The Advisory Committee on Heritable Disorders in Newborns and Children

Virtual Meeting

10:00 a.m.

Wednesday, November 10, 2021

Attended Via Webinar

Page 1 - 176

Reported by Garrett Lorman

Committee Members

Mei Baker, MD
Professor of Pediatrics
University of Wisconsin School of Medicine and Public Health
Co-Director, Newborn Screening Laboratory
Wisconsin State Laboratory of Hygiene

Jeffrey P. Brosco, MD, PhD
Professor of Clinical Pediatrics, University of Miami
Title V CYSHCN Director, Florida Department of Health
Associate Director, Mailman Center for Child Development
Director, Population Health Ethics, UM Institute For Bioethics and Health Policy

Kyle Brothers, MD, PhD
Endowed Chair of Pediatric Clinical and Translational Research

Committee Members - continued

Associate Professor of Pediatrics University of Louisville School of Medicine

Jane M. DeLuca, PhD, RN
Associate Professor
Clemson University School of Nursing

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

Cynthia M. Powell, MD, FACMG, FAAP (Chairperson)
Professor of Pediatrics and Genetics
Director, Medical Genetics Residency
Program Pediatric Genetics and Metabolism
The University of North Carolina at Chapel Hill

Committee Members - continued

Annamarie Saarinen
Co-founder
CEO Newborn Foundation

Scott M. Shone, PhD, HCLD (ABB)
Director
North Carolina State Laboratory of Public Health

Ex-Officio Members

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

Centers for Disease Control & Prevention
Carla Cuthbert, PhD
Chief
Newborn Screening and Molecular Biology Branch
Division of Laboratory Sciences

Ex-Officio Members - continued

National Center for Environmental Health

Food & Drug Administration

Kellie B. Kelm, PhD

Director

Division of Chemistry and Toxicology Devices

Health Resources & Services Administration

Michael Warren, MD, MPH, FAAP

Associate Administrator

Maternal and Child Health Bureau

National Institutes of Health

Melissa Parisi, MD, PhD

Chief

Intellectual and Developmental Disabilities Branch

Eunice Kennedy Shriver National

Institute of Child Health and Human Development

Ex-Officio Members - continued

Designated Federal Official

Mia Morrison, MPH

Genetic Services Branch

Maternal and Child Health Bureau

Health Resources and Services Administration

Organizational Representatives

American Academy of Family Physicians

Robert Ostrander, MD

Valley View Family Practice

American Academy of Pediatrics

Debra Freedenberg, MD, PhD, FFACMG, FAAP

Medical Director

Newborn Screening and Genetics

Texas Department of State Health Services

American College of Medical Genetics & Genomics

Maximilian Muenke, MD, FACMG

Organizational Representatives - continued

American College of Obstetricians & Gynecologists
Steven J. Ralston, MD, MPH
Chair, OB/GYN
Pennsylvania Hospital

Association of Maternal & Child Health Programs
Jed Miller, MD
Director, Office for Genetics and People with Special Care Needs
Maryland Department of Health Maternal and Child Health Bureau

Association of Public Health Laboratories
Susan M. Tanksley, PhD
Manager, Laboratory Operations Unit
Texas Department of State Health Services

Association of State & Territorial Health Officials
Christopher Kus, MD, MPH

Organizational Representatives – continued

Associate Medical Director
Division of Family Health
New York State Department of Health

Association of Women's Health Obstetric and Neonatal Nurses

Shakira Henderson, PhD, DNP, MS, MPH, RNCNIC, IBCLC
Vice President, Research Officer University of North Carolina Health
Board Director, Association of Women's Health, Obstetric & Neonatal Nurses

Child Neurology Society

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

Organizational Representatives - continued

Department of Defense
Jacob Hogue, MD
Lieutenant Colonel, Medical Corps, US Army
Chief, Genetics, Madigan Army Medical Center

Genetic Alliance
Natasha F. Bonhomme
Vice President of Strategic Development

March of Dimes
Siobhan Dolan, MD, MPH
Professor and Vice Chair for Research
Department of Obstetrics & Gynecology and Women's Health
Albert Einstein College of Medicine and Montefiore Medical Center

National Society of Genetic Counselors
Cate Walsh Vockley, MS, CGC
Senior Genetic Counselor Division of Medical

Organizational Representatives - continued

Genetics
UPMC Children's Hospital of Pittsburgh

Society for Inherited Metabolic Disorders
Georgianne Arnold, MD
Clinical Research Director, Division of Medical Genetics
UPMC Children's Hospital of Pittsburgh

C O N T E N T S

P R O C E E D I N G S

WELCOME AND ROLL CALL

CYNTHIA POWELL: Okay. Good morning, everyone. Welcome to the second day of the November 2021 Advisory Committee on Heritable Disorders in Newborns and Children meeting. I'm Dr. Cynthia Powell, the Committee chair. And we will begin with the roll call.

Representing the Agency for Health Care Research and Quality, Kamila Mistry.

(No audible response)

CYNTHIA POWELL: Mei Baker.

MEI BAKER: Here.

CYNTHIA POWELL: Jeff Brosco.

JEFF BROSCO: Here.

CYNTHIA POWELL: Kyle Brothers.

KYLE BROTHERS: Here.

CYNTHIA POWELL: Jane DeLuca.

JANE DELUCA: Present.

CYNTHIA POWELL: From the CDC, Carla Cuthbert.

CARLA CUTHBERT: I'm here.

CYNTHIA POWELL: From the Food and Drug Administration, Kellie Kelm.

KELLIE KELM: Here.

CYNTHIA POWELL: Representing HRSA today, Debi Sarkar.

DEBI SARKAR: I'm here, sitting in for Dr. Warren. Thanks.

CYNTHIA POWELL: Shawn McCandless.

SHAWN MCCANDLESS: Here.

CYNTHIA POWELL: From National Institutes of Health, Melissa Parisi.

MELISSA PARISI: Here.

CYNTHIA POWELL: I'm here, Cynthia Powell.

Annamarie Saarinen.

ANNAMARIE SAARINEN: Here.

CYNTHIA POWELL: And Scott Shone.

SCOTT SHONE: Here.

CYNTHIA POWELL: Okay. Thank you.

For our organizational representatives, from the American Academy of Family Physicians, Robert Ostrander.

ROBERT OSTRANDER: I'm here.

CYNTHIA POWELL: From the American Academy of Pediatrics, Debra Freedenberg.

DEBRA FREEDENBERG: Here.

CYNTHIA POWELL: From the American College of Medical Genetics and Genomics, Max Muenke.

MAXIMILIAN MUENKE: I'm here.

CYNTHIA POWELL: From the American College of Obstetricians and Gynecologists, Steven Ralston.

(No audible response)

CYNTHIA POWELL: From the Association of Maternal and Child Health Programs, Jed Miller.

JED MILLER: Here.

CYNTHIA POWELL: From the Association of Public Health Laboratories, Susan Tanksley.

SUSAN TANKSLEY: I'm here, thank you.

CYNTHIA POWELL: From the Association of State and Territorial Health Officials, Chris Kus.

(No audible response)

CYNTHIA POWELL: From the Association of Women's Health, Obstetric, and Neonatal Nurses, Shakira Henderson.

SHAKIRA HENDERSON: Good morning. Here.

CYNTHIA POWELL: From the Child Neurology Society, Margie Ream.

(No audible response)

CYNTHIA POWELL: From the Department of Defense, Jacob Hogue.

JACOB HOGUE: Here.

CYNTHIA POWELL: From Genetic Alliance, Natasha Bonhomme.

NATASHA BONHOMME: Here.

CYNTHIA POWELL: From the March of Dimes, Siobhan Dolan.

SIOBHAN DOLAN: Here.

CYNTHIA POWELL: From the National Society of Genetic Counselors, Cate Walsh Vockley.

CATE WALSH VOCKLEY: I'm here.

CYNTHIA POWELL: And from the Society of Inherited Metabolic Disorders, Georgianne Arnold.

GEORGIANNE ARNOLD: Here.

CYNTHIA POWELL: Thank you.

Could I have the next slide?

(Slide)

KAMILA MISTRY: Sorry, Dr. Powell. This is Kamila Mistry from AHRQ. I joined.

CYNTHIA POWELL: Thank you, Kamila. We'll note that you're present.

So as we get started, I wanted to just quickly go over some things regarding the actionable steps in the Committee review of the nomination package. And specifically, some of the changes that were suggested yesterday during our discussion about the nomination form.

So, what you'll see here with the red strike-through is what was on the form, the recommended change, previously and then what we agreed to yesterday. So in terms of just adding a gene, a specific genes or genes are known as being positive for the condition under consideration or under nomination, it would be helpful to include that. But if it's not applicable, that's also fine.

For those that would have an enzyme level, we thought it would be helpful to include that specific enzyme. But that could be confusing, so we had changed it to "critical biomarker." And again, if that's not applicable, the nominators can indicate that.

I think one of the confusing things is -- and there's been a lot of debate in the genetics field in recent years about how to name conditions. For example, some metabolic disorders may have the same name, but are due to different enzymes. They may be denoted as A, B, or C.

But just to make it as clear as possible, when HRSA and then those on the Nomination and Prioritization Workgroup get the forms, you know, it's really helpful to know specifically what is being nominated. So as much additional information as possible.

Now, for example, some things like hyperthyroidism, while there may be a number of genetic causes, there are certainly nongenetic causes. And so, if we were going back to looking

at that condition, then specific genes would not be applicable. But the thyroid hormone level would be the critical biomarker. It might be a virus, for example, or something else.

But again, if there's any confusion on the part of those preparing a nomination package, please contact Mia Morrison at HRSA. And she is happy to help with that information, as am I.

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(Slide)

CYNTHIA POWELL: And then for the severity of disease, instead of "if applicable" regarding the U.S. distribution or prevalence, that was switched to "if known."

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(Slide)

CYNTHIA POWELL: And then regarding specifically about terminology for the FDA, this is in regard to the platform and procedures for screening tests. And it was recommended that instead of "FDA approved" that it say "FDA cleared or authorized" and to "provide FDA submission

number if applicable."

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CYNTHIA POWELL: Then an additional change was added to the analytical validation regarding, "Has the CDC's Newborn Screening and Molecular Biology Branch been contacted regarding these and are other validation measures currently pending or available?"

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(Slide)

CYNTHIA POWELL: And then regarding the regulatory status of confirmatory testing, again for the appropriate wording regarding FDA, "Is the test FDA cleared or authorized? If so, include the FDA submission number."

Next slide.

(Slide)

CYNTHIA POWELL: Okay. And one additional change was regarding the cost of analysis and how that would be denoted. It didn't make any changes in the form. But it would change

the final report.

And so, that one correction has been made and clarified, and will be included in the document for this. Since it didn't change the form, we didn't see a need to go over that today.

All right. So that is what the Committee voted on and approved yesterday.

All right. Going on for the rest of the agenda for today, we're going to hear about the phase 1 update on the evidence-based review for guanidinoacetate methyltransferase, or GAMT, deficiency.

Afterwards, we'll receive updates from each of the Committee workgroups. We'll then have a short break. And our last session of the meeting will cover the ScreenPlus and Early Check newborn screening pilot programs.

I'll now turn it over to Mia Morrison, our designated federal official, to provide guidance for participating on the webinar.

Mia.

MIA MORRISON: Thanks, Dr. Powell.

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MIA MORRISON: Thank you.

Members of the public, audio will come through your computer speakers, so please make sure to have your speakers turned on. If you can't access the audio through your computer, you may dial into the meeting using the telephone number in the email with your Zoom link.

Committee Members and org reps, audio will also come from your computer speakers, and you will be able to speak using your computer microphone. If you can't access the audio or microphone through your computer, you may also dial into the meeting using the telephone number in the email with your user-specific Zoom link.

Please speak clearly and remember to state your first and last names to ensure proper recording for the Committee transcript and minutes.

The chair will call on Committee Members and then organizational representatives.

In order to better facilitate the discussion, Committee Members and organizational representatives should use the raise-hand feature when you'd like to make comments or ask questions. Simply click on the "Participant" icon and choose "Raise hand." Please note that, depending on your device or operating system, the raise-hand feature may be in a different location.

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MIA MORRISON: To enable closed captioning, please select the closed captioning icon on your Zoom taskbar. From that menu, select "Show Subtitles." Thank you.

Dr. Powell.

CYNTHIA POWELL: Thank you, Mia.

In April of 2021, the Committee received a nomination for guanidinoacetate methyltransferase, or GAMT, deficiency for inclusion on the RUSP. This was the second time

that GAMT had been nominated.

At the August meeting, the Nomination and Prioritization Workgroup presented an overview about this nomination to the Committee, and the Committee voted to move GAMT deficiency forward to full evidence review.

Today Dr. Kemper, Evidence-Based Review Group leader, will provide the Committee with the phase 1 update.

Alex, I'll turn it over to you.

GUANIDINOACETATE METHYLTRANSFERASE (GAMT) DEFICIENCY EVIDENCE-BASED REVIEW – PHASE 1 UPDATE

ALEX KEMPER: Thank you very much, Dr. Powell. Good morning to everyone else.

My goal over the next little bit is just to provide an overview of newborn screening for GAMT deficiency and talk a little bit about where we are. Again, this is the first of the series of three presentations that you'll hear from us, the ones today, and in a few months the interim one. And then leading up to the final presentation,

which will be timed with the Advisory Committee vote.

I'm not going to update the detailed presentation that Dr. Cuthbert gave earlier in terms of providing a really wonderful overview of the biochemical aspects of the condition, but really just talk about what we know about the condition in general and where we are with our evidence to be processed.

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(Slide)

ALEX KEMPER: And of course, I just want to thank members of the Evidence Review Group and note also that Drs. DeLuca and McCandless are serving as the liaisons to this work, in addition to the MPS II review. So I just want to publicly thank you two for your help on this.

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(Slide)

ALEX KEMPER: So again, my objective for this group presentation is to provide an overview of GAMT deficiency, talk about our current

progress, and then outline the next steps, which are really in line with all of the previous reviews that we've done.

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(Slide)

ALEX KEMPER: So, GAMT deficiency is a cerebral creatine deficiency caused by a mutation in the GAMT gene. It's an autosomal recessive condition that's associated with elevated plasma and urine guanidinoacetate. GAA is what I'm giving you. This is my creation on these slides, although sometimes you also see it as blot GUAC. But for the purposes of this presentation, I have GAA for guanidinoacetate. And it's also associated with low serum creatine disorder.

Untreated, it can lead to global developmental delay, seizures, muscle weakness, and significant movement disorders.

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ALEX KEMPER: So in terms of our progress, we had our first technical expert panel

call in early October. I'll show you the list of those individuals. And then we had a really very interesting and helpful call with the Utah Newborn Screening Program on October 28th.

