marketplace use HEDIS measures.

But sometimes there may be state involvement that's neither appropriate, or at least not easily done,

especially for things like point of care screening. So, we wanted to have a more in depth look at how this is achieved outside of the state newborn screening systems, and state public health and I brought kind of two folks to present today.

We're going to have -- first, we're going to hear from Dr. Stephen Patrick. Dr. Patrick is Professor and Chair of the Department of Health Policy and Management at the Rollins School of Public Health. He's also the Codirector of the Center for Health Services Research, and a practicing Neonatologist at Emory University.

He is an Adjunct Physician Policy Researcher at RAND Corporation. Dr. Patrick joined Rollins from Vanderbilt University Medical Center, where he was Professor of Pediatrics and Health Policy, the William Long Director of Child Health Policy at the Vanderbilt Center for Child Health and Policy, and the Executive Director of Firefly.

I also am going to ask to come back to the podium, Dr. Alex Kemper, Division Chief of Primary Care Pediatrics at Nationwide Children's Hospital, and Professor of Pediatrics at the Ohio State University College of Medicine. His research focuses on preventative services in the primary care practice setting.

He has partnered with the American Academy of Pediatrics in activities related to Bright Futures and the periodicity schedule, which is the evidence informed age-based recommendations for preventative services. Dr. Kemper also did as many years as they would let him as a member of the U.S. Preventative Services Task Force, which is another evidence-based group that makes recommendations that can be covered with first dollar coverage under the ACA Act.

So, with those introductions, is Patrick starting? I want to welcome you, Dr. Patrick. We see you onscreen, and we're going to let you go first.

DR. PATRICK: Wonderful. It's great to see you all. Do you see my slides?

DR. CALONGE: We do.

DR. PATRICK: Fantastic. Well, it's great to be with you all virtually. I am also a practicing neonatologist, and so part of what I was asked to do today is just talk through some of the critical things that happen during the beginning parts of life, and give a couple examples of things that we do for newborns, particularly, you know, pre-term newborns, in those first few critical minutes and hours, and talk about like the care processes, and specific actions, and how we work to make them better.

So, our objectives today for my brief time, is to discuss these critical transitions in the first hour of life, for extremely low birth weight infants, describe temperature control as an example of care process improvement early on in life, discuss some risks for opioid-exposed infants, and how process improvement

at discharge transitions can occur for opioid-exposed infants, again all focused on improving outcomes.

Well, this is a pre-term newborn, so extremely low birth weight infants are small, and they are vulnerable to many complications early on in life, and this is kind of what things feel like in the delivery room, and at that moment multiple steps need to be taken to ensure that newborn does well.

Here's just an example of admission order stats, just taking a picture of you know, what happens for an extremely low birth weight infant around the time of birth, and just to give a sense of this, there's you know, more than 30 standard admission orders listed here, and certainly you can go through multiple decision trees of the things that need to happen, from everything from glucose monitoring, to blood test monitoring, to processes that need to occur.

But if untreated, extremely low birth weight infants, AKA infants less than a kilogram, will develop

respiratory failure, hypothermia, and hypoglycemia. And so, this golden hour in the first hour of birth is really the optimal time to rid these complications and avoid both morbidity and mortality.

One of the things I want to focus on is temperature, because we often say, you know, measuring temperature seems like an easy thing to do. You know, if I said to you, gosh, we should measure temperature in newborns when they're born, you would say well, of course we should be doing that, that seems like an obvious thing.

But what we've discovered in hospitals across the U.S. is that oftentimes we fail to do that, or we fail to set the circumstances up to where infants have normal temperature. We know that hypothermia is less than 36.5 degrees Celsius, 37 degrees is 98.6 for those of us work in both the metric and non-metric world.

Newborn temperature can drop two to four degrees Celsius in the first 30 minutes of life without

interventions, and that's for a couple of reasons. One is body surface area to body mass. Infants have a ton, -- really pre-term infants have a ton of skin, and not a lot of body mass. Imagine anyone of us walking around right now with twice as much skin as we have, you're going to lose a lot of heat.

Subcutaneous fat, they have less of that than we all do, and immature vasomotor control, which is sort of the ability to sort of open up vessels to control temperatures a bit better. In one study, every one three Celsius decrease in admission temperature was associated with a 28% increase in mortality.

This is true in the U.S., and certainly there are multiple states outside the U.S. that associate hypothermia with poor outcomes. We often think about the ways infants lose temperature. These are kind of the four big ways. There are things we all think about that when applied to a newborn, you've can see how things come together.

Radiation, they just lose heat. This is why we think about hats on infants, convection, wind coming by, and trying to think just like a convection oven, evaporation, infants are wet when they're born, so they lose temperature and then conduction. If you put them on a cold surface they will lose temperature that way.

So, what can we do? I mean some of these interventions are pretty darn simple. Put a hat on the baby, blankets, skin to skin care with the birthing parents. Increased temperature in the delivery room or operating room. A radiant warmer, warmer above the infant. A chemical heat mattress underneath the infant for really for very pre-term infants, and a polyethylene bag, if you can believe that too.

It literally looks like a Ziplock bag. Even with these simple solutions, a 2016 analysis found that nearly two in five very low birth weight infants were cold, and this is an analysis from the Vermont Oxford Network, which includes data from about 80% of hospitals

that care for these types of infants.

Here's an example of a bag that an infant is placed in, I'm sorry for the low quality image, but you know, you get a sense of like yes, in the delivery room just placing an infant in a bag like this can be effective. So, I want to share an example of one hospital, this is published in the Journal Hospital of Pediatrics a couple years ago, how they approached improving what is a very important problem.

It seems like we should be able to address that pretty easily, right? So, they went through and developed a driver diagram, and I know Dr. Kemper is going to talk a little bit more about these types of quality improvement efforts, where they started, what's their aim to decrease the rate of hypothermia, pretty straightforward.

What are the primary drivers? We can go down the line of staff knowledge, you know, do the staff know about evidence-based control? Have they heard about the

- sorry -- evidence-based protocol. Have they heard about the protocol? And then what are the interventions, working backwards to that.

Expansion of chemical heat mattress, bedside limited cards, guideline badge cards, like every hospital has a unique approach. And this sort of broader approach to quality improvement works through planned study act, and so you plan an intervention, you do it, you study it to see how it was effective, and then you modify it.

