US DEPARTMENT OF HEALTH AND HUMAN SERVICES

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HEALTH RESOURCES AND SERVICE ADMINISTRATION

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THE ADVISORY COMMITTEE ON HERITABLE DISORDERS IN NEWBORNS AND CHILDREN

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MEETING

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THURSDAY
FEBRUARY 11, 2016

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The Committee met in Conference Room E in the Natcher Conference Center at the headquarters of the National Institutes of Health, 9000 Rockville Pike, Bethesda, Maryland, at 9:00 a.m., Joseph A. Bocchini, Jr., Chair, presiding.

PRESENT

JOSEPH A. BOCCHINI, JR., M.D., Professor and Chairman, Department of Pediatrics, Louisiana State University Health Sciences Center in Shreveport, Chair
DON BAILEY, Ph.D., M.Ed., Distinguished Fellow, Early Childhood Development, RTI International
JEFFREY BOTKIN, M.D., M.P.H., Professor of Pediatrics and Medical Ethics, Associate

Vice President for Research, University of Utah

PRESENT (CONT.)

CARLA CUTHBERT, Ph.D., Centers for Disease Control and Prevention, ex officio
KELLIE B. KELM, Ph.D., Food and Drug Administration, ex officio
DIETRICH MATERN, M.D., Ph.D., Professor of Laboratory Medicine, Medical Genetics and Pediatrics, Mayo Clinic
STEPHEN McDONOUGH, M.D., Sanford Health Bismarck
KAMILA B. MISTRY, Ph.D., M.P.H., Agency for Healthcare Research and Quality, ex officio
JOAN A. SCOTT, M.S., C.G.C., Health Resources and Services Administration, ex officio
CATHERINE Y. SPONG, M.D., National Institutes of Health, ex officio
TIINA URV, Ph.D., National Institutes of Health, ex officio
CATHERINE A. L. WICKLUND, M.S., C.G.C., Northwestern University Feinberg School of Medicine, Center for Genetic Medicine

ALSO PRESENT

DEBI SARKAR, M.P.H., Health Resources and Services Administration, Designated Federal Official
DEBBIE BADAWI, M.D., Association of Maternal & Child Health Programs
SUSAN BERRY, M.D., University of Minnesota
JOSEPH R. BIGGIO, JR., M.D., American College of Obstetricians and Gynecologists
NATASHA F. BONHOMME, Genetic Alliance
AMY BROWER, Ph.D., American College of Medical Genetics and Genomics
ANNE COMEAU, Ph.D., UMass Medical Center
CAROL GREENE, M.D., Society for Inherited Metabolic Disorders
LISA FEUCHTBAUM, DrPH, M.P.H., California Department of Public Health
ADAM KANIS, M.D., Department of Defense
EDWARD R. B. McCABE, M.D., Ph.D., March of Dimes
JON MILLER, Network of Tyrosinemia Advocates
ROBERT OSTRANDER, M.D., American Academy of Family Physicians
DEAN SUHR, MLD Foundation
SUSAN M. TANKSLEY, Ph.D., Association of Public Health Laboratories
BETH TARINI, M.D., M.S., FAAP, American Academy of Pediatrics
CATE WALSH VOCKLEY, M.S., National Society of

Genetic Counselors
MICHAEL S. WATSON, Ph.D., FACMG, American College
of Medical Genetics and Genomics

C-O-N-T-E-N-T-S

P-R-O-C-E-E-D-I-N-G-S

(9:05 a.m.)

CHAIR BOCCHINI: Thank you. Good morning, everyone, and welcome to the February meeting of the Advisory Committee on Heritable Disorders in Newborns and Children. I want to thank you all for coming and welcome you to the meeting.

I want to remind the committee I brought some beads, a Louisiana tradition, to celebrate Mardi Gras. And it's kind of, in Louisiana, this is called a lagniappe where you get a little something extra for showing up. So thank you for coming.

Before we get into the committee related work, I'd like Debi to give us some information related to how to use the microphones and how to work the webinar.

MS. SARKAR: Hi there. Good morning, everyone. I'm really glad that everyone is here in person. So just real quick, today's meeting is going to be webcasted. I think the last time we

had close to 100 participants.