And then we are proceeding with our evidence reviews, you can see at the top level, after searching our usual places, PubMed, Embase, CINAHL, and the Chochrane Library. We identified 338 articles, which we are in the process of doing a deep dive on it.

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ALEX KEMPER: This is a list of the technical expert panel members. Again, I just want to highlight how wonderful the call was that I had with the technical expert panel. It really helped us to understand the nuances of the condition and the state of the art related to diagnosis and treatment.

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(Slide)

ALEX KEMPER: So the diagnosis that was

discussed before was based on biochemical confirmation in a plasma of low creatine and elevated GAA at least a week after birth. There are other conditions that we need to separate out when you make the diagnosis of GAMT deficiency. For example, arginine deficiency can cause an elevation of GAA.

One of the things that we learned on our technical expert panel call is that molecular analysis can support the diagnosis, but it's really based on the findings of the chemical changes that I've outlined above.

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ALEX KEMPER: In terms of treatment, and Dr. Cuthbert really did a masterful job of explaining why this is a treatment, so I'm not going to repeat all of that. But it involves creatine and ornithine supplements, sodium benzoate, and dietary restriction of arginine.

Based on the technical expert panel call and other descussions that we've had, the ideal

timing of treatment is uncertain, but experts generally recommend to begin around two to four weeks of age. And then individuals need serum level monitoring to make sure that the dietary approach is effective.

And so, begins very frequently initially, but after the first few years when things begin to stable, the serum level monitoring can be spaced out to every six months.

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(Slide)

ALEX KEMPER: Screening is based on dried blood spots, using tandem mass spec for GAA and creatine. In terms of places that are screening, in the United States, in New York, screening began in 2018. And of the approximately 537,000 screened, there were 23 who were referred for further testing, leading to one diagnosis.

We have our call with New York. I think it's actually scheduled later in this week, but it's coming up sometime soon.

Utah began screening earlier in 2015.

They had a derivatized tandem mass spec approach at first. But in 2019 they were able to switch to a non-derivatized method, which has facilitated the ease of screening. Of the 274,000 or so infants that they've screened, there were three referred for diagnostic testing and 1 that was confirmed to have GAMT deficiency.

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(Slide)

ALEX KEMPER: So in terms of findings from colleagues in Utah, first of all Utah is a two-screen state. So at the first-tier they use UPLC tandem mass spec. GAA, or GUAC, if you want to call it that, is the primary analyte. And if that's elevated, they will look at creatine as a secondary analyte.

And the plan was that if there is a modest elevation of GAA on the first screen, then they try to expedite the timing of the second screen and then compare. Apparently, they're very good at being able to link their dried blood spots and see how things change.

But what happened was in the one diagnosed case, the GAA level was really markedly abnormal. So that expedited the diagnostic process. So they have contracts for confirmatory testing. They don't do that in-house. But again, there are relatively small numbers of individuals who move on to confirmatory testing. And for that, they use urine and serum GAA and creatine.

I put "creatinine." I apologize. I find myself falling into that trap a lot. But I meant to say "creatine" on the slide.

So they have contracts for that confirmatory testing and follow-up.

In terms of the cost of screening as you know, we give a range. And the screening is less than one dollar per infant. And that takes into account as well that Utah is a two-screen state per infant that's screened.

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ALEX KEMPER: So we're moving ahead with our usual evidence process. I showed you where

we were in terms of the systematic evidence review.

In terms of the gray literature, one place that we're going to look very carefully at is, there is a registry. Again, we don't expect that there are going to be a lot of children or individuals in a registry, just given the rarity of the disorder. But there is a registry that's maintained by the Association for Creatine Deficiencies.

There are novel therapies that are in early development. But I can't tell you on the call today how far things have gotten. But there's interesting developing gene therapy. And also inhibitors to reduce the production of GAA. And of course, we have the call set up, as I talked about, with New York to better understand the New York experience.

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ALEX KEMPER: So moving ahead with plans for the public health system impact assessment,

we're going to do that in early January, given that we've just surveyed state newborn screening programs around MPS II. And also, we don't want to run into the problem of doing it right before the holidays when groups may not have a chance to really do a deep dive that they need to to be able to complete this kind of survey.

Then again we're working with Dr. Prosser and her colleagues at the University of Michigan to do population health modeling.

What I'll say is it's sort of analogous to the conversations we had around MPS II. There's going to be limited quantitative data that's going to be able to predict long-term outcomes from -- GAMT Deficiency just given. Given the rarity of the conditions in what I think is going to be the available data.

But like MPS II, we'll be able to talk about the numbers of individuals that would be identified by newborn screening with its usual clinical care, and make recommendations in terms of things to think about for the future as well.

Again I'll know more about that once we're able to learn more about the registry and complete the systematic evidentiary review.

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ALEX KEMPER: So with that I'll stop and open things up to questions.

CYNTHIA POWELL: Thank you, Dr. Kemper.

We'll now take questions, first from Committee Members, followed by organizational representatives. As usual, please use the raise-hand feature in Zoom when you'd like to make comments or ask questions. Please remember to unmute yourself and state your first and last names each time you ask a question or provide comments to ensure proper recording.

(Pause)

CYNTHIA POWELL: Scott Shone.

SCOTT SHONE: Thank you. Thanks, Dr. Powell. Scott Shone.

So, Alex, I think two of the things that jumped out on your slides. One is the referral

rates, and the difference between the two states seem pretty significant. So I'm hoping that your interviews will tease out a little bit of that. Because that's a substantial difference, I think. My colleagues on the N&P Workgroup will agree that that was something that we looked at when it went to the ERG.

So I look forward to hearing more about on the technical side what that is. So that's an ask, I suppose, on the next steps, realizing how very early you are in this process and also on top of your MPS II review.

I appreciate the acknowledgment on the quantitative data based on my comments from yesterday, and I just think that we need to be thinking about, as a Committee, the challenges of making some of these decisions with the different types of data that are available. I don't know that I have a good answer to that, but I know you've been talking about it, and I appreciate the discussions around those.

I'd just like to say I think it's really

dangerous -- the number that I think stuck out that's a little dangerous to say is it's less than a dollar per screening. We hear that all the time. "It's less than a dollar." "It's less than three dollars."

I think we need to be clear that what I think you mean, and correct me if I'm wrong, is the simple cost of the reagents to do the test, which is substantially different from the cost of screening. I think Scott Grosse will agree. Particularly if you are referring 23 babies for follow-up testing and only one is actually diagnosed, the cost of screening I think needs to be described differently.

So I would ask we were careful with -- if I'm right that that's just the cost of the Utah mass spec laboratory of adding those reagents, then I think we have to be that clear with our articulation. Because that becomes the line, just like the "30 meters."

You know, I took your 30 meters yesterday, and it was a common theme all day. And

I know in the end you didn't actually mean it that way. So, sorry?

But I think that's what then happens with "a dollar." We will hear "a dollar" forever, but that is not the cost of screening. That's the cost of a specific additional enzyme -- or analyte.

ALEX KEMPER: Yes. So first of all, you're exactly right that we're going to be talking to New York to better understand the differences in methods and experiences and those kinds of things. So I regret that I'm not able to share that with us. It's just the challenge of scheduling things.

But in terms of the dollars, so we actually did talk with Scott Grosse on that component of things. And it turns out this may actually be one of those ones where it's just not very expensive to do. And part of it is, you know, there are just not that many babies who end up getting referred for diagnostic testing. What we were told was the additional workload just wasn't that great.

So we'll be able to provide more details to you as we go forward. But I think this one may actually be one that really isn't that much in addition to having the newborn screening are all going. Now, that was just based on one state, and we actually inflated the numbers to get things that are per baby, as well, since Utah's a two-state screening program.

So this just may be one of those ones that is actually less expensive. But we'll have more information for you in the comparative summary when we talk to New York.

CYNTHIA POWELL: Susan Tanksley.

SUSAN TANKSLEY: Hi, Susan Tanksley, APHL.

So I just wanted to expand on what Alex was saying about the cost, because we probed Utah about the cost when we had the discussion specifically with Utah. And because when they brought on GAMT, they had transitioned from the tandem mass spec, the testing being done at ARUP to it being done in-house.

So they brought it all on at the same time. So for them,it essentially was the cost of the reagents. And then we even asked about the confirmatory testing and that cost, and they gave us the specific dollar amounts.

And then if you average that all out, it was inflated. That is specifically for Utah. And as you pointed out, you know, there is a different referral rate from New York. So we'll dive into that as well.

CYNTHIA POWELL: Robert Ostrander.

ROBERT OSTRANDER: Yeah, Robert Ostrander, American Academy of Family Physicians.

I just want to make a comment as a member of the Follow-up and Treatment Workgroup that it is our hope that as evidence reviews go forward -- I know haven't formally included this. But it's our hope that as evidence reviews go forward, that at some point in the review there will be some blueprint, if you will, of at least the expected follow-up and treatment that will occur for these various conditions.

And in this case maybe it's implied. You know, it's standard metabolic clinic. But I think we shouldn't imply it. I think we should be explicit about what we imagine the follow-up treatment to be like, as well as a comment about, you know, and based on Dr. Powell's charge to all of us, a comment based on the capacity of the system to absorb follow-up and treatment.

My final comment is just probably to repeat what people have heard a million times from us about the treatment. There's two components to that – follow-up and treatment. Some of that is the clinical follow-up in doctors' offices, and some of it is follow-up in terms of measuring impact and outcomes.

But I think a lot of us in follow-up and treatment would like to see a little blueprint of that in the evidence reviews so we know that we're doing a screening test for which there is a plan in place for the clincal care that follows.

Thanks.

CYNTHIA POWELL: Thank you.

ALEX KEMPER: We'll do that. Thank you.

CYNTHIA POWELL: Annamarie Saarinen.

ANNAMARIE SAARINEN: Hi. Thanks. Annamarie Saarinen, Committee Member.

Thanks for the update here, Alex. And I'm sorry if I missed this part somehow, because I think I was focused on trying to understand the real differences between the doing it with or without the second-tier test. And I'm not sure I've got my head around that.

ALEX KEMPER: Yeah.

So I'll look through it a little more and maybe --

(Crosstalk)

ALEX KEMPER: The primary markers that they -- and again I'm going to talk about Utah because that's who we've had the deep dive with.

But the primary markers looking at the guanidinoacetate level, and if that's elevated, then they can look at the creatine level as a secondary analyte. And if that looks abnormal, basically if the GAA is sky high, then they can

refer directly to diagnostic testing, which just involved confirmation of GAA increasing levels in the serum and in the urine.

But if it's just modestly elevated or not elevated at all, then Utah has a second screen that occurs around a couple of weeks after birth. And again they look at GAA. And then there's a secondary analyte, the creatine level.

Does that make sense?

ANNAMARIE SAARINEN: Yeah. So without a population health base -- that is, if you were to -- I'm just wondering about the yield, the difference in yield between if you followed the like -- your standard practice is just going to be as a first-tier test. And you didn't automatically do that.

I'm just wondering about, it seems like there would be a lost of cost-savings to do that. I don't know what the potential miss rate is if you did it one way versus the other.

ALEX KEMPER: Okay. I will present. We'll also have more numerical stuff again after

we talk to New York can sort of dig through things.

ANNAMARIE SAARINEN: Yeah. And thanks for addressing Scott's question earlier. That was helpful.

ALEX KEMPER: Thank you, Annamarie.

CYNTHIA POWELL: Shawn McCandless.

SHAWN McCANDLESS: Shawn McCandless, Committee Member.

Alex, I thought there were other screening programs around the world, and you didn't show those data. Could you just mention that or not? And if not, why?

ALEX KEMPER: Well, you're exactly correct that there are international data like the screening experience in Australia. We have the published reports from those places that we're digging through. We have not arranged any specific follow-up conversation with them in part because we just wanted to get through Utah and New York first and see if we had sufficient information.

But if you recall, there was that long

screening experience where they weren't identifying cases. But what I can tell you is that I just don't know what's going on there now and whether or not they've identified any additional cases.

But generally, our pattern is to look in the U.S. first and then go there. And if the Advisory Committee wants to send me to Australia, I would be honored to do that as well.

SHAWN McCANDLESS: I'm happy to authorize that.

ALEX KEMPER: Well, thank you very much. I appreciate that.

CYNTHIA POWELL: Any other comments or questions from either Committee Members or organizational representatives?

(No audible response)

CYNTHIA POWELL: Annamarie, you still have your hand up. Is that --

ANNAMARIE SAARINEN: Sorry. It's lowered.

CYNTHIA POWELL: No problem. No problem.

Just wanted to make sure you didn't have something else to add.

So okay. Well, very good. Thank you, Dr. Kemper. We'll look forward to the next update when we meet in February. And thank you for your work and the others who are working on this.

ALEX KEMPER: Thank you for your kind words and the opportunity.

CYNTHIA POWELL: All right. So we're now going to go on to updates from the workgroups in their meetings yesterday.

At the May and August 2021 meetings, the Committee invited two panels to present on challenges facing the newborn screening workforce and strategies to address workforce-related gaps.

Yesterday afternoon I asked Education and Training, the Follow-up and Treatment, and Laboratory Standards and Procedures Workgroups to convene in order to assess potential ways the Committee could support meeting current and future needs of the newborn screening workforce.

All workgroups were asked to discuss

whether the Committee should consider the availability of follow-up experts, whether that be clinical follow-up public health staff, laboratory staff, or others, when reviewing a new condition nominated to the Recommended Uniform Screening Panel.

How could that information be collected? And what role could the Committee play in calling attention to identified shortages of follow-up experts?

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CYNTHIA POWELL: For the Education and Training Workgroup, we also asked, Where are the major gaps in newborn screening workforce education? Do Education and Training Workgroup members have additional recommendations on resources or training opportunities that support addressing shortages in the newborn screening workforce? How could those resources be expanded to further strengthen the newborn screening system?

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CYNTHIA POWELL: For the Follow-up and Treatment Workgroup, we also asked, What are the key workforce-related challenges impacting access to short- and long-term follow-up, including treatment for individuals and families identified with conditions on the RUSP? Are there examples of workforce innovations that have supported access to short- and long-term follow-up care?

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CYNTHIA POWELL: And finally, for the Laboratory Standards and Procedures Workgroup, we stated that at the August 2021 ACHDNC meeting, the Association of Public Health Laboratories outlined challenges facing the newborn screening laboratory and follow-up workforce and resources that have been used to address those challenges.

We asked: are there other resources that have been used at the state or national level to address laboratory workforce challenges? And how

could those resources be expanded to further strengthen the newborn screening laboratory workforce?