So, if your initial intervention -- let's say your first intervention is okay, we'll try a hat. If that doesn't fix the problem, they modify the intervention until you get to where you need to be. It's different than a clinical study like that. So, here's their results. When they started in January 2016, only about 40% of infants were below the desired temperature.

And you can see as they go through cycles.

These cycles are these PDSA cycles, where they have done audits, then they expanded heat mattresses, and then kind of modified things further. And so, you start to see this improvement, including sustained improvement, and just doing the right things that we know improves outcomes.

This is part of how process can improve, and we can pull out processes for many things, including glucose control, which is a, you know, a diagnostic test we do pretty early on in life. I want to talk about one, just another one that's from our group, where at Vanderbilt, where I was before. We know that nationwide about every 15 minutes an infant is born having opioid withdrawal in the U.S.

And opioid-exposed infants are at risk for adverse discharge complications, including readmission. Many infants that are opioid-exposed are not connected to critical post-discharge services, and this is important. One of those services is ensuring they've

been tested for Hepatitis C.

In our setting, about 40% of opioid infants are also diagnosed with Hepatitis, or also exposed to Hepatitis C, but you can't test newborns during the birth hospitalization. It's completely silent. You have to wait until they are a couple months old.

Because of that, less than 20% are tested to see if they also develop Hepatitis C. That's just not unique to Tennessee, that's true with other areas of the country, including some work from colleagues in Philadelphia. So, we came up with a pretty simple checklist, which is schedule a pediatrician visit before discharge, referral to home visitation services, referral to early intervention services to provide developmental support, referral to our clinic, and if exposed, referred to Hepatitis C follow-up.

Here again, you'll see the kind of similar discharge, excuse me, key driver diagram, where we sort of work through where we want to be. We believe in kind

of smart entrance to be really specific, increased successful upon completion of the discharge checklist from 2.6% to 40% by January 5th. And you can see how we work through those problems.

Similar to us, when we look back to see okay, how often were we meeting those things within the checklists every time we were to report? And you know, we were essentially zero. And then you have some simple interventions beginning a bundle, a measurement of the bundle, just measuring it broad awareness to that. Doing some resident education and sticky notes in the electronic health record, improve things further.

And then doing some biweekly resident reminders. You could see this dip was when we lost a social worker. But you can get a sense of, as you begin to improve processes, you can start to do things that are complex. So, care processes can be exceptionally effective, and there are a lot of key resources.

I mentioned the Vermont Oxford Network before

the caps is around 80% of very low birth weight infants, but they also do quality improvement around term infants, state perinatal collaboratives are founded by the Center for Disease Control and Prevention, a Division of Reproductive Health, coordinated by NICU, and often have a state partner like in Tennessee, Medicaid, and then certain guidelines.

I mean I will point out just some of the ones that we worked on, and you know, the opioid syndrome also has elements of a checklist. So, you know, my goal for this was just to introduce what quality improvement processes can be for newborns. I realize that, you know, we're looking at this through the lens of newborn screening, and things that have to be there, so I think we'll have an interesting discussion, and look forward to that as we move forward. Here's my contact information.

DR. CALONGE: Thanks, Dr. Patrick, and now Dr. Kemper.

DR. KEMPER: Thank you very much, and thank you Dr. Patrick for keying things up. We're going to switch from the NICU and talk about things that happened after discharge from the newborn nursery. This is something I feel very passionate about. I'm really excited for this opportunity to talk about approaches to screening in childhood over the next six hours straight, is that how long I have?

Because I could do it. So, I just -- beginning with the disclaimer that these reflect my thoughts, not the American Academy of Pediatrics, the evidence review group. We're not going to be talking about newborn screening, or really any other organization. To help sort of pull things in, I did come up with a series of learning objectives that we're going to do, actually, within the next 20 minutes or so. So, I'm going to summarize the general prevention strategies, and how they apply to primary care pediatrics to construct approaches for primary care

prevention.

At the end you should be able to relate approaches in primary care to newborn screening, right, so where's the analogy? To evaluate approaches to primary care prevention, to explain the importance of processes and outcome measures. Dr. Patrick talked a little bit about those, and then to navigate the process from recommendation to implementation.

And those questions came up earlier this morning. So it would be nice to return to that. I like to think about different levels of prevention because it ties to the kinds of things that we can do to improve health outcomes. So, you'll hear me talk about primordial prevention, sometimes these are avoiding the risk factors early in life that can lead to disease.

Primary prevention, which is avoiding the condition by elimination of the disease agent or increasing resistance. Secondary prevention, which is a lot of the work that we do in this group, which is

addressing the condition early on before symptoms, and then tertiary prevention, which can include things to reduce the harm of the condition in the first place.

And if you think about prevention across these different levels you can come up with different interventions that you could put into play. So, as I talk about preventative services, I want to be clear that we're talking about delivering services to the individuals who are asymptomatic or who are recognized to have the condition.

And there are a range of things that we do in primary care. We counsel, we give preventative medications, and we screen, so oftentimes in this room we focus on screening, but it's important to remember that there are these other components of prevention as well.

I do also want to distinguish between screening and surveillance, and when I talk about surveillance, I'm talking about surveillance from a

clinical perspective, not a public health perspective. So, screening is case detection at a single point in time, so you know, there's a newborn, and I'm going to test them for PKU.

Surveillance, again from a clinical perspective, is an individual ongoing longitudinal evaluation. So, for example, at the individual level we get to know the child over time and can see how well they're doing in terms of meeting their normal developmental trajectories.

Again, surveillance in this way is different than using data for public health practice, which is the sort of public health term, but again this is a clinical talk, and I just want to throw that term out there. There are lots of places where recommendations for what happens in primary care pediatrics come from, so there's the EPSDT benefit, or the early and periodic screening and diagnostic and treatment benefit.

These are requirements for Medicaid-enrolled

children. There's the Advisory Committee on Immunization Practices that makes recommendations for the immunization schedule. This one, I think most of you have heard of it, the Advisory Committee on Heritable Disorders in Newborns and Children.

There's Bright Futures, which is a cooperative agreement between HRSA and the American Academy of Pediatrics. I'm going to dig into this a little bit more. Dr. Calonge mentioned the U.S. Preventative Services Task Force, recommendations that come forth from them, that our A and B recommendations are covered first dollar through the Affordable Care Act.