So I'm going to ask you if you would like to speak, please turn on your microphone so that people can hear you out on the Web. And we also have a transcriptionist on site to help record the meeting procedures, so he needs to be able to hear. So please turn on your microphones to speak.

Also, I say this every meeting, and I'll say it again. Please remember to state your name before speaking. Like I said, we have a lot of folks on the webcast, including my mother, who will be watching, so please tell us who you are. Thank you.

CHAIR BOCCHINI: All right. Thank you. So let's go ahead and take roll. First, Don Bailey.

MEMBER BAILEY: Here.

CHAIR BOCCHINI: I'm here. Jeff Botkin?

MEMBER BOTKIN: Here.

CHAIR BOCCHINI: Carla Cuthbert?

DR. CUTHBERT: Here.

CHAIR BOCCHINI: Tiina Urv?

DR. URV: Here.

CHAIR BOCCHINI: Kellie Kelm?

DR. KELM: Here.

CHAIR BOCCHINI: Okay. Fred Lorey is attempting to call in by phone. Okay. Dietrich Matern?

MEMBER MATERN: Here.

CHAIR BOCCHINI: Steve McDonough?

MEMBER MCDONOUGH: Here.

CHAIR BOCCHINI: Kamila Mistry?

CHAIR SIEGEL: Here.

CHAIR BOCCHINI: And Joan Scott representing Michael Lu this morning?

MS. SCOTT: Here.

CHAIR BOCCHINI: Cathy Wicklund?

MEMBER WICKLUND: Here.

CHAIR BOCCHINI: And our DFO, Debi Sarkar?

MS. SARKAR: Here.

CHAIR BOCCHINI: And now our organizational representatives. Representing

the American Academy of Family Physicians, Robert Ostrander?

DR. OSTRANDER: Here.

CHAIR BOCCHINI: American Academy of Pediatrics, Beth Tarini?

DR. TARINI: Here.

CHAIR BOCCHINI: American College of Medical Genetics, Michael Watson?

DR. WATSON: Here.

CHAIR BOCCHINI: American College of Obstetricians and Gynecologists, Joseph Biggio by phone?

MR. BIGGIO: Here.

CHAIR BOCCHINI: Thank you. Association of Maternal and Child Health Programs, Debbie Badawi?

DR. BADAWI: Here.

CHAIR BOCCHINI: Association of Public Health Laboratories, Susan Tanksley?

DR. TANKSLEY: Here.

CHAIR BOCCHINI: Chris Kus? All right. He should be here soon on the phone. And

then Department of Defense, Adam Kanis?

DR. KANIS: Here.

CHAIR BOCCHINI: Thank you. Genetic Alliance, Natasha Bonhomme?

MS. BONHOMME: Here.

CHAIR BOCCHINI: March of Dimes, Ed McCabe by phone?

DR. McCABE: I'm here.

CHAIR BOCCHINI: Thank you, Ed. National Society of Genetic Counselors, Cate Walsh Vockley?

DR. VOCKLEY: Here.

CHAIR BOCCHINI: And the Society for Inherited Metabolic Disorders, Carol Greene?

DR. GREENE: Here.

CHAIR BOCCHINI: Thank you all very much. So I'm going to go through a few slides for, to go through the business. As you saw within the agenda book, we have listed correspondence with the Secretary.

As you know, the MPS I recommendations are currently under review. Our ALD

recommendations are also under review. We sent a letter to the Secretary on the newborn screening, informed consent recommendations.

We received a response from the Secretary, and the Secretary did accept the committee's recommendation number five, which was to create an distribute targeted materials on the importance of newborn screening, options for parents to participate in newborn screening research.

To support this recommendation, she has asked the Centers for Disease Control and Prevention to work with states, the Health Resources Services Administration, the U.S. Food and Drug Administration and the Assistant Secretary for Health, Office for Human Research Protection, to accomplish this.

These HHS divisions will work together with states to develop guidance and education material on these issues. Although she did not adopt recommendations one through four, she did move them on to OHRP.

The response we received was that, to ensure fairness and appropriate feedback from all stakeholders, the Assistant Secretary for Health Office for Human Resource Protection is not partnering directly with states or other newborn screening stakeholders.

But she asked that they consult with the states, as necessary, to develop guidance in the areas specified in these four recommendations.