So first we'll hear a presentation from the Education and Training Workgroup chaired by Dr. Jane DeLuca.

And I'll turn things over to Jane.

EDUCATION AND TRAINING WORKGROUP UPDATE

JANE DELUCA: Good morning, everyone.

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JANE DELUCA: Okay. I'd like to acknowledge the Education and Training Workgroup members. This is a wonderful group, who are very passionate about newborn screening. And we had a very, I guess, eye-opening and spirited conversation yesterday as we addressed the questions put to us by the Committee.

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JANE DELUCA: So our first question, we addressed the questions specific to Education and

Training Workgroup: What are the major gaps in newborn screening workforce education? Do Education and Training Workgroup members have additional recommendations on resources or training opportunities that support addressing shortages in the newborn screening workforce? How could those resources be expanded to further strengthen the NBS system?

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JANE DELUCA: So first we set about clarifying the question and wanted to know whether this included people who worked within newborn screening, or were we talking about families or systems in general?

And yes, it includes everybody who is part of the newborn screening system. This is a laboratory, public health practitioners, clinicians, in short- and long-term follow-up programs.

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JANE DELUCA: So again we sort of situated ourselves into, How do we start to think about this question? And there are of course phases of newborn screening -- pre-analytical, provider, clinical, applications, and the long- and short-term care.

Dr. Tarini had written an excellent article about the different steps of the newborn screening process. So we felt that special education is needed for each phase of the screening process.

Now, this Committee worked on a newborn screen educational planning guide some years ago and identified a large group of stakeholders and what they needed to know about newborn screening, but didn't apply formal education, ideas, or sources for stakeholder groups to improve their knowledge. But that guide can be accessed on the Advisory Committee website.

So expertise in newborn screening often begins in the workplace, within laboratories, on-the-job training, internet sources such as

New Steps, and other ad-hoc mechanisms.

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JANE DELUCA: So, we talked about some formal programs for educating newborn screening workforce, mostly for advanced practice providers such as the LSD fellowship, which is a commercial entity that basically funds LSD fellows, who are typically newborn screening nurse practitioners or PAs.

There is also NAMA, which can educate advanced-practice providers, tends to be a bit of a higher level, people who have been working in the area for a bit longer. They probably would get the most out of that. But can more professional organizations be charged with providing training?

So what are we educating for? There are different levels of education that are needed. We have different philosophies within newborn screening and such a wide array of practitioners and staff. We have public health people, there

are precision medicine people, laboratorians, and they are all interacting, all at the same time and constantly.

So it was pointed out that there is very limited time for educating workforce. Clinicians and staff are focused on complicated tasks and the issues within newborn screening, so this is a real concern in terms of carving out time for people to be able to do that in-depth learning rather than a sort of superficial skimming across some information, you know, where you can develop real knowledge about the field or a particular aspect of the field.

Personnel shortages are up and down in the newborn screening workforce. So how do we appeal to people to keep them within the programs? There are very few metabolic slots for trainees, for fellows. Can we enlist more MPH students, counselors to be trained up in newborn screening? And what kind of incentives can be offered?

Personnel often train up and leave. They go to greener pastures because there may be better

opportunities in terms of pay and lifestyle. Also, there are other groups in need of point of care education. So just couriers, obstetricians, dieticians, social workers, and technicians.

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(Slide)

JANE DELUCA: So what are we looking for in personnel? Do we want a match? Do we want a staff committed to newborn screening on all levels? So by matching, it could actually be even personality. You know, that you have a team that works very well together. So APHL has a workforce development project that is ongoing. And that is something we can look into.

Public health personnel are on hold or holding on for now during the pandemic. And they're committed to seeing this through. But they may leave if they can because the stress levels are immense within this staffing. So this is really, really important then, as we know there's been so much pressure on people working in public health. So that needs to be addressed.

There are shortages of lab workers and also data managers, which is something we, or I hadn't really thought about in terms of newborn screening. So Genetics in Medicine had published two articles, one on staff shortages and one on the current conditions in the genetics practice, which are, I'm sure, sobering. So you could take a look at those.

And also, the concern with adding more disorders to the RUSP, if states and staff already have difficulty keeping up, is of paramount concern.

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JANE DELUCA: So what is at the center of screening? So we kind of brought it back to the family and to the infants who are referred to our care. So what's the purpose of educating providers and families? We had ideas, considering to improve the ACT sheets and providing more information to families to create links on the ACT sheets for communication guides, to be able to

speak to parents during that initial discussion.

Some states link communication guides to the ACT sheets or directly to Baby's First Fest.

So what are these interactions, the return of results, the moment when a person conveys the information and family reactions? What metrics can we gauge to understand the impact and the effectiveness of this?

Now, there's a lot of factual information available, but families could go to the internet and they could find bad or old information. So how do you keep the information factual and up to date for them?

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JANE DELUCA: So communicating information effectively. It can be a matter of trusting the provider. Now we know these are difficult times for establishing trust with new patients within medical providers and systems, and there has been a mistrust of governmental

agencies.

So can providers answer the questions that families pose? There can be direct harm to families due to poor communication and knowledge deficits. So we do create a communication guide for clinicians and providers. It's a simple one sheet, and it was put out a few years ago in terms of framing the conversation for notifying and speaking to families.

But this is a very, very difficult process. And more needs to be applied here. When we have more complex disorders that are coming on-board and more complex educational messages, this can very difficult for even an experienced clinician to be able to talk to this about families that are brought into the system because of an abnormal screen.

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JANE DELUCA: So, how can we pull people in and engage people into the newborn screening workforce so we can target them young. Okay. And

then we spoke about that there are programs to talk to younger people in high schools about genetics, but not newborn-screening specific.

Do we need to be thinking about newborn screening as a specialty that people can be trained in? We tend not to speak about newborn screening in those terms. It's sort of like, who owns newborn screening? Can we make this a specialty that could be attractive to people?

Patient navigators could be needed. They could be nurses or genetic counselors, health educators, midwives. And one of the goals that they could do is to be able to build trust to deliver better education to parents.

So we can get creative in terms of how to pull in profesionals from other areas. You know, we target people that we work with who are not in newborn screening, but maybe they are ready for a change or interested in a new challenge and we can move them into a newborn screening role.

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JANE DELUCA: So educating parents. This is a busy slide; I apologize. But we were trying to be current and bring this up to date. So providing education in doses and formats that are appropriate for today's parents. So there are great packages of information out there, but they're no good if people don't look beyond the first page.

So we could target OBs and midwives and doulas, and mothers may be more open to discussing newborn screening and learning about newborn screening from them.

One of our Committee Members identified and discussed the successful pilot that was performed where researchers went into an OB office and set up an education program. Although the OB's were too busy, they were champions of it, and results are pending on this. It sounds quite successful.

Birthing centers and classes are outdated. Videos in waiting rooms to discuss newborn screening may help with information

delivery. Attempts to pull in prenatal genetic counselors have occurred, but they're very busy with discussions that they have with patients and particularly NIPT. And just-in-time education may be more effective for that group.

OB clinics are different from each other. So what is needed? How can that be tailored individually for them? These clinics are very busy with their own health teaching, SIDS, and other important issues.

So what changes do we want to see, how do we want to do this? There's a prenatal checklist that was developed for parents through a grant. The packet goes to OBs, and there are videos on YouTube, and data are forthcoming from this project. We'll look at maternal behaviors before and after the education is delivered.

And one novel idea was to offer prizes for completing newborn screening education for parents and families. And I think our group got very excited about that, the thought about offering some sort of reward for people educating

themselves.

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JANE DELUCA: So what change do we want to see? Small newborn screening programs cannot compete with larger research-oriented organizations in personnel and resources. And we were curious as to where money goes to the states. Where does funding actually go? Treatment centers used to receive funding, and that was sort of direct. And now this has been diffused and we're not exactly sure where funds are allocated.

So we need to think outside the box to address gaps. This is very serious. We are probably at a crossroads where this is. And we need to think bigger, possibly involving regional models or contracted services that can help.

So we're looking for other models to try to deal with this on a state-to-state basis or what else might be needed. Again we're looking towards larger groups being able to provide their input for newborn screening programs and thinking

about new regional newborn screening consultants.

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JANE DELUCA: So our last question was about, should the Committee consider the availability of follow-up experts when reviewing a new condition nominated to the RUSP?

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JANE DELUCA: This was actually a really good idea, but there was a problem with the question. No newborn screening program is sitting around with extra capacity, waiting for new conditions. Availability of an expert needs to be taken into account if reviewing a new condition. But this really seemed like it would be something that could be very valuable in terms of conditions being thought about for the RUSP.

Newborn screening programs are very optimistic and wanting to care for everyone all the time, but they need to be realistic in terms of the limitations of their resources.

If a state is not thinking about disorders, then you don't have that information. You don't know what's going out there. It may be in a research phase, and some states don't do research.

We'd like to see professional groups looped in. Is it possible? And see what the systems and capacity are on a national level. What stage would make newborn screening a priority? If newborn screening is not a priority, it could be. So we could raise a bit more money, find funding, and have this be a major public health priority within the states.

So what are issues within individual states? We know there are pressures with greater expansion on all levels from departments of health all the way down. So there are historical inequities that persist across states.

This is an extremely important issue, and why is it left to the states to deal with is very concerning because it does cross all the states in the nation. There are not enough specialists. We

have limited resources for support. And we need to really think about how to level the inequity of newborn screening programs across the nation.

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JANE DELUCA: So outcomes can be different in different systems and states. Historically, PKU rolled out, but how do we make this more equitable across the states? How can we again think about maybe regional and regional approaches for this? The New England region, there is a system there. How is this done? We could look at that.

Public health assessments are limited per the government, but this has expanded. It used to be a program where you could only look at nine states at a time in terms of their public health activities, but now it's broadened.

When reviewing our condition for the RUSP, how can information be collected? We had the idea of possibly taking states that are already screening for a disorder and kind of

making that into a model where we could look across all the newborn screening activities, from the point of having heuristic or pre-education for parents, all the way through to create a model so that other states can look at that and look at, by degrees, every single step of the way.

We thought that maybe we could do that with a state that's not screening and look at their capacity, but maybe that compel them to screen. So we were worried about that. But this idea of creating a model of a state that may be already screening a disorder could be very valuable for others who are thinking down the road for including that disorder in their screening panel, or they could include a case study or two.

So this needs to be a careful approach because again that added pressure to a state to add a disorder when they're not ready, you know, could be detrimental.

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JANE DELUCA: So, how could information

be collected? This was very broad and needs to be considered in depth. So much is being asked at once. So we want to think about this, I think, over time.

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JANE DELUCA: And in summary, there are many important issues that are put forth that need careful consideration. We need to think differently. And we need to acknowledge that state-by-state programs might not work moving forward, and we need new approaches.

Again we return to this idea of a regional approach, and we thought that we could consider developing a white paper article to talk about workforce educational needs and these newborn screening staffing shortages.

Thank you.

CYNTHIA POWELL: Thank you, Dr. DeLuca. It was certainly a very rich and thoughtful discussion yesterday, and you did a great job synthesizing all of the different comments that

were brought up.

Just as a reminder, we'll hold questions and comments until all three workgroups have presented.

Next up we have the Follow-up and Treatment Workgroup chaired by Dr. Jeffrey Brosco and co-chaired by Dr. Christopher Kus. Today Dr. Brosco will present the workgroup update.

Before I turn it over to Dr. Brosco, I'd like to take the opportunity to acknowledge and thank him for his service as chair of the Follow-up and Treatment Workgroup, as he rotates off, and this, as we mentioned yesterday, is his last meeting.

Over the years, he has led this dynamic and active workgroup to bring many important ideas forward for the Committee's consideration. On behalf of the Committee and the Follow-up and Treatment Workgroup, thank you for your service.

I am pleased to announce that after, Kyle Brothers will assume the role of Follow-up and Treatment Workgroup chair. Dr. Brothers has been

a member of the workgroup since joining the Committee in 2019 and will bring his expertise in primary care, ethics in human genetics, and the translation of health technologies into clinical care to this workgroup.

Dr. Brosco, I'll now turn it over to you to provide the workgroup update.

FOLLOW-UP AND TREATMENT WORKGROUP UPDATE

DR. BROSCO: Thank you, Dr. Powell, for your kind words.

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DR. BROSCO: So this is our workgroup. As you can see, Kyle will be taking over as chair. He is in blue there. And Annamarie and I are stepping off. We are going to really miss this. This was a wonderful workgroup over the years, lots of energy and excitement. And one other new member is Gerard Berry, joining as well, for the Society of Inherited Metabolic Disorders.

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DR. BROSCO: We tried to sum up as best we could the key things we talked about. So a lot of stuff is not detailed in this. I just want to remind everyone that these are the key questions, the workforce-related big challenges impacting access to short-term and long-term follow-up, including treatment, and workforce innovations.

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DR. BROSCO: So in terms of workforce challenges, this really dovetails nicely with what we just heard regarding education and training. And clearly, there are not enough specialists; this is well documented. And whether we're talking about dieticians, genetic counselors, social workers, others with newborn screening expertise.

And physician specialties, there's been a lot of documentation about the limited number of geneticists and endrocrinologists and neurologists that are trained to deal with newborn screening conditions.

And one of the questions I pushed the group on is, Well, does newborn screening make this any worse? I mean, we already have this shortage. And there was a general agreement that there are a couple of things about newborn screening that, when there's a new condition added, it does do a few things.

One is that basically taking care of kids starts earlier in their lives, so there are more visits than if they were clinically identified. And second, there are a fair number of children who don't have a clear diagnosis -- those presumptive positives and other varieties of that. So there is more work because of a condition added to newborn screening.

And a few folks brought up that burnout is not uncommon. This is really hard work. One our metabolic folks said, "I'm basically doing critical care medicine, but doing it as an outpatient on call 24 hours a day, seven days a week the entire year."

The treatment protocols, especially for

new conditions, are not usually easily available or sometimes they're unfamiliar when it first starts. And one of the neurologists mentioned that particularly for presymptomatic children, she says, "All I have to offer the family is worry." And that's draining for the clinician as well. It's hard watching families have to go through that.

But I will say in all these workforce challenges, they're really built on assumptions that we have about current models of care. That is, you can say we don't have enough pediatric endrocrinologists if the assumption is every child with hyperthyroidism has to be taken of by an endocrinologist.

And one of the things we talked about is how in most of the rest of the world, pediatricians are in fact specialists. Most primary care happens with general physicians, family medicine doctors, nurse practitioners. And pediatricians routinely handle much more complicated things than at least they do in urban

centers in the United States.

So the model of care that we have, this is just one example, is not necessarily the one that has to be going forward. So we don't want to spend too much time in challenges. So next slide. We'll talk about some of things about how to address this.