But so are things that are in Bright Futures. There's some caveats that are complicated, but you can think of it as leading to coverage. And then there's the Community Guide, which makes recommendations around community-level preventative services.

So, I had mentioned before, Bright Futures is

this cooperative between the Maternal Child Health Bureau and the American Academy of Pediatrics. It's evidence-informed series of recommendations. It really comes in two different components. There's the Periodicity schedule, which I'm going to show you in a second, which is the list of expected preventative services that happens at each routine well child check.

And then there's a book, which is very thick, that goes over how to implement comprehensive well-child care. It's the Periodicity schedule that carries the weight of the Affordable Care Act. So, I put this up just to show you, and I don't expect anybody to read anything. You couldn't even if you wanted to, but shows all the different preventative services that are included in the Periodicity schedule.

So, if you look at the columns, those are the individual well-child visits from infancy to early childhood, to middle childhood, to adolescents, and then if you look across in the rows, those are the general

preventative service categories which include history, measurement, screening, development, and so forth. Wherever you see a dot, which hopefully you can see a whole bunch --- a whole sea of dots, those are where the expectation is that that preventive service will be delivered at that particular visit-.

In contrast, there's the book, which is like a huge tome, that describes the 32 age specific visits that are recommended, and the book itself really boils down to focusing on caregiver concerns, childhood development, and positive reinforcement for families.

Across the various visits are themes. I'm not going to read it through each theme, but you can see how this really hits all the things that are important for child development and overall wellness.

The Bright Futures recommendations also outline the visit structure which focuses on understanding the parent and child concerns, surveillance and screening, assessment of strengths, and

then various age-based visit priorities as the child and teen ages -- obviously the priority for each visit changes a little bit.

So, as I talk about through things, I always try to keep a life course perspective, and so the things that we're going to focus on ultimately we're moving towards a healthy trajectory, and as a child ages there's things that we can do to promote the healthy trajectory, so focusing on things like emotional health, literacy, reading and so forth, while at the same time avoiding those things that can decrease the trajectory, including poverty, poor access to care, toxic stress, and so forth.

As part of the work that we do as primary care pediatricians, it -- is focusing very much on the social determinants of health. These are the conditions in the environments where people are born, live, learn, work, play, worship and age that affect the wide range of health outcomes. These can be broken into domains of

economic stability, education access and quality, health care access and quality, neighborhood and build environment, and the social and community context.

Everyone I hope hears a lot of about social determinants of health. I actually tell you I did not like the term social determinants of health because if you call it a determinant, then you're sort of implying that an individual who has been exposed to these things is doomed, and so I really try to use social drivers of health, and there are things that we can do to affect these things.

Oh, I think I am now of --- oh, so I need to pretend like my screen didn't- change. So, I am, in the interest of time, going to skip through some stuff on the U.S. Preventative Services Task Force, other than to say that it makes evidence-based recommendations, and I think everyone has seen the grades that comes up before A's and B's as things you ought to do. D's are the things you shouldn't do. I refer to them as don't do.

The C's are the things that maybe have a benefit, and you want to talk to families and see if this is something that they want, so I think a C is have the conversation, and the I's are where the evidence is insufficient, and you have to look towards other things to make recommendations.

So, with that as a background, I just want to tease out some stuff that I see as different between newborn screening, what happens in well-child care. So, newborn screening obviously happens in the newborn period, so it's only early in infancy. It's basically once or twice, if you're in the two-screen state, and then you're done.

There is near universal access to screening. Families really don't have much of an option about newborn screening. I guess the only option is whether to be screened, or not to be screened, but it essentially happens. And then there's just strong public health involvement through at least diagnostic

confirmation, and you know, in some cases a little bit longer, but at least there is this important role that the public health plays.

As opposed to well-child care, right, that happens at any change, it's repeated, it can be informed by surveillance, and other personal factors, including concerns that might come up from the family. It's certainly not universal, right, so we know that there are issues related to access and variations in quality.

There is an opportunity for shared decision making, right? So you can't really have like a USPSTF category and talk to families about whether or not they are going to be screened for some things as part of the newborn screening, but as part of this kind of thing you can, right?

And then, generally as part of well-child care there is no public health involvement. There's some exceptions, things like lead screening, and that kind of thing, but generally not. So, I think a lot

about the importance of well-child care to address disparities, and again, we could talk for a long time about disparities, and I know that that's not the focus here, but I do think it's important to bring up.

So, this is a slide of infant mortality in Ohio, over a ten year period of time, and it shows the difference between Black infant mortality and white infant mortality at the bottom, and then you could see the average Ohio infant mortality rate over time in the dark black line. And in all of our work, in all of our quality improvement work, we break things up by race and ethnicity to make sure that we're, first of all, not causing disparities, and that we're addressing the root causes of those disparities that exist. Because, you know, on one hand, if you just looked at sort of like relative improvement, right, so there is this improvement over time in the Black infant mortality rate in Ohio, and in the white infant mortality rate in Ohio.

But that's a huge difference, right? This is

something that we should be all upset and invested in, and as I go through and talk about some particular activities, I just want you to keep this in mind. The root causes for these disparities are complicated, again, I'm happy to talk about it, but it's hard to think about any aspect of health care delivery, or health outcomes where you don't find these kinds of disparities.

The other thing that I think about is, and we're going to drill into the work that we do within our primary care network, is the causes of death, and when they occur. I showed this slide not to pit one group against another group in terms of what's important and what's not important, but just to provide context.

So, you know, in the early ages birth defects are around 3 per 100,000, this is in the ages one through four, but then if you look at in the older groups, it's things like unintentional injuries and suicides that really dominant the causes of mortality in

the United States right now for children and adolescents one and older, the leading cause of death is related to firearm injuries.

So, again, we think a lot about what's causing harm to the patients and families that are in our responsibility. And that's led to something that I refer to as the vital signs project. This is a listed, targeted preventative service activities that the network that I'm going to describe in a second focuses on.

We already talked about infant mortality, Kindergarten readiness is another one, high school graduation, the preventive care index is just a summation of generally recommended preventative care things like vaccinations, and those kinds of things.

Teen pregnancy, OBC, all child mortality and suicide. So, as I show you a little bit about who we are as a network, know that these are the things that we're really focusing on, but we're also holding

ourselves to improve these outcomes for everybody who lives in Franklin County, regardless of whether or not they come to us for care.