And she also did not adopt recommendation number six that asked for federal funding for states to conduct translational research activities, but she will encourage HHS agencies to take opportunities to use discretionary funding to fund research as they are able.

We did also submit comments for the NPRM on federal policy for the protection of human subjects, as discussed at our last meeting. So next on the agenda is, oh, Don?

MEMBER BAILEY: Well, I was just going to ask a question about the Secretary's response

to our letter. So most of the recommendations were not accepted.

And I'm just wondering do you see this as a statement that what we were doing is really not under the purview of our committee, that they were -- that she disagreed with our recommendations or she felt that they were best handled in another venue?

CHAIR BOCCHINI: I felt that what it represented was that OHRP was working on this and that was where the effort was being made and that this information was brought to them related to our concerns and what we brought up for them to review and then to address, but that this was not under her purview to address. Dietrich?

MEMBER MATERN: Dietrich Matern. I probably should know this, but what about this 120 day rule that the Secretary has to make a decision about our recommendations to add a condition? I thought that X-ALD fell under that rule.

CHAIR BOCCHINI: For both of the conditions, she has turned them over to the

Interagency Coordinating Committee. No? Go ahead.

MS. SARKAR: So MPS-I was voted under the discretionary committee charter, so the 120 day rule does not apply for that. For X-ALD, it does, and so we should be hearing very shortly what her decision will be.

CHAIR BOCCHINI: Other questions, comments? Okay. So the next item is the approval of minutes of our November meeting. These minutes were distributed with the agenda book. Are there any additions or corrections to be made to the minutes as they were distributed? If there are none, I will accept a motion to approve as they were submitted.

MEMBER BOTKIN: So moved.

CHAIR BOCCHINI: All right, by Dr. Botkin. Is there a second?

MEMBER BAILEY: Yes. Don Bailey, second.

CHAIR BOCCHINI: All right. So it's been moved and seconded. So now we will do a vote.

I just need to know where I put my votes. There's my votes. Okay. All right. So, thank you.

So this is a motion to approve the minutes. Don Bailey?

MEMBER BAILEY: Approve.

CHAIR BOCCHINI: I approve. Jeff Botkin?

MEMBER BOTKIN: Approve.

CHAIR BOCCHINI: Carla Cuthbert?

DR. CUTHBERT: Approve.

CHAIR BOCCHINI: Tiina Urv?

DR. URV: Approve.

CHAIR BOCCHINI: Kellie Kelm?

DR. KELM: Approve.

CHAIR BOCCHINI: And then Fred Lorey, if he's available by phone. Dietrich Matern?

MEMBER MATERN: Approve.

CHAIR BOCCHINI: Steve McDonough?

MEMBER MCDONOUGH: Approve.

CHAIR BOCCHINI: Kamila Mistry?

DR. MISTRY: Approve.

CHAIR BOCCHINI: Joan Scott?

MS. SCOTT: Approve.

CHAIR BOCCHINI: And Cathy Wicklund?

MEMBER WICKLUND: Approve.

CHAIR BOCCHINI: Okay. The minutes are approved as distributed. So next is just to remind us of where we are and what we plan to achieve at this meeting.

Our subcommittees are ready to begin to meet to discuss priorities and potential projects on which the Advisory Committee should focus. So this afternoon, these projects will be proposed, discussed, finalized and brought to the full committee.

Tomorrow, the full committee will then look at them and again prioritize and give feedback to the subcommittees as to how to proceed. Our goal, obviously, is to address the needs and gaps that there are within the scope of work of our Advisory Committee which do not duplicate other ongoing activities.

For other priorities, we are going to, our workgroups that we established to address

issues related to our new charter met yesterday. And we will get additional reports from them, and we are coming towards the closure of two of these workgroups.

One is the Pilot Study Workgroup, and the second is the Cost Analysis Workgroup. And for both of these workgroups, their charge was to determine the essential elements for nomination of a condition so that we could move the committee to a position where we'd be able to meet the nine month deadline with the committee work plus evidence review.

And then we have a third workgroup, the Timeliness Workgroup, which continues to address issues for timeliness of receipt and then testing of newborn specimens.

MS. SARKAR: This is Debi Sarkar. Just to clarify, the workgroups will meet later this afternoon.