(Slide)

DR. BROSCO: So we see telehealth is the big change in the last year-and-a-half for how medicine works. And then some things that are working really well -- there's no doubt that direct patient care is much better for families who live far away from urban centers. And even inside urban centers, right, it takes probably an hour-and-a-half to get from one side of Miami to the other. So it doesn't even have to be a great distance. It's clear that we have better access to care because of telehealth. And that's the direct patient care side.

The other one that's really worth spending some time thinking about is more of a

consultation model in which a primary care clinician still has responsibility for taking care of the child with a newborn screening condition, but because they are linked into a metabolic center or a clinical specialist who has the knowledge of how clinical guidelines work, they can fine-tune their treatment of that condition, but also have that sort of personal connection to the family.

So these sorts of models have been tried in a number of places. For example, right now MCHB is supporting states to do this with child psychiatry consultations for primary care providers.

The challenge is for telehealth more generally -- I'm not going to list all of them. But obviously, payment may change fairly dramatically as the pandemic recedes. Right now it is a good economic deal to do telehealth, but that's changing already.

And secondly, when you think about those consultation models for a specialist who helps out

a primary care person or a doc at a distance or a nurse practitioner, where does the medical/legal responsibility begin and end? That sort of makes it complicated.

And the other part, and this sort of came up as implied in Jane's talk, well, if you had a regional model and your geneticist is in one state, how does that person help in another state where they're not licensed to practice?

So one thing we talked about is, could there be a federal designation of declared shortages, right, that says, "In this part of the world, there are not enough child neurologists. And so therefore, we can go across state borders to provide care"? That was sort of one example of how we might be able to move forward.

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(Slide)

DR. BROSCO: Payment systems matter, right? So one of the reasons why there are shortages of all of us in newborn screening is that we get paid a lot less than in other parts of

medicine.

But also a few people noted that we in the United States devote enormous resources to health care already, probably double that of just about any industrialized democracy. So it's not that there's not enough money in the system, particularly if you think about other ways to spend funds.

And then just a couple of words about value-based payment mechanisms. And we don't need to get too deep in the weeds. But here's an opportunity for dramatically changing the system of care. And whether we're talking about bundled payments for individual conditions or more global accountable care organizations, in both cases it's a chance for the health care team to use their resources in a way that maximizes quality.

And what do I mean by that? Just imagine for a second that when a child is born with PKU, there is a health care PKU team that's expert in that state that gets paid, who-knows, $10,000 per year for the lifetime of that child.

And they get to decide how to use those funds. So how much would be for the dietician? How much would be for a family peer? How much would be a for community health worker? You don't need to have all the funds go -- all the payment for a child with PKU funnelled through the clinical geneticist, who then feels like he or she is doing all the work.

So this kind of model really could change the way we do things and allow the training that Jane was talking about for all levels of newborn screening to be properly supported in the health care system.

So there's really a potential for a turnaround investment and something worth investigating, probably in the form of a white paper or something like that.

Now, of course the challenge to this is that the epidemiology of child health in the United States makes value-based payments really difficult. Because most kids are healthy, newborn screening conditions are rare, so it makes it

economically and logistically very challenging to do this kind of population health management.

We will point out that the overall system of care, we do know what to do. The AMCHP has mapped out how to improve the system, so we have a roadmap of what to do. We already know where to go. It's just a matter of the will to get there.

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(Slide)

DR. BROSCO: So the other questions that were asked were about whether the Committee should consider the availability of follow-up experts, especially clinical experts, how that information would be collected, and what should the Committee's role be?

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(Slide)

DR. BROSCO: So starting with, Should the Committee consider the availability of follow-up clinical experts when reviewing a condition? If we're talking about availability of treatment presented as a yes/no, then there were really

mixed opinions. And some said "No, we should not screen for a condition you can't treat." So if there really aren't clinicians available to do any of this work, then it is wrong to screen for a condition -- sort of basic Screening 101.

But others said just as strongly, "Yes. That is, if a treatment exists out there, we should have the wherewithal to be able to get it to that child and that family."

Is it okay to add --

(Dropped audio from 01:03:50 to 01:04:04)

CYNTHIA POWELL: Jeff, it looks like we're having some connectivity problems with you. I don't know if you didn't hear me. You may need to log out.

MIA MORRISON: Maybe go off camera.

ANNAMARIE SAARINEN: I was going to say maybe Kyle can step in if we are unable to message him to see if he can get back on.

(Pause)

SCOTT SHONE: Looks like he's trying to reconnect.

KYLE BROTHERS: Annamarie, you actually cut out when you mentioned me.

(Laughter)

KYLE BROTHERS: So I couldn't hear what you were saying.

ANNAMARIE SAARINEN: Oh, I was just saying you could step in on this slide if you wanted to cover for him in case he kept having connection issues. Sorry, Kyle.

(Laughter)

CYNTHIA POWELL: Let's give Jeff a minute to log back in. That might help.

(Pause)

MIA MORRISON: And, Dr. Powell, if Dr. Brosco is unable to reconnect, looks like he had just one slide left in his presentation. So maybe we could cover that when we open it up for discussion.

CYNTHIA POWELL: Yeah. Okay. Let's give him just a few more seconds, and then we could go to Dr. Kelm next.

(Pause)

CYNTHIA POWELL: Okay. Yeah, we'll definitely give Dr. Brosco some time to finish up, hopefully when he's able to log back in and we can hear him.

If we could now go to Dr. Kelm's presentation from the Laboratory Standards and Procedures Workgroup Update.

Dr. Kellie Kelm and Dr. Susan Tanksley are the chair and co-chair of the Lab Standards and Procedures Workgroup. And Dr. Kelm will give the update for that workgroup.

(Pause)

LABORATORY STANDARDS AND PROCEDURES WORKGROUP UPDATE

KELLIE KELM: While they're loading the slides, it was a very interesting discussion. And as always, I learned a lot. And the great news, we had just about everybody from our group was able to attend except for one person, who unfortunately was unable to join yesterday. So it was well attended, and it was a very fruitful discussion.

Let me see. There we go.

(Pause)

KELLIE KELM: And Jeff is back.

(Laughter)

DR. BROSCO: Sorry about that. Internet issues. My wife got lost, too, in the wilderness here.

CYNTHIA POWELL: So I think we'll go ahead with Dr. Kelm's presentation. And then before we open it up to discussion, we'll let Dr. Brosco finish up his presentation.

KELLIE KELM: Yes. So we were, as was dicussed yesterday, unfortunately we are going to be losing Dr. Baker by the end of the year and all of her contributions to our workgroup discussions. So, anyway.

Next slide.

(Slide)

KELLIE KELM: So this is the specific question that was asked of our workgroup about the laboratory follow-up workforce challenges. So the questions were, Are there other resources that

have been used at the state or national level to address laboratory workforce challenges? How could those resources be expanded to further strengthen the newborn screening laboratory workforce?

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KELLIE KELM: So we actually started with Susan, the co-chair of our workgroup, who let us know that there actually is an APHL Workforce Workgroup that actually started before COVID-19 trying to address the workforce issue. So this was already something that APHL was looking at before COVID-19 obviously made things even more difficult.

So that workgroup is still meeting. I think Susan said, you know, she's got two of the more difficult workgroups, and this is one that is still working. And some of the goals include examining each program and then identifying critical components common to all newborn screening laboratory programs. And that in order

to develop an APHL position statement that will lay out critical components of newborn screening programs that everyone needs to staff at a minimum.

Obviously they don't want people to use that and only staff that, but this is at least identifying that so that states can also identify gaps and places where they need to hire.

So then getting into programs that are already being used by labs and then discussing whether or not those could be, for example, expanded. The one program that I think was the most favorable and was mentioned by everybody was, you know, the fellowships that have been out there that have already been expanded and, of course, were highlighted as a place where we could expand more.

You know, they point to APHL fellowships, that that program gets very high marks. And then Max from ACMG let us know that they have fellowships in genetics and genomics that have been in the clinical space, but they actually

added a fellowship for laboratory genetics and genomics.

And so ACMG has expanded, and so this is a space that, as I said, a lot of the programs and the people who have been in the fellowship programs really highlight as a place that we could identify future leaders, people who can really come in and help a lot of the programs.

A lot of the labs do apply for the grants that are available, whether that's for, for example, bringing on new conditions, and using that to also help with staff. But of course, those grants are often limited in terms of time and come with the administrative burden that programs need to figure out how to take on. And they are obviously often trying to minimize new administrative burden. So grants can be extended with that caveat.

Next slide.

(Slide)

KELLIE KELM: One thing that we heard as a constant thread through the whole entire

afternoon's discussion was of pay. That all of the labs are struggling with maintaining, bringing on and keeping staff for any length of time, and the need to increase pay across the board to compete with other industries and laboratories.

There was a lot of discussion of some programs even changing their outlooks on the new folks they're bringing on to really thinking that they're going to be there for two to five years. And then they'll probably lose them because either most of the new people that they are bringing on tend to jump to other labs, industries.

And of course, you know, there was a lot of discussion about some of the labs that are in cities with other opportunities, you'll see that happen a lot more often than some other places, depending on the location. But this is a constant problem that everybody is seeing. But obviously, no easy way to figure out how to increase public health lab salaries across the board.

But then we went on to spending some time talking about some of the incentive programs that

some of our own workgroup members have used themselves. And these things in some cases have been positive. Some of these are local or program-dependent. It really depends often on the resources about where you are.

So some people touched on paid training when you owe a certain number of years of work after you finish your graduation degree. And in some cases, that has led to people staying on in the newborn screening area where maybe they wouldn't have, and maybe staying on even beyond the time that they owe.

Loan repayment programs. So the federal program for public servant repayments, after 10 years, is mentioned. Of course that program has been fraught with issues, but obviously it is one that some people can use.

Some places will actually pay for their staff to take classes or earn degrees through the public university system. And that's an incentive to also build leaders in your program and hoping that by doing that, they will actually want to

stay and move up in your organization.

And then we heard about labs. Even though it's not typical for them to do telework, trying to figure out ways to offer that just as benefits or incentive to keeping some of the staff on, figuring out ways to make that work.

It turns out that some states actually require clinical laboratory certification or licensure in order to work at the public health labs -- sorry, I mean in the state labs as staff. But some of the public health labs actually have exemptions. But often that is for just a short period of time.

So they stay and they earn their certification or licensure because they have that limited time that they're exempted from needing it. But often, once they earn their certification, then they are more attractive and can actually go to some of the labs that might pay more than the public health labs.

So could we extend exemptions so they may actually stay in the public health labs and not go

to the other labs?

And we did hear, you know, some interest in helping some sort of mentoring across programs, whether this is regional or federal. For some of the labs that are smaller have less ability in terms of people or time to do that and help with development. So helping, once again, to develop leaders and future lab directors in the public health space.

Next slide.

(Slide)

KELLIE KELM: So the last idea and the one that I think did take a good chunk of time was that, you know, somebody mentioned that there are cooperative agreements between the federal government and public health labs, and they pointed to these two existing programs, the Public Health Emergency Preparedness, and Epidemiology and Laboratory Capacity programs.

And this is additional funding that the programs get in that, you know, the benefits obviously are, number one, an ability that those

programs and that funding help with staff, you know, funding employees as well as infrastructure.

And lastly, although sometimes I'm sure people think of these things as a con that there's a governance structure that they would have in order to be able to make sure that their program is addressing the types of goals or recommendations that they have to meet as part of the cooperative agreement.

But, you know, this kind of program could be built for newborn screening, and in some ways people thought that some of the negative pieces could actually really help newborn screening, a lot of things that we've been talking about for the last 10 years.

So, yes. So number one, obviously a program like this could help fund adding full-time employees. And that would be in exchange for meeting goals or recommendations around newborn screening. And obviously, as I said, we've talked about a lot of these things -- timeliness, quality assurance, adding and beefing up follow-up and

other things, and other recommendations and goals that our own Committee has thought about and could ask programs to meet.

The governance structure and the ones that ELC and PHEP already have require staff from across the program to come together, and they want to discuss ways to tackle the program issues and activities and goals that these cooperative agreements, you know, ask these programs to meet.

So in this way, the governance structure in the state could -- you know, they now have to come together and actually tackle these program issues. Perhaps some of these longstanding issues of the newborn screening system that we've been talking about for many years, and even that with Melissa from RTI talked about yesterday, that we talk about often -- you know, how can we tackle these things with what we have?

So the pros about this would be helping to build infrastructure as well. You know, a program like this could help tackle some of the disparities between states that, once again, we

talk about often and that both Jeff and Jane have talked about.

And that is part of one -- states, I think, write up these agreements. They fold the administrative piece into the agreement. So it's also funded.

The one thing that obviously is an issue is finding funding for this. And that we heard from both our CDC and HRSA colleagues that that would obviously have to be a discussion that would need to be had. It's not that we have money already here to do it. So we would have to fund that. We would have to find funding to do that.

Next slide.

(Slide)

KELLIE KELM: So the other question was about whether or not we should consider the availability of follow-up experts when reviewing a new condition nominated to the RUSP and how we would collect that. So, you know, this was also very interesting.

Next slide.

(Slide)

KELLIE KELM: And I say that I think I heard a lot from the other groups as well in terms of discussing this. And I will say that in our own discussion, you know, a lot of this and how we would collect it and what we would collect, a lot of this we've thought would depend on whether or not we're talking about a condition in the new area.

So are we talking about, you know, new tests, new follow-ups, new clinicians that haven't been involved in newborn screening before? Or whether or not we're expanding a condition in an area where we're already doing newborn screening?

So, for example, adding SMA, we're talking about bringing in neurologists as an example of clinicians who may not have been involved in newborn screening before. Whereas rare metabolic conditions, we already have metabolic specialists involved. If it's rare, we're talking about a small number. The context there does make a difference.

The other thing that was really mentioned, and this is hard to know sometimes ahead of time in terms of how you might want to ask these questions though, is, Do we have a good test?

And what I mean by that is, you know, if we have robust pilot studies along with a test that has very good positive predictive value, then we know that the babies whom we're identifying and who will be referred will need care. And we're having fewer false positives, so who is moving on from newborn screening? That's a small number in terms of the burden on the system and whether or not we're worried about potential for harm.

I mean, all of that is obviously different in this case of this type of the condition that checks these boxes. And obviously it's going to be a lot harder if we're talking about smaller numbers, smaller confidence in what we're seeing. You know, the test is not as good and we're a little bit worried, a little bit more concerned about what number of babies have to go

on to confirmatory testing, et cetera.

And this already came up today, this issue with disparities in specialists. And we thought about, obviously from the perspective of our lab folks, you know, we know some states may have no specialists. Or they're all located in only part of the state.