We have an approach to quality improvement that's based on standard quality improvement activities with small tests of change. I'm looking to see the difference it makes. This is who our network is. We have 14 clinics around Columbus. We have over 130,000 unique patients that we provide care for with about 240,000 patient visits annually.

Nearly all of our patients are Medicaid enrolled, and part of our accountable care association, known as Partners for Kids. So, here's examples of things that we've done with quality improvement. At any given time we have about 30 different quality improvement projects ongoing. So, you know, we look a lot at access, right, so we're not going to be able to deliver preventative care services if we don't get patients in.

So, this shows our patients with six or more well-child visits by 15 months of age, and you can see that that went from about 45% to about 60% over time. These are our patients with two or more visits between 15 and 30 months, and you can see that that's around 60% as well. And then we look through the teen years.

And you can see that we try to label these things as we each find different activities to get people in. So, I show these slides just to highlight the importance of thinking about access, and getting patients in, if you want to be able to deliver the preventive care services.

We follow things like immunizations. You can see how we're doing in time over there. Here's the adolescent immunization schedule over time. We drill into specific services like HPV vaccination. Here's our work around depression screening for children 12- to 17-years-old coming in for well-child care.

And you can see how critically important it

is to follow how things are going on over time. April 2020, what happened then? I'm trying to like block that one out. All right. And then it's not enough just to look at how we're doing with screening, but we also look at the patients who had a positive screen, and whether or not they got recommended therapy.

And you can see how that's changed over time. I showed this, I could have pulled this up really for everything that we look at, this is our suicide screening activities broken down by race and ethnicity. It's sort of a messy little spaghetti diagram, but we do this for all of our work, just to make sure that we're recognizing disparities and developing interventions as appropriate.

Here's an example of interventions that we had to do in terms of increasing our use of interpreters to ensure that there wasn't a disparity in developmental screening by preferred language. There are dozens of languages spoken by our patients. I show this just to

point out that all this stuff requires ongoing measurements and practice. We re-designed, this is a slide showing our access to care.

And what I would say is that if we really want children to get the preventative care services that we want, there are things that need to happen related to the recommendations that need to be clear and comprehensive. There needs to be a burning platform, somebody needs to care about it and measure it. You need to have process measures you can look at over time.

There needs to be quality collaboratives with participation. You need to collect data in real time at the practice and the clinician level. There's nothing better than being able to go back to a clinic with attending problems and show how they compare to their peers.

As an aside, we do something that we refer to as March Metric Madness, where we pit all of our practices against each other during the NCAA tournament,

with a big trophy that gets awarded at the end. Again, informatics tools, population focus and aligned incentives. I didn't mention this before, but most of those slides that I showed you of the control chart showing how things were done over time, the denominator is not who's coming in for care.

It's who is assigned to us, so it's really important to think about things from a population standpoint, right? If somebody is not getting a preventive service because they're not coming in, we need to be responsible for that and come and figure out why they are not coming in. As a matter of fact we have things like Lyft now, Lyft services to bring patients in to get them, and we've developed a school-based health program, so that we could get patients that aren't coming into the clinic.

So, that was a whirlwind tour. I obviously could have talked about things a lot more, right? I just wanted to put up the learning objectives just so

that you could remember what we just went through. And what was funny is last night as I was going through the slides, and looking at things again, I don't know how this happened, but look at that.

Okay. I don't want to tell you how many hours I spent on that, and just in case you're wondering I did not use ChatGPT. This was all me. This was all me. So, I guess I'll just leave it right there, but I think that there's really tremendous opportunity for recommendations that come forth from this Committee to help inform what happens as part of well-child care, for things that maybe don't fit necessarily with newborn screening.

And I would say that while the preventative care services that happen within primary care are not perfect. They can be really good, especially when you can tie together just larger population perspective.

Committee Discussion

DR. CALONGE: Alex, are you willing to stand up there, while you and Dr. Patrick answer questions?

DR. KEMPER: I would be honored.

DR. CALONGE: Let me --- let me start with one intervention that, just because I've been involved in it a lot and I know well. That was birth dose for Hepatitis B. So, Colorado uses hospitals to develop, to deliver the birth dose for Hepatitis B, but we're- well over I think 98% success rates in hospitals.

So, as we get to birthing centers and home deliveries it drops off quite rapidly, but are there other examples of that kind of --- and Dr. Patrick, as well, you talked a little bit about hospital delivered standard of care interventions that you know about that we've been successful in getting quite high participation rates that don't look differential by identities?-

DR. KEMPER: Yeah, I can talk about one

example then, Stephen. I was going to talk about bilirubin, do you have like another example? So, newborns are at risk for complicated reasons of having high levels of bilirubin, and for some of them if you don't treat them it can lead to a problem called Kernicterus, which is a form of brain damage. The current, I was actually the lead author on the new AAP bilirubin headline, so I didn't feel like I had to put that out there for whatever it's worth.

But the recommendations are for all babies to have bilirubin levels checked before they are discharged from the newborn nursery or go home, and then based on the bilirubin levels, they either need treatment, or need to have, you know, a lot of them need to have close follow-up with primary care for follow-up bilirubin levels.

The American Academy of Pediatrics just led a gigantic quality improvement activity to confirm that babies are getting bilirubin testing prior to discharge,

and that they're getting the appropriate follow-up, including with primary care, based on that bilirubin level, and it was really a smashing success.

Now, there were opportunities for improvement in ensuring that children got --- there's actually a bigger problem with over treatment than under treatment, based on bilirubin levels, but I think that's- an example of like a big win that this Committee could look at.

DR. CALONGE: Dr. Patrick?

DR. PATRICK: Yeah. There are lots of examples, actually. I mean like everything from Vitamin K to antibiotic ointment at the time of birth to congenital heart disease screening with a pulse oxy prior to discharge, and everything in between. There are a lot of standardized processes that occur that, you know, if you just go around and look at an average state perinatal collaborative, and the work that gets done, sometimes complex, sometimes not, definitely.

I mean, another example would be, you know, changes that we've seen around kind of promotion of breast milk in hospitals. There are lots of examples of just what you're talking about. You know, kind of creating processes to make sure we get that first Hepatitis B vaccine prior to discharge.

We're seeing the same thing around RSV prophylaxis with some complexity right now, and who gets it and who doesn't. But we can implement things within hospital settings, and do them very quickly and modify them. The congenital heart disease screening is a great example of that where you know we do a pulse oxy screen universally for infants that might be at risk of having congenital heart disease that may not be apparent.