(Off microphone comment.)

MS. SARKAR: Yes.

CHAIR BOCCHINI: Sorry about that.

MS. SARKAR: They did not meet. They will meet.

CHAIR BOCCHINI: Oh, okay.

MS. SARKAR: And we'll get updates from them tomorrow.

CHAIR BOCCHINI: Okay. Sorry about that. I thought that sounded strange. Okay. All right. Then, just moving forward, just to remind you that there are four meetings scheduled for this coming year.

Today was our first. We have our second meeting scheduled for May 9th and 10th. It'll again be an in-person and webcast meeting. And then tentatively we have July 25, 26 and November 3rd and 4th for our final meetings of the year.

I want to just mention two things. As you know, we did increase the number of organizational representatives for the committee. We have not received any additional applications to become organizational representative to the committee.

So we want to again remind people that we do have three vacant spots, and we would like to accept proposals for people to join as organizational representatives. If there is a group that's interested, Debi can receive a call from them or correspondence from them, and we can move forward with that.

Since we haven't received any committee, anybody coming forward, we will post this on the Advisory Committee's website to make more people aware that the positions are available.

In addition, as you know, we are reaching a point where we have two committee members who will be rotating off at probably the end of June, depending on whether we hear about the new members that we hope to appoint.

And so that may happen as early as June with a transition in July. As for 2017, we'll have three additional members who will be rotating off the committee.

And so very soon we will put up a call for applicants to fill those three positions for

2017. And we hope those people who did apply who were not selected, because we have a large group of applicants for the open positions, would be willing to reapply for open spots for the following year.

So our meeting topics for, oh, I'm sorry.

MS. BONHOMME: Hi. This is Natasha Bonhomme. On that, does that mean by the June or July meeting that, or no May, sorry, that there will be a consumer representative on the committee? Will that person have come on by that point in case there are any votes?

CHAIR BOCCHINI: The, I guess the new positions really become part of the committee in July, so, but Debi, did you want to --

MS. SARKAR: So we're hoping that the new members will join at the August meeting.

CHAIR BOCCHINI: First will be August.

MS. BONHOMME: Okay. So there won't be a consumer rep vote at that point?

MS. SARKAR: If we find out before,

then they will join, but the two members we have currently, their terms end in July. So we have two openings right now --

MS. BONHOMME: Right.

MS. SARKAR: -- and two members rotating off in July, so there is a possibility if we find out from the Department who the consumer person is, then they could potentially start earlier.

MS. BONHOMME: Okay. Thanks.

CHAIR BOCCHINI: All right. Other comments? So for this morning we have on the agenda a panel of experts on newborn screening long-term follow-up. So we can begin a discussion of where we are and what we need potentially to do going forward.

We'll have the projects from the subcommittees proposed, and then four of the subcommittees from the full committee and then summaries of the workgroup meetings. Now I'm going to turn this over to Debi to discuss ethics and conflicts of interest.

MS. SARKAR: Good morning. So as usual, I have my standard reminders for the committee. So first, we are advisory to the Secretary of Health and Human Services.

So for anyone associated with the committee or due to your membership on the committee, if you receive inquiries about the committee, please let Dr. Bocchini and I know prior to committing to that interview.

Also, just want to remind committee members that you must recuse yourself from any participation in all matters likely to affect the financial interests of any organization with which you serve as an officer, director, trustee or general partner unless you are also an employee of the organization, or unless you have received a waiver from HHS authorizing you to participate.

When a vote is scheduled or an activity is proposed, and you have a question of a potential conflict of interest, please let me know.

Okay. We went over this during the last November webinar, but I wanted to highlight

this again and to remind folks that the Advisory Committee's legislative authority is found in the Newborn Screening Saves Lives Reauthorization Act of 2014.

The legislation establishes the committee and the duties and the scope of work. However, all Advisory Committee activities are governed by another act, which is the Federal Advisory Committee Act, FACA. And that sets the standards for how these committees are managed.

And so according to FACA, I just wanted to highlight, so all committee meetings are open to the public. If the public wish to participate in the discussion, the procedures for doing so are published.

We have a Federal Register notice that goes out before every meeting announcing the meeting. We also, in the Federal Register notice, talk about how to submit public comments or provide oral public comments during the meeting.