I think Michelle mentioned that some of their conditions, all of their specialists are in New York City. So obviously, that is an issue that we should collect.

So one of the actual, I think, granular things that we actually did think about for if we continue to use a survey-type of tool is whether or not we can actually ask if the state has the capacity for a certain number of hours per child for specialists or genetic counsellors. Because that gets a little bit more into the state's capacity. And seeing whether or not the state could answer that.

Now, of course, all of this is -- when you do surveys of conditions, we realize that the

issue number one is that if the state hasn't even started thinking about screening for this, then they won't have this information.

If the state is, of course, asking, has already started considering screening for this, then they may have already started doing their homework. They may already have lots of information in terms of the first four bullets on this page. But that also really makes it hard when you're asking states about this and how much homework they have to do to answer this question.

And I think that that touches a little bit on what we've done before and that Jane talked about, you know, asking states that are already doing it or already thinking about doing it. They already have this information versus a state that has no idea and will not be able to get you this kind of information ahead of time.

You know, I think this is, although with the lens of the fact that we already know that we are already lacking geneticists and that we are already -- you know, we already need two times the

number of geneticists that we currently have for our current workload. And so we can ask about that. But we're already behind.

And we also know that many states are already two or three conditions, still working on bringing on two or three conditions, or behind and not even working on two or three of the ones that we recommended. So sometimes our survey or the way that we're asking about bringing on new conditions is not even within the thinking about the scope of the fact that many states are behind.

But the interesting thing, at least for the members of the workgroup, is I guess the conclusion that so far states have just made it work. That when we move forward with recommending and adding a condition to the panel, yes, they are behind. But they just figure out a way to make it work.

Is there a condition that a state -- there was a no for this. Is there a condition that a state had difficulty screening for due to the availability of specialists? And what we

heard was, some states, you know, might not have metabolic specialists. But then they have set up, and they go out of state to find specaialists. And that has happened as well.

So they've just made it work. They've just figured out a way to make it work. And so, you know, I think there's a little bit of I guess -- obviously, lots of surveys have happened of the people on our workgroup, and the answers obviously are often that it's going to take us many years, that we still move forward with adding the conditions.

And they figure out how to do it; it just sometimes takes longer than they want. And they figure out how to get the resources to do it even if, you know, we might not have everything that we want.

So I think that was it for us. I don't think we have any other slides.

CYNTHIA POWELL: Thanks, Dr. Kelm, and also to Dr. Tanksley and all of the members of your workgroup. Really very important information

that you discussed, and some new ideas that I think are going to be critical going forward.

Before we go on to comments and questions, if we could bring up Dr. Brosco's slides from the Follow-up and Treatment Workgroup and find the last slide. I think it was towards the end.

DR. BROSCO: Yeah. I only had two slides left. And I apologize. If my internet goes out again, I can just call in by phone and finish the last slide or two.

But before I jump into this, I just want to say one other thing, as a historian, that there have been surveys of the physician workforce every decade for the last 100 years. And there's always a shortage. Back to the time when there were no subspecialists, there's always a shortage if we use the same old model that we gave a specialist to do something. Anyway, it's just a fun fact.

So coming back to, Should the Committee consider the availability? We were talking about how this is better conceived as a continuum and

that there would be variation in the access to treatment based on geography, insurance status, race, ethnicity, and other factors.

And then sometimes we're all responsible in the newborn screening world and beyond for trying to improve health equity. We certainly over the last years have moved in a better direction with that.

So what in particular could we do as a Committee, though? One is we did come down on the idea of saying, yes, we should have a clinical impact component. It would sort of be analagous to the public health impact component in saying, What are the clinicians' availability? How does this play into what's going to happen with a new condition?

We also recognize that whenever a condition is nominated and gets to the RUSP, it's most likely the treatment is not going to be available everywhere as soon as that condition is nominated. It's just not ever going to be true. However, the big question is, Is there a

reasonable path to sufficient capacity to treat all children?

That is, if we could imagine a way of training child neurologists to be able to treat SMA, and that there are enough and there's some way to do it, if there's a path to capacity, that probably means something that's important. If there is none, then that probably means something important, too.

So that might be really the critical question. Not what do we have right now?, but what is the potential going forward?

(Slide)

DR. BROSCO: Then in the last slide, How exactly would we collect this information, and what would be the role of the Committee? So these are just very brief early ideas. So this obviously needs to be discussed more.

One is, we could in the nomination package start asking right from the beginning, so, Who are the clinicals you think need to be involved? Who are the ones who are going to do

the diagnostic and treatment? Is it a subspecialist? Who might actually do this work?

And if there is any evidence of their availabiilty? Lots of times there are reports out about saying there were not enough of whatever specialty you need.

And then related to that is, What's the proposed plan for reaching all children?, as I was just mentioning before. Could it be that, you know, this is a relatively simple condition to manage? Primary care, clinicians can fairly easily do this with some support, with some kind of point of care consultation. Or does it really require a child neurologist expertise being able to do intrathecal injections?

How could this affect the evidence review? We hate to add more to Alex's team, but you could imagine surveying professional societies or others the way we do public health labs now. And what would happen after something actually makes it to the RUSP?

Well, we're already working on rapidly

available treatment guidelines and training clinicians. I think the RTI discussion yesterday kind of had this idea of almost, you know, when something comes on the RUSP if there is pathway to implementation. It would include a variety of things, including how we make sure clinicians are ready to receive those children where there is a presumptive positive.

Then lastly, one of the things that we could do not related to a specific condition, but more generally, and one you heard already from Kellie and from others, is if state newborn screening programs minimize referrals for presumed positives, that would certainly reduce some of the workload on the clinicians, but it would increase the workload on the lab folks.

And then, lastly, you know, maybe as I said before, this is a time to really look at, What are the needs of children with rare conditions -- that is, newborn screening conditions -- in the move to value-based care?

This is happening in the adult world.

It's changing the way medicine is practiced. It's presumably going to come to pediatrics. That's what all the indications are. And should we be thinking now about how this affects how kids with rare conditions are treated? I think that is within the basic realm of our Committee.

I think that's it.

CYNTHIA POWELL: Thanks very much, Dr. Brosco.

We've heard some really interesting ideas from the various workgroups. And I'll now open the floor for discussion. Committee Members will discuss first, followed by organizational representatives.

As a reminder, please use the raise-hand feature in Zoom when wanting to make comments or ask questions. And please unmute yourself and state your first and last names each time you ask a question or provide comments, to ensure proper recording.

DISCUSSION

CYNTHIA POWELL: Lots of information

presented there.

(Pause)

CYNTHIA POWELL: I found it really helpful to get more input from additional folks who are involved with newborn screening. I was struck yesterday by some comments that really brought up the problem of burnout among those in the public health system.

And there was one comment that if we continue to add new condition after new condition, we're at risk for breaking the whole system. And that sort of sent chills through me.

Also, you know, given what those in public health not specifically involved in newborn screening, but other aspects of public health have unfortunately had to go through during this pandemic, being threatened, you know, because of all of the horrible misinformation that's out there that is causing so much anger, you know, people getting threats and things.

And that they're sticking it out through the pandemic, but that there may be a mass exodus

after the pandemic, hopefully soon, is over with. And we're going to lose extremely good people. And I think we need to provide a way to make sure that people are retained.

So I see Jeff Brosco.

JEFF BROSCO: Jeff Brosco, Committee Member. I have a question that probably Debi Sarkar can answer best. But before I do, I want to second what you just said, Cindy, about how important it is to support our friends who work in public health. Our state public health departments have really been under a lot of stress. And I thank you for your words.

So one of the solutions, Debi, we've heard a lot about is regionalization of newborn screening. And I know that over the years MCHB and HRSA more generally have really tried to support creating collaboratives and so on. I just wonder, what's been holding us back from moving toward a regional approach which seems to make so much sense? And what we could do to sort of push that forward? Or anyone.

CYNTHIA POWELL: Yeah, I think I've found that to be a common theme also, both perhaps more on the federal level and/or regional levels to support newborn screening.

I like to say that when we think about the workforce, it's not just in well-funded states like New York, California, Massachusetts. But it's also states like states like Mississippi. And how do we make sure that there is equity?

Debi, did you want to comment? I don't want to put you on the spot.

DEBI SARKAR: Thank you for that.

You know, I think I would be also interested to hear more from states and from other Committee Members on how this regional model would look. Yes, we've done collaboratives. We're doing the regional genetics networks. And, you know, just more ideas, that would be helpful for us to then think about how we could approach that.

CYNTHIA POWELL: Scott Shone.

SCOTT SHONE: Thank you, Dr. Powell. Scott Shone, Committee Member.

And I also just want to echo appreciation as someone who has been living in public health. So many of my colleagues do this. And as a state lab director, it has been a unique challenge.

So I want to call back to something Dr. Raspa said yesterday at the very beginning of her talk that sort of leads into what you were talking about, Dr. Powell, which is that she mentioned something to the effect of that there's a growing divide between states and programs, and we're sort of rebuilding a potential inequity in terms of what programs offer to disorders or how they're operating.

And it made me think about a recent discussion I had with Rod Howell about what started the ACHDNC to begin with. And I had a similar shiver when Dr. Raspa said that around, are we getting back to where we started?

And it made me think that there has to be some sort of substantial pivot point and really new idea to reframe this. The Committee is a great resource for guidance and recommendation.

But how to help facilitate that?

I know every advocacy group is trying to sort that out. And a lot of it around adding disorders. But I think we need to be more mindful about all of the other things that support the system that we've talked about, that also are catalogued quite well in Dr. Raspa's presentation -- sort of a decade of work -- and where we've made progress and where we've struggled.

I think Dr. Kelm mentioned our discussion yesterday around similar structures for other parts of the public health system, with preparedness and epidemiology and laboratory capacity, and how we as a public health system have made strides there, thanks to the dedicated support of the federal government to fund those.

You know, there's been a recognition of the essentiality of preparedness. We relied on PHEP at the beginning of the pandemic when we hoped it would be short-lived. But then it became longer-term and there were more funds.

And then ELC stepped in and has

distributed trillions of dollars around the country to fund not only the response, but also the long-term restabilization of the public health system, whether it's sequencing for variants or whether it's expanding infectious disease work to make us stronger.

And it was somewhat, I think, lost in Dr. Kelm's presentation that those are the types of really big ideas, I think, that HRSA and HHS needs to think about, moving forward.

That would again, the long-term stabilization potentially of infrastructure with dedicated funding sources and projects that are built out of the recommendations of this Committee, with resources that are driven by success and plans with milestones, owners of those milestones. And we see that across the public health lab system.

And I would love to have those dialogues not only as we do with our state epidemiologists, ELC, and our step coordinators wherever they lie within the states, but our follow-up teams and

then that junction with that.

I mean, we have ELC projects with universities and academia that drive the expansion, the technology transfers, and all of that work that we need desperately here. And so I think that that's not the solution. I want to be clear. Like I don't think like we solved this in the Laboratory Standards and Procedures Workgroup yesterday.

But those are the types of things we need to be really pontificating and pushing forward to make the changes stick that were catalogued yesterday afternoon. Thank you.

CYNTHIA POWELL: Thank you.

Mei Baker.

MEI BAKER: Hello. Mei Baker, Committee Member.

So I want to adding on one thought regarding regionalization. In my head, I like the federation system. I think we can do this combination. The states should have retained autonomy, and also for patient care.

Because unlike other public health programs, newborn screening is -- when you have a test and result, you are not done. You have to have a follow-up. Physicians have to be involved and have a HIPAA, have an insurance, have so many different things.

What I can envision is that federation system. Because we can -- I mean, a few things. First, going forward, the technology work will get more and more sophisticated. And also, certain tests really are -- I mean, because effectively, every state has one.

I want to give a typical example for SMA screening. I still strongly believe the copy of SMA II is important, is that every single state have to have a digital piece how to do that. Maybe not. And the interesting thing is, states among themselves have to do such a thing.

Like states say, "I want SMA II call the numbers, but I don't have to do that. Can I ask for somebody else, other program, to do so?" And those things, I think, get to be when the

workgroups, the laboratories, the workgroups are talking about bioinformatics. And this kind of thing, that is a very, very high skill and very, very expensive, the workforce.

If we really can regionalize and the people utilize the way to have access to that, I think it is a cost-effective way. And also, people talk about the challenges to maintain the grant. Your federal funding comes through this channel. And the benefits that states can have, I don't have a buy-in implementation. But I know the regional and also, the high-end program, the ways of interpretation, and it's a lot of very sophisticated, important, and a very expensive program. And the license can be very expensive. Why every state has to spend money to that? If federal funding can do that, people can have access in the regional, or even federal, fashion. I think it really is -- I can see this.

I don't know term. It really is a nationwide, the newborn screening ecosystem. But the states still have the autonomy. And also,

think about the timeliness. Timeliness is important to the state because you don't want sample centers everywhere.

One thing I was thinking -- perhaps it is a fantasy; I don't know -- is every state you have, like let's say if we show to the genome and every state can have the machines where the data can be generated and this through the closest or whatever, every single state have access to the biomedical piece, to the interpretation.

I think CDC has done very good job of starting this, have paved the way. And you can do everything regulatory compliance. So I'm going to stop here. I hope I can get it from "federation" this concept to get into people's head.

CYNTHIA POWELL: Thank you.

Shawn McCandless.

SHAWN McCANDLESS: Shawn McCandless, Committee Member.

I'll try to be brief. I think something Dr. Brosco said resonated with me, and I want to thank him for his wisdom.

And that is that physicians always feel like they're overworked and that there aren't enough of us. And the reality is that this Committee has no way to impact, nor do any of the individual members or government agencies represented here have any way to impact the number of providers available in our society.

We don't have an organized health care system. We don't have a single health care system that we can make rational decisions about need and then implement them.

And so, the number of providers available is driven by a variety of market and pseudo-market factors that we have no control over. Therefore, I would encourage this Committee not to spend too much time worrying about that. What determines the number of providers available is the demand.

And I think that this Committee should focus on things that we actually have the ability to impact, and that is creating expectations on a national level for what an excellent newborn screening program should look like in every state,

trying to support regional centers. Whereas Dr. Baker said "federation," when that is appropriate and efficient.

And we should be really focusing on supporting the needs of the public health system that we can have some impact on by providing funds -- or not this Committee personally providing funds, but just supporting the newborn screening labs and the follow-up programs within the laboratories.

And really creating clear expectations and guidelines about what newborn screening could and should look like in the United States.

Thank you.

CYNTHIA POWELL: Thank you.

Natasha Bonhomme.

NATASHA BONHOMME. Great. Thank you. Natasha Bonhomme, organizational rep for Genetic Alliance.