You know, these things were not something we did 30 years ago, you know, these are processes that occurred over time.

DR. CALONGE: Yeah, I'd like -- - and I often bring up the --- - I did this morning, congenital heart

disease screening is a RUSP measure, but it's a RUSP measure that people in screening programs and labs have little implementation strategies. I think in Colorado there's just a checked box that says yeah, we did it. That'-s what the state does.

And so, implementing point of service tests, are things that were --- and birthing centers can be very important in terms of the rollout and the strategy. -Melissa?

DR. PARISI: Melissa Parisi, NIH, so thank you both for those presentations, a really great reminder of some of the challenges and differences, and opportunities for not only newborns, but childhood screening, and identification. And I do want to say, Alex, that having just recently taken my maintenance of certification exam and having to review the 40-page document on screening for hyper bilirubinemia, in advance of that I'm grateful that you did it.

It is extremely long and detailed, but it is

exactly what the field needs, so.

DR. KEMPER: The check is in the mail. So, I will tell you that I got the MOC bilirubin question. I was so nervous I was going to get it wrong.

DR. PATRICK: I had that question last month too, that series of questions, and I don't have positive feelings toward Alex, I'm just kidding.

DR. PARISI: I have a little bit sarcasm in my voice in that, but in all seriousness, all joking aside I should say, I did have kind of a question and a comment for you, Alex. When you showed your graphs of how you had achieved some of your goals of 60%, or approximately 60% of your population actually meeting those targets for coming to clinic and being seen for well child evaluations.

There were a couple things there like little arrows saying this is the intervention that caused those things to go up. And one of them was Epic notification, and one was also opening a clinic in a high opportunity

area. And I just wondered if you could say a little bit more about those interventions, and what they consisted of, and how effective they were?

DR. KEMPER: Yeah. So let me take the second thing first. So, I have a heat map of all the patients that are attributed to us, and I also know where populations are that aren't coming in, and we use that to drive where we open our new clinics. And we also use that to drive how our clinics are set up.

So, we have a hub and spoke model where we divided the city up into five quadrants, and in each of the quadrants there's one clinic that's bigger, and we bring services into there, that we know that families are not accessing, that they would benefit from.

So, for example, dental services, speech and language services, those kinds of things. We're also bringing in a psychiatrist into the hubs as well. I did mention before we actually am very proud of this. We have a psychologist in all of our clinics, and I can

tell you the secret later about how we were able to do that.

So, we use real time data to drive all of our clinical operations. Epic is --- we- use our electronic medical record judiciously for sending messages, and engaging families, because we know that if we put too many alerts in there, people get alert fatigue, and they completely ignore them.

The other thing that we're doing now is we have a text system for families to deliver messages about when they're due for things, and that kind of thing. So, we try to leverage the electronic medical record in a way that's actually useful and not overwhelming for people.

DR. CALONGE: Ash?

DR. LAL: I have a two-part question. The first is just for information. When we talk about differences in infant mortality, I am looking at Dr. Patrick's presentation before that, I was just wondering

what component of the infant mortality differences could be explained by the perinatal events, and what are due to things that happen after the first 28 days or?

DR. KEMPER: Yeah. So, we, and well, let me talk to you about what we do first, and then I think Dr. Patrick can probably give a sort of a broader perspective on things. So, like most communities, we have a child fatality task review, and we look at each infant death to identify the root causes.

So, although there's no question that things like prematurity lead to some of these deaths, a lot of these deaths, the lion's share of them were potentially preventable, so things like -- - and- those sorts of things that in retrospect interventions could have been done to prevent those deaths.

So, I'm very careful. I mean there's no question that prematurity and other early events like that that it's too late for us as pediatricians to necessarily prevent, lead to some of these deaths. You

can't pin most of them on that, certainly not in our community.

DR. PATRICK: Well, I'm happy to sort of to dive into this just briefly. If you look at maternal deaths, maternal mortality, and you look at infant deaths, you see a lot of themes. And those themes that you see are huge disparities. We see the same huge disparities in maternal deaths too. Black moms are about three to four times as likely to die as white moms.

Those same issues of equity are there for American Indian and Alaskan Native populations too. So, I view this as dyadic care, that it's our responsibility to care for mom and baby because you know, we see, let's use the opioid crisis or substance abuse as an example.

You know, treating for substance use overdose is a leading cause of pregnancy-associated death, and in states like Georgia, Tennessee, Ohio, it is the leading cause. So I can approach this from healthy moms have

healthy babies, and you know it's true. That the three leading causes of death for infants is prematurity, birth defects, and sleep related deaths.

But those broader issues of equity and systemic racism, I think drive through the force of all of this. So, when we can look at this holistically, and think about what do we do to begin to address the prematurity rate by looking upstream from a public health perspective, like the primary, secondary, tertiary approach that Alex pointed to earlier. I think that's important as we think about this.

So for example, we know that treatment of substance use in pregnancy reduces risk of pre-term birth. Pre-term birth is associated with mortality. Like, that view of maternal infant mortality I think is really important. And what we see happening are parallel conversations often, where we see a focus on the unacceptable maternal mortality rate that's happening in the U.S., that's around 900 deaths.

And we see separately a focus on the infant mortality, and those are around 35 --- I'm sorry, 25,000 deaths. I think we're better off if we look at them together because the through point in terms of I like the social drivers of health, are more similar that way, and the interventions, while some are clinical, more broadly there's a lot of things that happen outside that I think are pretty important-.

I hope it answered your question. It was not too much of a broad view of maternal infant mortality.

DR. LAL: Thank you. My second question to Dr. Kemper is the ---- in high risk infants require both family care as well as specialty care, and I just wonder if from your experience if you think that has it been relatively simple to organize and coordinate care between the specialty center and the primary care physician, or are there things that you think need to be improved during the communication and coordination of care?

DR. KEMPER: Yeah, so if I understand your question right it was about, you know, sort of coordinating things between the primary care pediatric side of things, the OB, the internal medicine side of things that are taking care of the families, as well, or?

DR. LAL: No. This is postnatal. This is between the specialty ---

DR. KEMPER: Oh, between the specialties.

DR. LAL: Between the specialties and the primary care pediatrician.