Only with advanced approval of the Chair or DFO, public participants may question

committee members or other participants. We've talked about the public comments.

Also, public participants should be advised that committee members are given copies of all written statements submitted, and we do state this in the FRN as well as the registration website.

And all written public comments are part of the official record and of course shared with committee members. Any further public participation will be solely based on the discretion of the Chair and the DFO. And that is all I had.

CHAIR BOCCHINI: All right. Thank you, Debi. All right. We're ready to begin the discussion of newborn screening long-term follow-up. And so as I indicated, today we will begin a conversation on re-examining long-term follow-up activities.

For several meetings we have discussed how do we know that newborn screening is making a difference. Another question is, that is how states are implementing conditions with later

onsets. Who and what entity is responsible for ensuring these patients can get the care that they need?

So today, we'll be hearing from a panel of experts on newborn screening long-term follow-up. First we will hear about the past work that this committee and follow-up and treatment subcommittee have been involved in.

Then we will hear from Dr. Feuchtbaum, from the state of California, Dr. Berry, a clinician and researcher and Ms. Christine Brown, who will provide a parent's perspective regarding long-term follow-up.

And the panel will discuss challenges in collecting data, conducting long-term follow-up activities, and we'll have a significant opportunity for committee members to then provide input into this process.

We have both Drs. Hinton and Brower who worked on this presentation together. Dr. Hinton is a health scientist in the Disability and Health branch in the Division of Human Development and

Disability at the CDC, where she works with partners across CDC to promote disability inclusion. She's worked in the area of public health newborn screening for close to 20 years.

Dr. Brower works on several projects at the American College of Medical Genetics, including serving as project manager on the National Coordinating Center's long-term follow-up project and the Newborn Screening Translational Research Network.

Dr. Brower is a former member of this committee and a current member of the committee's follow-up and training, treatment subcommittee. So let's bring, I guess, first Cindy Hinton.

MS. SARKAR: Amy Brower.

CHAIR BOCCHINI: Oh, Amy first?

MS. SARKAR: She's on the phone.

CHAIR BOCCHINI: Okay. On the phone.

DR. BROWER: Okay. Good morning.

CHAIR BOCCHINI: Good morning.

DR. BROWER: Can everybody hear me okay? Good morning. Thank you for the

opportunity to present to the committee today. I'm really presenting Dr. Hinton's work this morning.

So my job today is to briefly review some of the important efforts that this committee has undertaken in the past that have guided long-term follow-up and that continues to shape activities in this area.

Next slide. I don't see the slides, but I assume you're on the second slide. Let's see. So, let's see. Sorry, guys. I'm not seeing the slides, but that's okay.

So as you know, as Dr. Bocchini said, newborn screening is a system of interconnected activities that begin before a baby is born. Newborns who screen positive undergo a series of screening and ultimately receive a diagnosis.

Screening and short-term follow-up takes places within the state based public health system, while long-term follow-up, diagnosis and treatment occur in pediatric care centers.

This series of handoffs, from prenatal

care to public health to specialty care, creates the unique opportunity to capture important longitudinal information.

As Dr. Bocchini said, there is no national facility currently to collect and analyze and share this information. Recognizing that the leaders of this committee implemented several key efforts related to long-term follow-up, even before and as soon as the committee began.

In 2004, Mike Watson at ECMC was funded by HRSA and be an expert first to look at all of the conditions that might be a fit for newborn screening. It was a multi-year effort that led to what is now called the Recommendation Use of Funds Panel.

That gave us some guidance into the long-term practices that we might need to get for early onset conditions or conditions that need to be monitored throughout the life span.

(Telephonic interference.)

DR. BROWER: --- presented an evaluation and tracking system that had already

been in place in 1992 ----

(Telephonic interference.)

DR. BROWER: ---- and in the 2002 CDC effort that said that Iowa and Colorado to begin to develop tracking databases for long-term follow-up.

So that, at the same time, was funding the National Coordinating Center and the Regional Genetics Surface cloud was developing standards, so listening to public thought, understanding what they might think is important in long-term follow-up and ----

(Telephonic interference.)