This really builds off of a lot of the conversation that's taking place. And while I know particularly from the lab group there's been

kind of a listing of what's needed and all of that, I think if kind of the goal is to see how we can support public health, we really need to be sharing more broadly and not just kind of speaking to the choir about what the issues are.

As has already been said, the tone of the newborn screening system is going to break. It's going to break, has been happening. That line has been said for a very long time. I remember when CCHD was going to be what completely destroyed the newborn screening system. And it didn't.

And so that's not to say that these concerns aren't valid. Of course they are. But I think really putting some really clear, accessible language to that -- What does that look like? What does the crumbling of the system really start to look like so that people have something that they can really attach to? And it does just sound like the same thing we've been hearing over and over again.

And I think that this is a really good opportunity to work with and partner with and have

that explanation to really be able to communicate that to advocate partners of, what are the concerns? And not just at the 30,000 foot, but you know, bringing that conversation down.

And I think we had a lot of that discussion yesterday in the Education and Training Workgroup of being very specific of, you know, not just broad workforce issues, but this is why we know people are going to be leaving.

And if we can get to some of those data and some of those specifics, and again really speaking to those partners who aren't always included in all of these conversations, I think that can really move the newborn screening system forward.

But I think that effort needs to come from all angles, from all stakeholders who are invested in newborn screening.

CYNTHIA POWELL: Thank you.

Susan Tanksley.

SUSAN TANKSLEY: Hi, Susan Tanksley, organizational representative for the Association

of Public Health Labs.

I wanted to go back to the concept of regionalization. And I'm sure you already realize that regionalization has occurred, at least in a couple of areas. I mean, we have the Northwest Regional Newborn Screening Program out of Oregon that tests with other states, as well as the New England Newborn Screening Program, which covers a substantial part of the eastern part of the U.S.

And, you know, those are great. But that regionalization itself is -- newborn screening is a state-based issue. So that has to be a decision of the state, much as what Mei was stating, for that piece.

But I do think that the idea, and I'll use a term that Scott Shone coined, using "centers of excellence" for specific things. And Mei mentioned some of those as well, like for bioinformatics or some of the second-tier testing, those sorts of things.

We heard discussions in the workgroup report-outs. At least a couple of them mentioned

the need for really good tests for high-positive predictive value. And the way you get that is by doing second-tier testing. And not all states do that. And so that would be one way to improve the positive predictive value.

I love the concept of some sort of core funding for newborn screening, much like ELC and PHEP. That does support an infrastructure, and that is a mechanism that could support those centers of excellence, something where states compete to be a center of excellence for particular projects.

I think that's all I had to add. But thanks so much for this discussion today.

CYNTHIA POWELL: Thank you.

Jane DeLuca, I'll give you the last question or comment for this session this morning, as we will take a short break after that.

JANE DeLUCA: Okay. You know, I just wanted to come back to the comment about telehealth. Because I think we were plunged into telehealth in an emergency way, and it was

awkward. But I'd like to know more about what people were doing, from initial calls to downstream to three-months-out, nine-months-out.

I don't know if there's a body of literature out there about that. But I just wanted to throw that out. I think we should find a way to gather that before it dissipates or before we even lose telehealth; I don't know.

But anyway, that was my comment.

CYNTHIA POWELL: Yeah, I agree. I think as Jeff had mentioned, you know, it's worked very well. But unfortunately, in our own state I know we're losing some of the insurance providers who are now not willing to cover telehealth visits anymore. So it's really impacting already our program.

It was very successful for our metabolic patients. They really liked it. But unfortunately, I'm not sure. So I agree with you, it's an important thing as we move forward.

So once again I'd like to thank everybody for these great discussions in your workgroups.

And one thing that I'm hopeful is that we will be able to develop at least a white paper, if not a peer-reviewed publication about these issues. I'd really like to have at least one representative from each workgroup.

I have gotten one so far from Education and Training yesterday. So feel free to contact me if you're interested in helping with this. I think we'd also include those who presented to the Committee regarding their specific specialty areas and workgroup challenges.

So we will break for about 10 minutes and reconvene at 12:05 Eastern time for our afternoon presentations. Thank you.

BREAK

CYNTHIA POWELL: All right. Welcome back, everyone, from a short break. We'll now move on to our last session of the November meeting. The Committee will hear two presentations on newborn screening pilot programs, ScreenPlus in New York and Early Check in North Carolina.

This is an opportunity for the Committee to hear about conditions with population-based pilot programs that in the future could be nominated to the Recommended Uniform Screening Panel.

Our first presenter for this session will be Dr. Melissa Wasserstein. Dr. Melissa Wasserstein is the Chief of the Division of Pediatric Genetic Medicine at the Children's Hospital at Montefiore, and Professor of Pediatrics and Genetics at the Albert Einstein College of Medicine.

She is a board-certified biochemical geneticist and pediatrician, diagnosing and managing patients with rare in-born errors of metabolism.

Her research activities focus on expanding and enhancing newborn screening to optimize the outcome of infants with rare disorders, implementing genomic diagnostics in diverse populations, and studying the natural history and treatment of acid sphingomyelinase

deficiency.

She is the principal investigator of ScreenPlus, which she'll talk with us about today. And I'd like to turn things over to Dr. Wasserstein.

NEWBORN SCREENING PILOT PROGRAMS

SCREENPLUS -- NEW YORK

MELISSA WASSERSTEIN: Thank you, Dr. Powell. And good afternoon. I'm delighted to be here today to introduce you all to ScreenPlus.

Next slide, please.

(Slide)

MELISSA WASSERSTEIN: Here are my disclosures. The majority of these are all related to research work for ScreenPlus.

Next slide, please.

(Slide)

MELISSA WASSERSTEIN: So, ScreenPlus is a comprehensive, flexible multi-disorder pilot newborn screening program.

It's a large multi-facted program, so I think it's easiest to introduce you to it by

breaking it down into four components, starting with an overview of the program, including logistics that are running the pilot screen, followed by an introduction to the programmatic infrastructure, an overview of our ELSI studies, and ending with a status update.

Next slide, please.

(Slide)

MELISSA WASSERSTEIN: Next slide.

(Slide)

MELISSA WASSERSTEIN: We originally had eight pilot hospitals, but just this week we actually added on a ninth. And I'm showing the hospitals here. They are largely based in New York City and Long Island.

And in order to be a pilot hospital for ScreenPlus, we have certain criteria including that these are all extremely massive hospitals with very high birth rates. The anticipated birth rate at each hospital is shown over a five-year period underneath the name.

All of the hospitals are in ethnically

diverse communities, and most of the hospitals are already New York state newborn screening referral sites. So they have trained biochemical geneticists ready to see our patients.

Our recruitment goal is 175,000 babies over a five-year period. And if you add up the birth rates from all of these hospitals, it's almost 300,000 births. But we're assuminmg that we will get a consent rate of approximately 73 percent, and that's based on the consent rate that we had for a pilot newborn screening for lysosomal storage disorders that we ran from about 2011 to 2017.

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MELISSA WASSERSTEIN: This is an identified prospective pilot screen where we obtained informed consent using direct in-person one-on-one conversations between the recruiter -- we have a full-time recruiter at each pilot hospital who goes onto the maternity ward after the parents have given birth and have those

discussions.

Our coordinators are bilingual, Spanish and English. And our brochures are translated into the eight languages that are most commonly spoken at our pilot hospitals. And a few of them are shown here. Once parents agree to participate, we automatically create a RedCap form for that baby, and we have an automatic link that will email the parents a copy of the consent and brochure.

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MELISSA WASSERSTEIN: I'm showing you our ScreenPlus panel here. As you can see, we have 14 disorders on our initial panel. Importantly, the panel is fluid, so we can remove disorders if they're added to the RUSP at any time during our recruitment period, or we can add them if they meet our ScreenPlus criteria.

And the criteria to be included on our panel includes, first of all having a dried blood spot screening assay that can be multiplexed, that

is high-throughput, that's reasonably priced, and has had positive baseline validation studies. We need a disorder that has significant morbidity or mortality if untreated.

It has to have a pediatriatric phenotype because many of these disorders have broad phenotypic spectra, including infantile onset forms ranging to adult onset forms. We recognise that, so we are including that it has to be a number of children who would be identified with benefits and treatment during young childhood.

And the last criterion is that there either has to be an FDA-approved treatment or treatments that are currently in clinical trial and that look very promising.

So just to quickly run through our initial panel, starting with acid sphingomyelinase deficiency, or known as ASMD; ceroid lipofuscinosis type 2; cerebrotendonous xanthomatosis, Gaucher disease; GM1 gangliosidosis; Fabry disease; lysosomal acid lipasde deficiency; metachromatic leukodystrophy;

MPS II, IIIB, or IVA, VI, VII; and Niemann Pick C.

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MELISSA WASSERSTEIN: So we felt that a pilot screen like ScreenPlus is a really good opportunity to kind of trial a new approach to enhance the accuracy of screening. So as you can see in this table, all of the disorders that we're screening for have at least two tiers of screening prior to call-out.

So the vast majority of them have enzymatic activity as the first-tier screen. If that's abnormal, then it will reflex to a second-tier screen, which is often a biomarker. And third-tier is sequencing on the relevant gene. And at the beginning of the trial, we're actually running second- and third-tier in parallel.

And the goal of this is to see, first of all, if we can enhance accuracy, possibly reducing false positives. And it would be really wonderful if we could actually eventually use these data to help predict phenotypic severity, which all of us

who are in the newborn screening world know that that's always a challenge when we get a new baby from newborn screening.

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MELISSA WASSERSTEIN: Because this is a pilot program and because the disorders on ScreenPlus are new to newborn screening and are relatively complex, it's really critical to capture longitudinal follow-up data. In part because, you know, first of all a newborn screening laboratory won't be able to accept the accuracy of their assays until we know if the patient is expressing phenotype.

The confirmatory testing results may be unclear based on variants of uncertain significance, et cetera, until the patient does or does not express phenotype. And we also need to know which children who have later onset disease might need follow-up and might need treatment at another point.

We also, of course, since this is a

private program and we need to know if there actually is a benefit to early detection for our disorders on our panel. So we've created some guidelines, and you can see an example. This is the metachromatic leukodystrophy recommended timing and type of testing to do for babies.

And this is just for MLD, but we have similar protocols that we've developed in conjunction with national and international experts who are very generous in donating the time and expertise to help us develop these. And these were shared with all of the pilot hospitals and the doctors who will be seeing these babies so that we can make things a little bit more uniform in terms of the data capture that we'll be obtaining.

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MELISSA WASSERSTEIN: So now turning to infrastructure.

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MELISSA WASSERSTEIN: So we have created a unique cost-sharing infrastructure. Starting with NIH, this was an NIH R01, industry sponsors and patient advocacy groups. And all parties who are participating have a vested interest in newborn screening for a particular disorder either because they have an FDA-approved therapy, are sponsoring a clinical trial, or are advocating for a RUSP nomination.

And this cooperative plan will enable us to streamline costs while enabling the program to function at maximal efficiency.

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MELISSA WASSERSTEIN: So this is kind of an overview of our organizational and financial infrastructure. We've been working extensively with the Albert Einstein College of Medicine Contracting Team, the Research Finance Team, the Legal Team. We have regular meetings with them.

And this infrastructure was largely developed by my amazing Project Manager, Nicole

Kelly. And you can see on the top line, we have our sponsors. Again these are largely industry partners and patient advocacy groups. And those groups are supporting the actual pilot screening in terms of helping to fund the pilot hospital, the cost of testing and reagents.

The NIH is largely supporting the coordinating center, which is my team here at Montifiore/Enstein, as well as our ELSI studies, which I'll talk about today.

And the output is the planning of the pilot hospital; the testing laboratories including the New York State Department of Health; and Mayo, who will be doing some of the confirmatory testing; the reagent suppliers; as well as our ELSI team, who are at the institution.

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MELISSA WASSERSTEIN: Now turning to our ELSI studies. So we have decided to take advantage of the large number of babies whom we are hoping to enroll and engage their parents in a

series of surveys and interviews.

We think we're going to have 175,000 babies. Even if just a small fraction of the parents agree to participate in this survey, we'll actually still have potentially thousands of engaged parents who are willing to share their opinions about newborn screening.

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MELISSA WASSERSTEIN: So at the time of consent, we start out with a consenter survey and the decliner survey. And we're asking parents about how we did. Did they understand what we were talking about? Why are they participating? Or why have they declined? And we're collecting socio-demographic factors to see if we can do anything better in that process and to understand why people might not want to participate in a study like this.

About one month after the results were reported, we have the first set of surveys for parents whose babies have negative ScreenPlus results. And this is going to be the bulk of the

parents.

We have a series of surveys that are each focused on a different topic and include things like, What is your opinion about newborn screening for later onset disorders or screening for untreatable disorders? What is your opinion about using whole-genome sequencing for newborn screening? What is your opinion about informed consent for screening, informed consent for research in newborn screening?

We also have a series of qualitative interviews, which are focused on parents whose babies have an uncertain or positive result in ScreenPlus. And these will be done about six months or two years after the results are obtained.

And the reason why we're focusing on the parents whose babies had an uncertain or positive result is that -- you know, in my experience and probably in the experience of a lot of people who are listening, our focus is always on the babies. But I think that the parents are often struggling.

They're going through a trauma and trying to understand what's going on.

And I think this is an opportune time for us to try to learn what they're going through, how this is impacting them, and what we as the newborn screening community can do better to help support them.

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MELISSA WASSERSTEIN: So the overall goal of our ELSI study is to allow us to have an improved understanding of how to improve the newborn screening implementation process to meet family needs. And as well as learning from parents what they see as the optimal way to expand newborn screening and the future of newborn screening, including genome sequencing.

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MELISSA WASSERSTEIN: So our current status. We had our first baby in back in May. We were obviously delayed because of COVID-19 when

there was no live in-person research happening in New York City. So we were delayed a bit, but we got our first baby in.

(Slide)

MELISSA WASSERSTEIN: This is the Jack Weiler Hospital here in the Bronx.

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MELISSA WASSERSTEIN: And our ELSI studies were also already helping out. So as I mentioned, we are doing surveys for parents right after they consent or decline.

The information that we're asking them is, How did we do? How was the information? What did you use? How was the e-consent process? What was the most helpful bit of information that we provided that helped you make your decision? Why did you decide to participate? And then demographic information.

And for decliners, again we focused on why they chose not to participate.

The top table shows our overall consent

rate by week. We have consent rate, decline rate, and then pending rate for babies who have been discharged before we got to see them in the hospital and we were following-up by phone.

And you can see that our consent rate was roughly in the range of 60 to 80 percent. We have one week, week 10, where our recruiter took the MCAT, so he was out for two days. So we lost a few babies that week. But we've been using the information they've provided to help kind of tweak our scripts to try to enhance the recruitment rate.