DR. KEMPER: Yeah. So, we found you know the interventions that we found that have made the biggest difference are really primary care based interventions. I mean I'm like to be right in a coordinated academic center where we have pretty good access to, you know, the sub, sub, sub, sub-specialists, but you know, one of the key things that I hope everyone gets out of this is the differences that we've been able to make in child

health outcomes have really been built within primary care.

I mean to go back; I just feel like I want to build on the comments that Dr. Patrick made about focusing on maternal and child health as well. So, our city has a program called Celebrate One, which is focused on getting children through to their first birthday, so celebrating the first birthday.

And there are a ton of interventions that we have going on, both within primary care, as well as outside of primary care within the community to help ensure that the children are healthy when they get to one year of age. So, it's true that we definitely need our subspecialty colleagues, but it's actually --- it's pretty straightforward for us to get in with them as we need them, but and I hope this is ----- if my specialty colleagues are listening, and Margie over there, who is like a huge help for in neurology.

But most of the improvements that have been

made have been made by focusing on what we can do within primary care.

DR. PATRICK: Honestly, I think all of it is from neonatology, I'm just kidding. I would also just like to put a pin on that, like in our system, the system that I was previously a part of, that's subspecialty care. So, let's take Hepatitis C. Infants exposed to Hepatitis C got a referral to the pediatric liver clinic. Like talk about super specialized.

You go like GI, and then liver, to test for Hepatitis C exposure. Well that certainly doesn't need to be a tertiary care piece. So, like as we work to support through some of our programs at Vanderbilt, one of the things we built out is how do we support primary care, how do we provide the support to our rural communities to not just do things like test Hepatitis C, which is lost, but also to be a resource when you see, you know, we might see a ton of opioid-exposed infants, but that rural practice may see three a year.

So, how could we help support that? I think that's part of developing a sustainable model, particularly as we are looking towards the future of pediatrics, where we're starting to lose subspecialties, and there's substantial concern about what our workforce is going to look like in the future. We're going to have to think about things differently.

DR. KEMPER: And again, just to build on that too, because you sparked another thought, which is we need to reward pediatricians based on the quality of care that they provide, not the volume of care that they provide, right? So, you know, we have you know, many people like rely on their RVUs --- Dr. Ostrander is like I think he rolled his eyes a little bit when I said that, but that's- what we do, you know.

DR. CALONGE: So, one of the reasons I really focused on the hospital setting is you know it's kind of like why do we do newborn screening tests in the hospitals? You know, it's really sudden, it's where

they're born, it's a universal not a sight, I'm sorry, almost --- how about the majority, the vast majority of- children go through the hospital in terms of beginning life.

And so, I always think of those hospital interventions. My question, so I talked about a success. I'd like to get your ideas about areas where we haven't done so well in terms of the practice of pediatrics outside of the hospital setting. So, I think everyone knows what the EPSDT is, and in that set, which is a Medicaid program, there's payment for universal lead level testing.

I'm in public health. I believe in lead level testing, and when we look at least in Colorado at our success rate, in Medicaid patients for whom clinicians are already being paid to do the test, you know, our first year success rate is under 50%. And our second year of tests, putting them together is under 22%.

So, what are the levers that you think we could push outside of the hospital to think about screening because somebody said it earlier, we are the Advisory Committee for Heritable Disorders of Newborn and Children. What kind of strategies, other than Epic or some other, which most of these clinicians have, do you suggest, or are there ways we can address to get screening for other heritable disorders outside of just the newborn setting in the hospital, and more broadly into the pediatric care community.

DR. KEMPER: Well, I mean my understanding -- so, I'm going to lead by saying that our lead testing rates, both at one and two years of age are in excess of 95%. So, well I mean it's true, and that's at a population level. So, I would go back to the slide that I had before, that you need to have, you know, a clear and unambiguous recommendation.

There needs to be a burning platform. There needs to be a quality improvement collaborative to get

it done. Somebody needs to be on the hook. There needs to be responsibility for ensuring that this happens. You need close to real time data, and you know, if people are underperforming, then that needs to be made clear.

We also had, again this was like a whole other -- I could talk for hours about this, so I apologize to everyone, but we found that our most successful interventions to also engage people from the community to help us think about practice redesign, because we sort of get blinded to what needs to be done.

But I mean, I think all this stuff is doable, we just need to have all the incentives aligned, and the expectations.

DR. PATRICK: Yeah, so I'll be a little more pessimistic if that's all right. Like I, the reason why --- I think we have systems where the incentives aren't aligned, and the maternal child health in particular we- have fragmented systems that exist in health and

human services, that are often siloed.

We don't have a whole child view, like yes, we have communities, we have it here, but if I go to you know, North Georgia, or I go over to like if we're thinking about creating equitable systems that are across the entire U.S. then we have to think about how the systems are put together.

You know, we have a challenge with, you know, generally lower Medicaid reimbursement in many communities. Medicaid is one place though that many states have multiple different Medicaid, managed care organizations who may have part of the state. How well does that group work with everything from the foster care system to early intervention services to, in my experience those are usually pretty siloed.

And then, you know, Dr. Kemper mentioned data systems, well most state data systems are also siloed, you know, you might have Medicaid data here, you have IDEA Part C data here, those systems don't talk, and if

you wait to get those systems, those data systems federally, they're multiple years old.

So, in maternal child health I think we have to find a place where we can begin to align incentives that are focused on the holistic child care that include the things that matter as we're thinking about social determinants, or drivers of health where we can, you know, create incentives in Medicaid that incentivize human services outcomes, like decreasing foster care, and vice versa.

I think that is what the future needs to look like. And it's worth saying if we compare children and newborns to seniors, one of the differences is the way systems are structured. We have one Medicare program, we have more than 50 Medicaid programs, and many of the systems that serve the patients we serve are a mix of entitlements and block grants that are administered everywhere from federal, state and local.

And I think that's part of the confusion, and

part of the siloing that we see.

DR. KEMPER: Yeah. I think ---- just to piggyback on that too. You know, certainly there are, you know, issues with Medicaid and lack of Medicare parody, and those kinds of things, but private insurance has a lot of problems, and for example, we have you know patients with high deductible insurance plans, and even though they get a lot of their preventative care services covered first dollar and sort of all the add ons that happens downstream.

And so, families get concerned about spending money with their health savings accounts, so I don't want to give ---- I just want to point out that private insurance is not the panacea, that there are many children with private insurance who I think are getting lower quality of care than children who are enrolled in Medicaid.