DR. BROWER: The Advisory Committee, at the same time, established three committees. One of them was focused mostly on follow-up and treatment and identifying areas that the committee could play a role in shaping long-term follow-up. Next slide.

MS. SARKAR: Amy. Could you, sorry. We're having a little trouble hearing you. This is Debi. So our IT specialist said if you could

just keep the phone a little bit away from your face, and if you could talk a little bit slower.

DR. BROWER: Okay. Sure.

MS. SARKAR: Thank you.

DR. BROWER: Okay. So the next slide is titled Follow-up Treatment Subcommittee Charge. So in 2005, this Advisory Committee created the subcommittee staffed by Jill Shuger.

The first job of the subcommittee was really to identify which areas they would be focused in and to create a charge for the committee.

So the charge of the committee came up with focused in three different areas, to work to identify barriers to short and long-term follow-up and treatment in newborn screening positive individuals and to identify specific challenges in reintegration of healthcare systems, thinking about electronic information exchange, the payer and the care systems that these children will enter into for lifelong care.

So also want to develop recommendations to identify how to overcome barriers and looking

for opportunities to build our program throughout the United States that may already be doing long-term follow-up healthcare for many of those programs after my talk.

This committee also recommended mechanisms for establishing accountability for newborn screening guidelines. So they wanted to play a role in really shaping this area after diagnosis as an infant goes into lifelong care and treatment.

The next slide reminds us that there are already several efforts that looked at long-term follow-up across the landscape of newborn screening.

One of those was the state of newborn screening follow-up that really identifies some inventories that were already in place from the PEAS.

That was Dr. Hurrell's efforts in performance and evaluation and assessment, which goes all the way through treatment guidelines from all the in California that really the committee can

look to and learn from, bringing in those experts to meet with the committee and talk about their experiences.

The committee also implemented an inventory of state practices to identify again what it would cost to do long-term follow-up, how laboratories and clinicians will work together to have the same working knowledge information and through the parent and caregiver perspective in newborn screening.

The committee wanted to identify models of care that work and wanted to look at common issues or common elements. So the next slide reminds us that in February 2006, the committee got together a group of experts for a one day meeting.

And this group of experts involved advocacy, clinicians, public health, our federal partners as well as people to think about standardization of healthcare information across the lifespan. So our colleague from the National Library of Medicine and NIH, so to think about how to create this system of healthcare follow-up.

This one day exercise ultimately resulted in a report that many of us refer to today. So they really wanted to identify the scope of long-term follow-up, what do we mean by long-term follow-up, the goals for long-term follow-up and the key elements of long-term follow-up.

It seems like a simple thing to want to come up with a definition, but without a definition and thinking what are we talking about with long-term follow-up, it's really hard to build a system. Next slide.

So in April 2007, this one day committee was wrapped up into a paper that was then reported. And it is called the Roadmap to Implementing Long-Term Follow-up and Treatment in Newborn Screening, commonly known as the Kemper et al paper.

So this paper really guided us and identified the key components of long-term follow-up. Three key features, quality chronic disease management, condition specific treatment, age appropriate care throughout the lifespan and

four central components, care coordination through a medical home, evidence based treatment and continuous quality improvement and knowledge discovery.

So you can think about those central components really hit on many of our federal partners that the Advisory Committee has at the table today, whether it's CDC, NIH, HRSA, all partners working together on the long-term follow-up activities.

The next slide reminds us that this paper really about, although didn't tell us how to implement long-term follow-up, it provided the framework, so what we mean by long-term follow-up.

There was question on how long we mean by long-term follow-up, and this paper decides its birth to 21 years. Ideally, it would be a standard for this time. That was the definition, from birth to 21 years.

The next slide really gives a summary, and it isn't meant to be all-inclusive, every project has gone on with long-term follow-up, so

just some key efforts that along with the Advisory Committee has guided us in this area.

The CDC's funded a four state pilot that began to be retracting across these states in long-term follow-up across all of the conditions that are part of the recommended uniform panel.

What that initial pilot lets us do is to come up with essential questions and answers that we thought would be interesting to follow kids throughout the lifespan.

HRSA then funded several projects through the regional collaborative. Region 4, Dr. Berry will talk about her effort, which really began at HRSA for Region 4's funding a special priority fund.