And the bottom shows the most helpful source of information that parents said that helped guide their decision to participate. And I guess not too surprisingly, the majority felt that the most important piece was the discussion, that one-on-one interaction with our study coordinators.

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MELISSA WASSERSTEIN: So next steps. We

are very actively in the process of contracting with all of our pilot hospitals. And we hope to have them live within the next few months. January–February might be a little optimistic depending on hiring. But this should all be live hopefully within the next quarter.

And based on this early feedback, we are hoping with just continuing to refine our materials and our scripts -- we've also decided that based on the fact that parents are being discharged a little bit earlier than they were before, which is hard to believe. But parents are being sent home earlier because of COVID-19.

So we do need to really focus on developing a passive e-consent model for these discharged parents to use at home because we've been finding that when you call them at home, it hasn't been very fruitful. So we're working on that now.

And in terms of our ELSI surveys and qualitative studies, we have a community advisory board who's been fantastic. And we're seeking

feedback from them to help ensure that our study materials are appropriate & comprehensive.

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MELISSA WASSERSTEIN: And with that, I think it's a very large chain that I'm delighted to be part of. And I would love to thank everybody out loud. But just special thanks to Nicole Kelly and Natalie Boychuk, who are my nominal project managers; the New York State Newborn Screening Team, especially Joe Orsini, Monica Martin, and Hannah McKnight; Michael Gelb, who developed our multiplexed assay; and my ELSI team, Aaron Goldenberg and Maria Kefalas.

Thank you for paying attention. I look forward to questions.

CYNTHIA POWELL: Thanks very much, Dr. Wasserstein, for this very informative presentation. We're going to hold questions and comments until after our next speaker.

I'd next like to introduce Dr. Don Bailey. Don Bailey, Ph.D., is a Distinguished

Fellow at RTI International, where he is a member of RTI's Genomics, Bioinformatics and Translational Research Center.

Before joining RTI in 2006, he was on the faculty of the University of North Carolina at Chapel Hill, where he was a W. R. Kenan Jr. Distinguished Professor, and for 14 years Director of the Frank Porter Graham Child Development Institute.

His research addresses early identification and early intervention for children with disabilities, as well as family adaptations to disability. Much of his work has focused on chidren with fragile X syndrome.

Currently, he directs several projects on newborn screening and broader issues surrounding the ethical, legal, and social consequences of genetic discoveries, and the disclosure of genetic information.

And I'll now turn things over to Dr. Bailey.

EARLY CHECK -- NORTH CAROLINA

DON BAILEY: Great. Thank you very much, Dr. Powell. Can you hear me okay?

CYNTHIA POWELL: Yes.

DON BAILEY: Great. Thank you very much for the invitation to present to the Committee today. I've been watching the last couple of days. As you know, I served as a member of this Committee for six years. And so it's been great to see how you are still operating, and it was a real privilege to serve on the Committee.

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DON BAILEY: I'm at RTI International. This is a picture of our home campus in North Carolina. We have offices all over the United States and around the world, and we hope to be back in our office in person sometime in the next few months.

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DON BAILEY: Here are my disclosures. We are fortunate to have funding from a variety of different sources, the NIH, from the CDC, and from

HRSA and from a variety of other foundations and industry partners. These support not only -- some of them support Early Check and for other projects as well. So these are all awards to RTI International. I don't get a consulting fee for anything.

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DON BAILEY: I thought I would start by just saying that Early Check and ScreenPlus actually have a lot of common. First of all, we're both investigator-initiated projects. So we didn't respond to an RFP or any initiative from the federal government or from any other source. We've developed these on our own.

And I would resonate with some of the discussion earlier today about the need for centers of excellence, perhaps funded at the national level.

We're both designed to advance newborn screening policy and practice. And we combine research with implementation studies. We see

through a lens both of public health, public health ethics, and respect for families. We're both designed to fill a gap in national capacity to gather policy-relevant data.

And the little box that I've got on the right, this is something I've talked about for years. It was clear on my Committee that rare diseases are caught in this classic "Catch-22" situation that screening cannot be mandated without evidence; but screening is needed in order to gather evidence. So that's what both of our projects are designed to do.

Both multi-condition studies of disorders that are not yet on the RUSP were designed hopefully to be long-term disease agnostic to a certain extent, infrastructure or resource. So we're not trying to add -- we're not trying to do a study that's just focusing on one disorder, but on multiple disorders. And we're funded by many different sources.

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DON BAILEY: So what is Early Check? First of all, it's an Innovation Award from the National Center for Advancing Translational Science. We received this a number of years ago. These awards are designed to help break a barrier in translational science, translational medicine. With additional support from NICHD, the John Merck Fund, Asuragen, Cure SMA, and the Muscular Dystrophy Association, and Sarepta.

So it's a research study designed to develop and evaluate methods to offer free, voluntary screening to all birthing parents in North Carolina for conditions that are currently not part of newborn screening. So this is a statewide project.

And we started with spinal musuclar atrophy and fragile X syndrome as initial prototypes. SMA was not on the RUSP when we started this, and North Carolina was not screening for it. So it became a good prototype for us. And fragile X syndrome, as Cindy mentioned, is a disorder that I've studied quite a bit.

And these are great examples of a little bit of the ends of the continuum in terms of urgency of treatment.

We added Duchenne muscular dystrophy and CKMM screening in 2019, and we were able to transition SMA off of the Early Check panel earlier this year once it was picked up by North Carolina as a part of North Carolina's newborn screening program.

So we're also designed to acquire data to inform policy. And our hope is that this is a long-term research resource to which new conditions can be added when ready. And an envisioned future in which states may be good to offer a volunary panel of non-RUSP conditions. That's something way out in the future, but it's part of what we're interested in examining.

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DON BAILEY: So here's a quick overview of the Early Check flow. And I'll talk about some details about this in a few minutes.

Our recruitment, we start with the recruitment just as Dr. Wassestein does. Our recruitment is all virtual. We have multi-phase public outreach to every parent in North Carolina. We have an e-consent portal for online permission.

For parents who consent, we have our own lab on the RTI campus where we do the screening tests using the dried blood spot that the state has already collected. So we consent to access that dried blood spot.

If it's a negative result, parents can get that information through their own personal patient portal. If it's a positive result, a genetic counselor immediately calls the family and then refers them for a confirmatory testing and diagnosis. And then our team establishes a registry and conducts follow-up assessments, and we provide surveillance and support and information about interventions that are in existence.

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DON BAILEY: So some of the unique features of Early Check are that we are, first of all, a multi-institutional partnership integrated with public health and newborn screening. So as you can see from this figure, RTI is -- we really coordinate everything, but is in partnership with local universities, UNC-Chapel Hill, Duke University, Wake Forest, Baptist Medical Center, and the North Carolina State Laboratory of Public Health.

So, full disclosure. Dr. Powell is our primary collaborator from UNC-Chapel Hill, and Dr. Shone from the North Carolina State Laboratory of Public Health.

Something we've done a lot of is systematic formative work, trying to understand what parents want and how we can develop materials and processes that really work for families. We use and evaluate virtual strategies for multiple system components. I'll describe that in just a minute.

We have a two-tiered consent for carrier

results, fragile X syndrome and fragile X carriers status. And that two-tiered process is going to serve us very well as we move into the future, as I'll mention shortly.

We use methods other than tandem mass. We're not using tandem mass at all in our laboratories. So we're screening for using genetic screening in a variety of different ways to identify these disorders.

We feel like it's important for us to publish about our laboratory methods, as well as our other findings and work. We have pretty sophisticated systems for tracking and evaluating everything from consent to follow-up. And I won't be addressing this today, but we've designed an early intervention program and systematically studying its effectiveness for children with fragile X syndrome.

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DON BAILEY: So as I mentioned, we've done lots of formative work. We've published

papers here, for example, initially on parental intentions to enroll children in a voluntary expanded newborn screening program. We also did a discrete-choice experiment in which we looked at parent preferences in this case, for genomic sequencing, but for non-medically actionable conditions.

And then these photos and some of the words associated with them display some of the formative work we did in our social media campaign with Facebook and Instagram and Pinterest. We looked at what kinds of words, what kinds of messages, and what kinds of photos most resonated with our target population?

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DON BAILEY: So we use and evaluate virtual strategies for multiple system components. We have virtual recruitment. We have e-consent. We have telegenetic counseling. We have family-friendly web-based educational materials. And when necessary, we do virtual asessment and

organize a virtual intervention program.

As a result of these virtual strategies, we've really been able to continue the project since 2018, during the COVID-19, without any disruption. And in fact, we had an uptick in recruitment since COVID-19 came into the United States last year.

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DON BAILEY: So we have been systematically examining different virtual recruitment methods. You know, we know from -- we've seen Dr. Wasserstein's earlier paper and are familiar with what she's doing now in terms of in-person consent in hospitals. We also have conducted our own pilot study with fragile X syndrome a number of years ago.

And also, I think we've got a 67 or 68 percent recruitment rate. So we know that in-person recruitment works. We also know it's very expensive. And we don't have the size hospitals in North Carolina that you have in New York. So

we've been testing our virtual recruitment strategies to see what we can get.

So we started a postnatal letter and an email. This letter is actually on the state, on North Carolina State Department of Public Health letterhead, and it's signed by the state's Chief Medical Officer. It's sent out within a week of birth, inviting parents to go to our website and think about it, and enroll in Early Check.

We've also been engaging in a series of social media campaigns. I'll give a brief synopsis of that in a minute. We have information in health care setting and the WIC programs in North Carolina. And we've been testing out models for inviting parents, or mothers, to participate in Early Check through MyChart patient portals. We've been doing that systemically at UNC and Duke and hope to start that at Wake Forest sometime this year.

We have done some small in-person recruitment, testing at Duke and at the University of North Carolina, started that earlier this year.

But our primary focus remains on virtual recruitment methods.

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DON BAILEY: So we've been pretty systemactic about evaluting and publishing about each of those methods. Two papers that are out already, one is "Outreach to New Mothers Through Direct Mail and Email: Recruitment." We had an early paper on "Using Social Media to Conduct Outreach and Recruitment for Expanded Newborn Screening."

We've got a MyChart recruitment paper that's under review right now. It's been returned with minor revisions requested, and we've resubmitted that. We're working on a greatly expanded social media paper. And we're beginning soon a phone and text, and hopefully text, reminder study.

So this is our last bit effort to see what we can get through virtual recruitment by calling parents a couple of weeks after birth to

say that we've sent you a letter, and just reminding them that you have a defined period of time to sign up for the study. And that's going to begin soon.

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DON BAILEY: So since we began in 2018, we've enrolled more than 18,000 individuals in the study. So this map shows the distribution across North Carolina. The dense areas, as you can imagine, relate to our larger cities, so the Charlotte area, the triangle area, Greensboro area, Asheville.

Consents have come from every birthing hospital in the state, and 99 percent of our 100 counties -- there's one county up in the northeast, Gates County, where there are only a few people living there. And so we haven't gotten any consents from there.

We have a few from South Carolina, but these are mothers who have given birth in North Carolina, primarily in the Charlotte Hospital. So

they would still be screened by the North Carolina lab.

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DON BAILEY: This is our Early Check consents by month. So we have the dark-blue line is the postnatal consent, primarily through letters. And the light-blue line is the prenatal consent through MyChart invitations and social media.

You can see that starting in -- you know, CDC first said COVID-19 was here in January of 2020. You can see that actually our recruitment rate has either remained stable or gone up since there. We had a little dip during the election last fall. I think people were distracted by other things in the media. But otherwise, so we're around 500 to over 600 consents per month.

So we've got a pretty good estimate now of what we can do virtually. Like I said, our last test will be through phone and text reminders. You know, we're hoping that that will

elevate the consent rate more. We did find that a postcard reminder did not, but we think it's because mail right after birth is just not something people pay very much attention to.

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DON BAILEY: People always ask us about the racial and ethnic distribution of our sample because it is a virtual recruitment sample. So these are data from the people who have signed up. Seven percent don't answer the question when we ask them to disclose race/ethnicity. And the rest of them are, we have a study percentage and then the percentage from the North Carolina 2020 Census.

So our white non-Hispanic sample is actually lower than the 63 percent in North Carolina. Hispanic only is, because we asked for race and ethnicity, is right at about the same percentage as the North Carolina Census.

African American only is only 6 percent compared to our 22 percent population in North

Carolina. Asian-only is higher than the North Carolina Census. Then other or mixed is 12 percent. It's been very interesting, the various combinations we've seen.

The 6 in parentheses is those who said they were African American plus something else. So if you add those two together, we get 12 percent African American, or African American plus something else. But we're still working on strageties to increase our African American respondents. But as you can see, we do still have and feel good about the diversity that we have in our sample.

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DON BAILEY: We have electronic consent process, so the big picture on the right-hand side shows the portion that you go to on a website. "Welcome to Early Check! Let's get started." And on the left-hand side, just trying to show you that we can access it through any device, through your cell phone, through a mobile app, through an

app, and so forth.

So it's a pretty easy and workable system. And as you can see from the picture on the right, you have short white-board videos that we've developed. This one is about What is Early Check? And these are simple, short, one minute or a little bit more, videos on various aspects of the project.

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DON BAILEY: We have telegenetic counseling for return of screening results. This is an option for parents. We do of course provide in-person genetic counseling after families come in for diagnostic confirmation.

This technology has turned out to work really well. It's HIPAA-compliant. Multiple -- both parents can join on, an interpreter if needed. There's screen sharing. We can show documents. It's very convenient, easy to use, reminder scheduling. And so far, parents seem to be really at ease with using the online meeting

platform at home, and especially while the baby sleeps nearby.

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DON BAILEY: We also have quite a bit of educational web content about each of the disorders. So we have graphics showing various aspects of different disorders as you can see in the movement here. And depending on the question that you have, this is one for parents of the children with fragile X premutation. They can go to different links within our website to learn more.

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DON BAILEY: So we are studying and publishing about our various laboratory methods. So we had a pilot study, a task order program funded by NICHD. And so we did publish our laboratory method with MPS I and for XLD. We have published on the fragile X screening and our SMA screening pilot.

And as we finish gathering data over the next year or so with the Duchenne pilot, we'll be gathering that kind of data as well -- publishing those kind of data as well.

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DON BAILEY: We have very comprehensive data systems. Scott Shone helped us develop a flowchart like this early on, and we've modified it considerably throughout. I won't be going through this as to this slide except to say that the red line shows that we have a virtual firewall between the state lab and our secure network, and mechanisms for going back and forth with data, both within the state lab system and with our own systems that have maintained a high degree of security across everything that we do.