DR. PATRICK: To be clear, I wasn't saying that about Medicaid.

DR. KEMPER: Oh, no.

DR. PATRICK: Medicaid is such a big player. You know, half of births at least in the U.S. may be increasing, it is a critical partner for care and provides excellent services like EPSDT. Medicaid is critical, and I think it has to be part of the solution.

DR. KEMPER: Yeah. It's like 65% of all children.

DR. CALONGE: And I didn't mean to throw pediatricians under the bus.

DR. KEMPER: You're going to have to answer to them.

DR. CALONGE: We don't have the burning platform. We're a low lead state. It doesn't mean we're a no lead state, so that's the issue that we are always facing. All right. So, let me turn to our Org Reps. Oh, sorry. Oh, Jennifer, I'm sorry, and then Jeff.

DR. KWON: That's okay. Well, I just wanted

to maybe come to Colorado pediatrician's defense. I think that I was just really struck by how wonderful Dr. Kemper's data looked, but I think that you also have to recognize the circumscribed scope of the clinics that you're describing, as opposed to a statewide look where you're bringing in, you know, like rural areas that are quite far from like even a pediatrician, right?

Their pediatric care comes from advanced care, advanced practice provider who is affiliated with the family practice group, et cetera, so I think that that's just one of the things I wanted to throw out there. And that it's those disparities, and all this fragmentation as Dr. Patrick pointed out in Medicaid services, and even in what private insurers will cover that really makes it difficult to standardize what we want, you know, early childhood care to look like.

DR. CALONGE: Thanks, Jennifer. Jeff?

DR. BROSCO: So, one of the reasons why we asked Stephen and Alex to do these talks, and answer

some of the questions that keep coming up. So for example, we heard just today from Debra and Susan and others, how is this care meeting the needs of all kids, right, because that is something that we have to be concerned about.

And I'll give you at least one example. Connecticut is a small state, but at least it's state-wide, and they presented a couple of years ago. We should have them back, where they link their newborn screening positive results to, and they have a contractor at Connecticut Children's Hospital that works with Yale, and they have demonstrated over the last few years that pretty much every single child with a newborn screening result is being followed up across the state.

And in terms of following up in clinical guidelines for sickle cell, hypothyroid, and a few other things, they're making dramatic gains, about 20 points over the last two years. And they have shown at a population level how if you have the proper systems, all

the things that Alex mentioned, you can have a huge impact.

So, there are examples around that do that. The other reason why we had you guys doing these talks, and this has to do with what Michele mentioned before about we are the Advisory Committee for Newborns and Children, and sometimes we get so focused on the state public health lab approach, that we forget there's a whole range of other things.

And so Alex, I'm going to actually ask you, and you had that slide that had well-child care screening and surveillance and newborn public health screening, and I wonder if it's less of a clear contrast, and more of a continuum, right? So, we've heard examples of okay, if it's a state mandate, and the dry blood spot goes to the lab, we're pretty universal.

But not a lot of shared decision making. But then as you pointed out, Stephen, in the newborn period, almost every baby is going to get antibiotic ointment in

their eyes, they're going to get a Vitamin K shot, they're going to get their glucose checked, so there's a whole range of things that happen pretty universally.

And as you get to the vaccines at two months of age we're really good. As you get to vaccines as an adolescent it drops off, and it's more of a continuum. And so one of the things for us to think about is what's the best place for screening? Is screening part of a state public health mandate, or does it fit better as a hospital protocol standard of care, or does it fit better as a clinical practice later on.

And we asked them both to talk about quality improvement to show that there's clearly a drop-off in equity, but there are ways of addressing that and making it better.

DR. CALONGE: Thanks, Jeff. All right. Again, I lost track of the order, so I'm going to go in reverse order and start with Debra.

DR. KEMPER: Do you want me to comment? I

mean I can comment, I agree.

DR. CALONGE: See, I knew you did. There we go.

DR. FREEDENBERG: I have a number of comments, but I'm going to start out with one that is totally not evidence-based driven, but when Texas went to implement its CCHD screening before the state mandate, it went into effect that hospitals were using it as a marketing tool, and it had greatly improved the number of kids that were being screened before we even, you know, were officially requiring that screening, so there are other ways.

A couple of things on the pediatricians, there are ways to impact things like there are lots of -- lots of echo projects, which is basically educating the physicians to help educate the folks around them as well on any given issue. And a lot of also other QA projects are when I know that there have been times when we couldn't do things as a state, but we turned it over

to our maternal and child health, or perinatal collaboratives, and asked them to take things on as a QA project, and that really -- -some of them they didn't take, and some they did, and some of it really impacted that and improved that quite a bit.

And so, I think that there are lots of levels for intervention, and there are lots of creative ways to incentivize things. And you know, in terms of the EPSDT, the early programs, my understanding is that in Texas that if the pediatrician does not check all the boxes, they don't get paid. That's a big carrot and stick approach, and so everything on there has to be done before they get their reimbursement for their visit.

I don't know if that's true in other states as well, but that was my understanding of the way it worked in Texas, so yes, everything got done. But it was a lot of the things also were approached as QA projects, and they were when the state was unable to do

it themselves, we reached out through our colleagues, and we had some incredibly committed pediatricians and champions that helped work throughout the state to make certain that those QA issues were incorporated when we couldn't do it as a mandate, it went over to QA projects.

DR. CALONGE: Thanks, Debra. Bob?

DR. OSTRANDER: Robert Ostrander, American Academy of Family Physicians. I got pulled into this world in 2002 when my practice got chosen to be part of MHLC's, Medical Home Learning Collaborative for Children with Special Healthcare Needs, and it slowly morphed into genetics involvement.

But it was a very early effort to spread the notion of short cycle change in PDSA cycles. I know you both talk about these, and my comment is more generic about what happens when we don't do the study part of PDSA, because that's what I've seen has been the big problem at a couple of levels in my life. And one is

the smaller hospitals that may not be as sophisticated as yours.

And the other is legislation where the original chain isn't circumscribed either in terms of time and number, and there's no pause taken to study and decide what you're going to do. I give a lecture on this to the fellows at Rochester, or was at least for a while every year.