That effort has now gone on for the last eight years, and it's been collecting really important and novel information on inborn inherited metabolism issues and some other conditions.

Massachusetts has always been a leader in long-term follow-up and has presented to the

committee several times on their approach to doing long-term follow-up in the Northeast. And we look forward to learning more about that effort in the future.

Some of the other regional collaboratives from the Southeast region to NYMAC, the Mountain States and Heartland State have also addressed a different part of long-term follow-up but thinking through how in their region, how in their unique state could long-term follow-up be initiated.

NICHD has funded for a long time natural history studies that focus on long-term follow-up and began to collect the basic information for understanding the trajectory of the conditions that we're now springing for, whether they're later onset or different phenotypes that maybe give some conditions different status than others.

So funding those long-term follow-up efforts has been an important part of the effort so that we can learn from how we can implement long-term follow-up across the board. NICHD,

NBSTRN, housed at ACMG as well as the National Coordinating Center for the regional collaboratives that's housed at ACMG.

Both of those efforts have launch and follow-up projects that focus on both the states and the clinicians and getting them together to build long-term follow-up systems.

The next slide. So following on the meeting in 2007 that Dr. Kemper led, Dr. Hinton led a meeting in 2011 that brought together some of the same stakeholders but really expanded it into advocacy and caregivers.

And we wanted to begin to think about what kinds of questions, if we were able and successful in implementing long-term follow-up, should we be able to answer.

And so what the group did was identify some overarching questions. If we were able to do long-term follow-up, here's the kind of information we should be able to give back to parents.

Here's the kind of information we

should be able to give back to our federal partners so that they have some idea of the benefit of newborn screening so that they can begin to talk about not only at 99 percent of newborns screen, but here's how we're doing today across all conditions.

The next slide. This group also talked about as far as families in this conversation to do a survey of families and to begin to understand how, what parents like to see in long-term follow-up and what role they would like to play and that the most important things for the children's quality of life care like medical foods, the substance, making sure they have medical care and insurance coverage across the board, and you'll hear more about that in Dr. Berry's talk.

The next slide reminds us that Dr. Hinton is currently working on a framework paper that she's published today. She's got a great draft of it. And it's going to address overarching questions and think about how will we implement this on the clinical side.

It's not going to be a systematic analysis of newborn screening but really focused on what do we mean by outcomes. How do we measure whether a health outcome is good?

How do we begin to stop ----

(Telephonic interference.)

DR. BROWER: -- How do we begin to identify maybe gaps in delivery, gaps in service of care across the United States? And do the long-term follow-up systems need to be tailored by age?

Next slide. So once this paper comes out, hopefully it will be a good step, this paper will go to the committee and to the long-term follow-up subcommittee. And we'll be working with the subcommittee to take it to the next step.

And that will be working through some pilots and thinking about the states that are already doing a great job of long-term follow-up and beginning to learn from them and learn what we could harvest at a national level.

I hope you were able to hear most of

that, and I'll be around to take any questions. Thank you.

CHAIR BOCCHINI: Amy, thank you for a great presentation to kind of give us an idea where, how much work has been done by many people in this room and others to get where we are today.

We're going to open this paper for, this presentation for any questions specific to Amy's presentation. And then we're going to save the discussion and interaction for later.

But are there any specific questions related to her presentation? None. Any from the committee members? Organizational representatives? All right. If not, thank you again, Amy.

And we'll move to the next presentation. And so stay with us, Amy. So our next presenter is Dr. Lisa Feuchtbaum. She has been employed for over 25 years at the Genetic Disease Screening Program, California Department of Health, and is currently the Chief of Program Development and Evaluation Branch.

Her work is focused primarily on documenting and evaluating the efficacy of the California Newborn Screening Program. She's been a key player in the development of long-term follow-up data system for newborns diagnosed with disorders detected through the California program and has served on numerous state, regional and national committees focused on newborn screening policy development. Lisa, thank you for being here.

DR. FEUCHTBAUM: Well, thank you very much. It's a pleasure to be here today to talk about one of my favorite topics, a passion of mine going back many years.

And I also want to thank Amy Brower and Cindy Hinton for the great history and overview of the quite many years of activities that have gone into this long-term follow-up discussion.