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DON BAILEY: We also pay attention to our social media. And this is the example of our monthly social media report. We can see how much

we're spending for Facebook and Instagram. This was a month that we did a test of Pinterest, how much we spent there. We can show how many eligible people looked at it, how many in all at each mechanism, how many signed up using each.

We can generate cost, a cost per eligible person and a cost per sign-in. We try to use -- every month we do a lot of work on evaluating where we are with things.

Next slide, please.

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DON BAILEY: We've also developed two very, very helpful in-house systems. One is called our Early Check Follow-up Tracker. So this is a visual interface that we just recently developed with the functionality to import and input data and track individual progress data. So it's an automatic data import from multiple sources. And we can daily track and document participant status.

And then in our Early Check Dashboard, we visualize currently Early Check status and

aggregated data on consent counts and so forth.

I'm almost finished. Next slide, please.

(Slide)

DON BAILEY: For future disorders, as you can tell, we've been using one disorder at a time. So our goal now is to move from one disorder at a time to multiplexing a large number of disorders.

We recently received a planning grant to start looking at chromosome 15 disorders, angelman, Prader-Willi, and dup 15q. These can all be multiplexed using a platform that a collaborator has developed. So we're working on how to do that.

We've also received a planning grant to plan a very large targeted sequencing panel. We're working with colleagues at the University of North Carolina. And hopefully, that will be fully funded and we can start that this coming year.

Again we're developing flexible systems just like ScreenPlus so that we can respond quickly to either newly nominated conditions and especially now to new transformative therapies so

that, as conditions are ready for testing, we can move quickly into that.

I think that's my last slide.

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DON BAILEY: Oh, I just wanted to acknowledge the Early Check team. We've got a great group of collaborators and partners. Our team members within RTI who have helped on a variety of different aspects of the project.

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DON BAILEY: We're also really grateful to our Early Check partners. Of course, Dr. Powell is at UNC, Dr. Cotton at Duke. Dr. Eddie Smith facilitates our Duchenne work at Duke. Dr. Nancy King is a bioethicist at Wake Forest. And Dr. Scott Shone is at North Carolina State Lab.

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DON BAILEY: And this is my contact information. And I think we can stop now and turn

it over for questions.

QUESTIONS AND COMMENTS

CYNTHIA POWELL: Thanks very much, Dr. Bailey, for your presentation. We do have time for some questions and comments. And we'll first take those from Committee Members, followed by our organizational representatives.

We'll give everyone a minute or so to raise their hand.

(Pause)

Melissa Parisi.

MELISSA PARISI: Thank you. This is Melissa Parisi from NIH. And I just want to thank both of you for your presentations. Really phenomenal, and a really nice way to see partnerships and ways to leverage resources from a lot of different directions to try to successfully bring together some of these really challenging-to-do pilots.

I have a question for, I guess you both, about social media and your use of social media approaches, which I think is very creative and

certainly the wave of the future. In both of your cases, do you have access to the individual-level information for the families of the newborns?

Such that you have a cell phone number and/or you must have email and some sort of address information that you've been given from the birthing hospitals. But I'm just curious about how that actually works in terms of targeted outreach using social media.

DON BAILEY: Well, I can start. We don't do targeted outreach through social media. This is more of an algorithm approach, like as the different social media companies would do.

So they sort and we have recruitment criteria that we would be using in terms of age and, you know, various other filtering mechanisms that they use.

But we don't -- none of our social media outreach is to individuals with contact information that we have.

Now, our phone and text reminders, our letters, our patient portal information, now

that's all individualized, we get those data from a variety of sources, from either the hospitals or from the lab, the newborn screening card.

MELISSA WASSERSTEIN: Again, we're doing inpatient recruitment. So we get a list of all of the babies who have been born. If we miss them for our passive recruitment method after they've been discharged, we do actually have email addresses and contact information. But that would be direct. It's not social media based.

So we do have this HIPPA waiver where we can do that, but again our social media is really just touting the program and not to help with recruiting at this point.

MELISSA PARISI: Thank you.

CYNTHIA POWELL: Shawn McCandless.

SHAWN McCANDLESS: Shawn McCandless, a Committee Member.

Yes. Thank you both. Those were really fascinating projects and both excellent projects. I want to thank you for having this foresight to

think about how we can ease the ability to collect data for new potential conditions to add to the RUSP.

I have a question that's probably primarily for Dr. Bailey, but maybe Dr. Wasserstein can comment also. The question, Don, was, for the percent, do you have a sense of percent of births that you're actually reaching? And you must have. You have numbers that you can compare to the birth rates in North Carolina.

So I'm curious about sort of if you could compare the online enrollment rate, the online recruitment enrollment rate to the in-person recruitment rate.

And then the second question is that you had -- if I remember from one of your slides, it looked like the cost based on the cost of this advertising on social media was right around $120 to $150 per successful recruitment. And I wonder if you have a way to compare that cost to the cost of in-person recruitment?

And then the third question is if the two

of you plan to get together to sort of compare from the parental perspective, if you have a plan to follow up the way that Dr. Wasserstein's group does, in particular with down the road, the parents' perceptions of the process and their satisfaction with the process?

Sorry, that's a lot. I apologize.

DON BAILEY: You're challenging my memory, Shawn, to remember all these questions. But I'll try.

So first the cost, or the percentage. So North Carolina has about 120,000 births a year. We're getting a little over 600 now per month, so in the 6 percent range. So, you know, that's not anywhere near what Dr. Wasserstein is getting from her project. But again, one of our major goals for this effort has been to test out different strategies.

You know, it's ultimately going to depend on what questions we want to ask. And if we want to look at natural history of a disorder that occurs in 1 in 100,000, you know, we're never

going to answer that in my lifetime using this.

But if we want to test our laboratory methods, you know, one of the things we do is set up statewide follow-up procedures for every disorder, because we have to anticipate on day one, and we might find someone in the mountains or on the coast. So it's a lot of systems-level work and evaluation work.

So cost varies considerably by method. So mailing out the letter, you can add postage to that. And 120,000 letters a year, I figure it's about a dollar a letter to send. We have a mail center we have at RTI. So we can send all those out.

Patient portals has turned out to be quite cheap. You know, we work with the hospital systems. It takes a while to get it set up. But once it's set up, it's a process that really gets pushed every few weeks to eligible mothers.

Social media, we do get some bang for the buck, but not a lot. And so I think if we gave up one of our strategies, that would probably be one.

We're hoping that -- the phone reminders are going to be expensive. And so, we'd like to be able to do the text reminder. We're still trying to get that through the IRB.

And your third question? Oh, about collaboration with each other. So we have had a number of conversations about that. We don't have any overlap in the disorders that we're screening for or in the methods that we're using. And so, we actually had planned an in-person meeting. And then COVID-19 hit and we had to cancel that meeting.

We've taken, I think, divergent paths and focused on the various funding sources and so forht. But we are conceptually and personally committed to collaboration. I think ultimately, Shawn, this is really where we have to go as a nation, where there's got to be -- none of us is going to ever collect enough data to answer the questions that we need to answer.

But there's just no mechanism. There's no data -- the feds need to just preach on this.

And you need to fund data-coordinating centers that help pull all of these data together in a systematic way. I know that there's some of that work going on already. But it's got to be research-question-driven.

Melissa, do you want to add something to that?

MELISSA WASSERSTEIN: Yeah. I can't agree with you more, Don. I do think that as Shawn mentioned, we have programs running in parallel. But I do think that each program presents a recruitment method that's unique. And I frankly think that, although the in-person recruitment and screening costs might get a higher hit, I think that the Early Check program is probably more sustainable in the long term.

So I think that there's value that is essential to expanding our knowledge about how these pilot programs might work and how the disorders might work. But I think they're complementary, and our shared experiences will maybe find the optimal path going forward.

CYNTHIA POWELL: Thank you.

Georgianne Arnold.

GEORGIANNE ARNOLD. Okay. I would like to say Bravo! Melissa, I am jealous. I wish I'd thought of this myself. The only thing I can say is, subject who decline and fill out the survey, I think they are still going to have to be consented as research subjects, are they not?

MELISSA WASSERSTEIN: Yeah, if they're declining, that's a really good question. So we are collecting information, but it's de-identified for the decliners. So we're trying to make it -- and they have no records, so we won't be able to track it back to them. It's a two-second three-question or four-question survey. So they're not being consented for decliner information again, because it's non-trackable, non-identifiable. It's a great question.

GEORGIANNE ARNOLD: I spoke at the Orphan Drug Conference last summer, and there was, I would say, a significant lack of appreciation from some of the pharma representatives on, once there

was an enzyme replacement therapy, why we couldn't just add this to the newborn screening.

And, you know, this actually I think is a wonderful way to address that problem. Things can be tested out in a consented manner. And I wish we'd thought of it 16 years ago in New York.

(Laughter)

GEORGIANNE ARNOLD: But I'm jealous. Thank you.

CYNTHIA POWELL: Thank you.

Natasha Bonhomme.

NATASHA BONHOMME: Natasha Bonhomme, org rep for Genetic Alliance.

Great presentations. I have two questions. The first one to Dr. Bailey.

Can anyone involved in Early Check participate in the telegenetics sessions? Or is that really targeted toward those who have an out-of-range or something happens?

DON BAILEY: Well, the screening-positive cases, of course, yeah. But for any of the disorders that's the first mechanism for phone

calls, the first mechanism for informing them about a screen-positive case.

Then after that, it really depends on the nature of the disorder, how quickly we need to get them in. And, you know, for SMA it's an emergency and we have to get them in very quickly. But for fragile X, it's not such an emergency and we can offer more -- "leisurely" is not the right word, but it's a less time-sensitive disorder.

So we're using a combination of approaches with that.

NATASHA BONHOMME: Great. And then my other question is for both presenters. I think all of the discussion that you presented around recruitment and communication is really great and really helpful, and very helpful to see the costs behind that and what you get and what you don't get.

But one question I had was, you know, this communication and the communication that goes along with recruitment that you've both done around this research project. Has that had any

impact or effect on the general communication, education around public health and newborn screening?

I think sometimes people think, "Oh, if you do that, then people will get confused." I don't know if you're testing for that or asking your participants if they understand the difference between public health newborn screening and the research program that they're enrolled in. Or maybe that's not deemed that important, that distinction.

Just kind of any information about that would be helpful. Thanks.

MELISSA WASSERSTEIN: I'm going to start then if that's okay.

DON BAILEY: Great. Yeah.

MELISSA WASSERSTEIN: So for our first pilot screen that implemented in 2011 to 2017 that was focused just on lysosomal storage disorders, we enrolled about 65,000 babies for those. And one of our big concerns, Natasha, was that we would lose babies, that once parents became aware

of newborn screening, they would opt out of general newborn screening. And that was a concern.

But it turns out that there was absolutely no change in any of our pilot hospitals. So they were informed about newborn screening. Our script does differentiate, the script that our recruiters use, between routine newborn screening, which is what we're following, the state-funded screening, versus our ScreenPlus screening.

So they're aware of the difference, but nobody opted out of the other, which is great.

DON BAILEY: Yeah. We make it clear in our recruitment that this is separate from regular newborn screening. But, I know Scott can answer this question--we've not seen any reduction in refusals of regular newborn screening as a result of this project. And even from our earlier fragile X pilot study many years ago, we didn't see that either.

CYNTHIA POWELL: Let me just check.

Melissa Parisi, did you have another question or had your hand still raised? I don't want to overlook you.

MELISSA PARISI: I forgot to lower it. I apologize.

CYNTHIA POWELL: Okay. Thank you. All right.

Debra Freedenberg.

DEBRA FREEDENBERG: So my question really is sort of about outcomes. I know you focus in on recruitment and systematic design of these studies. So, Melissa's project may still be a little bit early since she just started recruiting really in May, hasn't started implementing that.

But my question is, When you see this sample population that has consented, are you finding some regret from parents who wish they had not known even though they consented? And are you finding the incidents to be about what is expected for the condition you check -- you know, the standard incidence numbers right now?

MELISSA WASSERSTEIN: So, I don't have

the data yet from ScreenPlus. We just haven't had any positives yet.

We actually did a similar ELSI study for the earlier pilot screen that I had mentioned before. And we weren't really focusing on decisional regret, but we were asking about stress and anxiety. But there is always concern if we're picking up later onset lysosomal storage disorders in the population, is there more anxiety and stress for parents sitting and watching and waiting?

And we are in the process of writing up that manuscript since we have a great data analyst now. And it looks at if, honestly, as if parents have less stress and less anxiety when these disorders are detected through newborn screening versus having a diagnosis for clinical purposes, or actually even a diagnosis of the different routine RUSP, you know, PKU type newborn screening results.

So I can't assume that that's decisional regret or lack of decisional regret. But those

are actually very positive outcomes so far that come from the data that we have. So there will be a lot more, hopefully, to follow, in the next series of questions.

DON BAILEY: I mean, I think that's similar for us as well. We published a paper after our first fragile X newborn screening where we did return carrier status as a part of that. We did a follow-up on maternal stress, anxiety, postpartum depression, quality of life, and so forth. And we found no -- and we compared with families who participated, but had a negative screen. And we didn't find any differences there.

So in qualitative interviews, you find sometimes short-term -- this is very natural -- people are wondering why they did this or questioning it. But over the long haul, we've not seen any kind of longitutinal kind of negative effects.

I think, you know, it's very hard to answer, and Dr. Wasserstein alluded to this. It's very hard to compare parents who got data through

this project to those who had to go through a diagnostic odyssey. These parents will never know what the diagnostic odyssey was like. And so you can't really ask them, you -- it can't be family comparisons.

And we know that the diagnostic odyssey for most disorders is long. It's complicated. It's frustrating. It's costly. It's something people hate going through. And so -- but it's a complicated question to kind of answer. But to me it's kind of obvious, and especially if we don't get adverse reactions.

DEBRA FREEDENBERG: Thank you so much.

CYNTHIA POWELL: Well, let me thank both Dr. Wasserstein and Dr. Bailey for your very informative presentations today before the Committee. We appreciate all of the work that you're doing. And I look forward to updates in the future as they develop.

DON BAILEY: Thank you for the opportunity to present.

MELISSA WASSERSTEIN: Thank you.

NEW BUSINESS

CYNTHIA POWELL: Do Committee Members have any new business or announcements before we adjourn?

(No audible response)

ADJOURN

CYNTHIA POWELL: Hearing none, I want to remind everyone that the next ACHDNC meeting will take place on February 10th through 11th, 2022 via webinar. For a full list of meeting dates through 2025, please visit the Committee's website.

The November Meeting of the Advisory Committee on Heritable Disorders in Newborns and Children is now adjourned.

Thank you all. Take care.

(Whereupon, the meeting concluded.)