You know, sometimes they should simply be abandoned, often it should be modified, sometimes it should be spread and done in a larger way, but what I see is outside of sophisticated programs like yours that clearly are doing exactly what they're supposed to be because you're monitoring your change, and those graphs show these nice little step wise improvements, or a stall and then a bigger improvement because they've done that, is making sure that people do that stop study, and then modify, because you know so much gets put into place that is either poorly designed, or actually

negative.

I mean legislatively, part of it is you know, my own vent on the wrong people telling us what to do, and then again, my small institutions, and we end up having work added and checked boxes added to our day that keep us from doing the steps we need to instead of improving care.

DR. PATRICK: I want to just respond to one thing real quick, which is the notion of how do you do quality improvement in small, under-resourced environments? And they're really good models for that. State perinatal collaboratives do that very well. It's generally one volunteer, often a nurse who volunteers at a you know, level one hospital.

We've seen birth hospital who may have a small volume of births, but that's where the structure of perinatal collaboratives is so extraordinary, because it provides an infrastructure for the federal support and at the state level that includes a lot of volunteers

at these small hospitals to prioritize, okay, what do we want to improve, and where do we want to improve it?

And state perinatal collaboratives have been incredibly successful at driving statewide change from everything towards early-term deliveries, if you remember that when we were delivering babies early, before 39 weeks. And it's not even talked about anymore because of state and perinatal collaboratives.

So, I just we can do this, and so there are good examples of it. I would agree with some previous comments, which is that, you know, the hospitals are where the babies are, but we can drive positive change at hospitals, and we can do it in small, rural communities if we right size it to what the needs are of those small communities.

DR. KEMPER: And if I can build on this too. So, one of the things that always upsets me is so when these quality improvement projects all fall on the clinician, the pediatrician, or the nurse practitioner

to be the agents of change, and you know, if you can only work harder and check these boxes, then things will be better.

I would say that the biggest improvements that we've had have been things that have been completely outside of the clinician that is actually made the clinician's lives better. So, when I showed you the dramatic improvement in early well child visit rates, all that was done based on having the when families checked in, getting their subsequent visit scheduled as they check in for their current visit, so there's like small things that you can do that can make a huge difference, and it can't all fall to the pediatrician and the nurse practitioner, or whoever to do everything.

DR. OSTRANDER: I'm just going to answer, I think that's one of the key lessons that we learned even in that original learning collaborative, that the people brilliantly set that up with a physician, a staff

member, and a parent partner. That's how that was run, and it became the model for our small free physician practice, and we made all sorts of, like you said, a small size can be wonderful if people know, and if we stop.

I think the very last one I did, or nearly so before I retired from day-to-day practice, was one to get the EMR to prompt us to see if the newborn screening results were back at the two-month follow-up.

DR. KEMPER: Yeah, those are great examples. That's a great example.

DR. CALONGE: Sabra?

MS. ANCKNER: Thanks. Sabra Anckner from the Association of Material and Child Health Programs, which I would just like to shout out as your resource for these things, your Title V and Children with Special Healthcare Needs Programs in all jurisdictions exist, and would love to have this conversation with you, as that is very much part of their programmatic mandates,

is all of these things in driving -- they have to report metrics on many of these things, and we very much like to have additional partners to work on them with their, you know, always at the table with PQCs, with EMSCs, with many of these programs.

And so I just want to flag a couple of things that I think we've talked about here -- we've glanced upon. One is screening without knowing what to do with the result is a real problem, and I think that that is a lot of when you get resistance to running a test to collecting even a blood let level, is what am I doing with this? Do I know how to interpret this result? Do I know what I'm doing with the result?

And a lot of times the answer to that is no, so it really has to be much like we know that the consequences in the, you know, blood spot screening world of [noise intended to convey uncertainty], I don't know what to do with that information. That goes for all screening. That goes for developmental screening,

that goes for behavioral health screening, so keeping that in mind.

And I did write with AAP a seven or eight page guidance on developmental screening for non-clinicians, for folks that are doing that in the public health space, so those resources do exist on that. And the other thing that I want to say is that I've been thinking a lot lately on -- when does newborn screening begin, you know, and I think CCHD is a perfect example.

I've just recently been having a conversation with a fetal cardiologist who really gets upset when somebody is identified on the CCHD screen, right? They want everybody diagnosed and identified essentially in utero, right? They want them all at the 20-week ultrasound, which is a screening, right?

The 20 week ultrasound does not find out the gender of your baby, it is a screening, and you know, with the quad screen is a screening, and maybe it is really time that we start thinking about screening as

something that occurs across the lifespan that begins in the perinatal period and extends on, and really consider them all as part of one package, and not just this one point in time, at 24 hours when we do something.

DR. CALONGE: Thanks. Amy? Oh, you took it down. Okay. Well, I really appreciate the presentations. Thanks Alex, and thanks Stephen. I have a real interest in thinking about newborn screening recommendations, and specifically around how we might create recommendations that don't require state laboratories and state programs to do things that they can't do, or are unable to do.

But still support the basic screening where early detection will lead to better outcomes over time. So, it's kind of almost it gets right back to the kind of public health readiness, and ability to do screening, and trying to expand beyond what you can do with the dried blood spot more systematically to what you can do in the system for these point of care delivered tests

that will be, or are currently associated with improved outcomes because of early detection.

And going further back into the perinatal, into the prenatal care period is kind of an interesting concept as well. So, I appreciate the dialogue. I hope --- I know I learned a lot. I appreciate the issues that we talked about, and now you kind of understand a little bit about why we have an acute interest in exploring this a little bit further as a Committee.

End of Day 1

DR. CALONGE: So, I appreciate the time. It's been an interesting day. And we have a really great session tomorrow. We're going to consider a nomination package, and hear about the assessment of the package, and have a motion and a vote about potentially moving that on to full evidence review, so I look forward to public comments tomorrow, and hope everyone has a good evening.

There is a session for Organizational Representatives Orientation. It's in Room 5N54 which is on this floor. It's that way. That direction behind you, and I'll look forward to seeing interested Org Reps there for that session. Otherwise, I hope everyone has a great evening. We'll see you tomorrow.

COMMANDER MANNING: And I have one additional announcement, and I'm going to make this announcement tomorrow also. The November meeting, so the meeting scheduled for November 14th through the 15th will be virtual only, no in-person in November. Thank you, have a good night.

DR. CALONGE: Thanks everyone.

(Whereupon the Advisory Committee on Heritable Disorders in Newborns and Children adjourned at 3:07 p.m.)