And, in fact, many people in this room have been involved in many of those discussions and putting together manuscripts over the years, so it's been a real collaborative effort.

So again, thank you for my introduction, and let's see. So this is just to repeat in a simplified way what essentially is long-term follow-up for newborn screening. In California, we have seen it as a systematic evaluation to determine if newborn screening is meeting its goals.

And systematic is the operative word because we have developed a system, which I'll describe here today, to capture a similar set of types of information about the experience of patients after they get a diagnosis with one of our newborn screening disorders and essentially what happens with those patients over the -- during the first five years of life.

As a public health program, it's important to have the assurance that the treatments and age-appropriate preventive care is available for those individuals identified through screenings.

So that's been an important concern of ours, and a lot of these concepts have been

presented in the paper by Alex Kemper et al, which also was referred to by Amy.

And I also wanted to remind folks that there was an issue of Genetics in Medicine that was put out in 2010 that covered newborn screening, long-term follow-up with a lot of great articles and kind of thoughts about how states are going about doing this.

But in my presentation today, I'll be talking about how California has gone about this. And so back in 2002, our team in California received funding from HRSA to do an evaluation of what was then a brand new technology, the tandem mass spectrometry technology.

And as part of developing the framework for doing the evaluation of the efficacy of tandem mass spec screening, we started thinking about a long-term follow-up system and was also inspired by Judi Tuerck, who was also mentioned in the previous presentation, who did a lot of work with the CORN project way back when and got me thinking about what would be the variables and data that

would be important to collect following newborn screening.

So in 2005 in California, we were fortunate to be able to bring up a brand new, computer based system, which covered all aspects of the newborn screening program.

And at that time I had put forth the idea well, why don't we build a long-term follow-up system into this new computer system. And everyone agreed and a significant effort was put forth, and we were able to do that.

So just a word about our screening information system, which we refer to as SIS, does support all aspects of the newborn screening business, if you will, from lab results, reporting to mailer creation, patient referral tracking and coordination with probably about 65 different types of specialty care follow-up centers throughout the state.

So this is a quick model to show basically how things work. For all patients that have a screen positive test result, they get

referred to a small army of clinical care coordinators that are scattered throughout all the major medical centers in California.

And it's their responsibility to make sure that each and every one of those families and children get referred to a specialty care follow-up center for a diagnostic work-up.

And that's what -- this is part of what we refer to as short-term follow-up. And we do ask the centers also, through another web-based database if you will, to provide documentation of services provided, the health status of the newborn and outcomes of confirmatory testing.

And at a certain point a decision is made. The child either is determined not to have a disorder or, in fact, they may have a confirmed disorder.

In which case, if the child is basically two criteria for our computer system that a diagnosis is confirmed and that the patient is in active care at that center, essentially are the criteria that -- where the patient essentially

enters, if you will, into a registry, computer based registry, and then essentially entered into the long-term follow-up system.

And the system is based on a -- essentially it's a one year survey that's done right after the birth date of the child each year. And we refer to it as the Annual Patient Summary report.

And we collect this data for program evaluation purposes primarily, although there are other uses that I'll share. The data is provided by our state contracted specialty care follow-up centers under contract with the state.

And again, it's a once a year assessment of the status of the child. And we currently do this through age five for all of the disorders, whether they be metabolic or cystic fibrosis, hemoglobinopathies, endocrine, et cetera.

The state pays for the data essentially, so there is an incentive that we provide the centers to give us the data and the report documents, whether the child is still in

active care and other characteristics of whether -- of care, including the clinical management strategies and clinical outcomes and also health utilization data.

So this schematic essentially shows how we've folded in our long-term follow-up system. So again, back in 2005, we started with the metabolic disorders when tandem mass spec went live.

We added cystic fibrosis in 2007. Endocrine and hemoglobin disorders were added at the end of 2011. In 2013, we developed a long-term follow-up system for SCID.

And currently, very, very busy. Currently, we are planning a system, which is challenging because of the late onset nature and other reasons for adrenoleukodystrophy, which we are hoping to go live.

Waiting for the Secretary to make her decision, but our plan is to go live with ALD screening this summer. And in each case I want to point out that we work with the specialists to

develop their essentially similar features to this long-term follow-up system. But the details of some of the clinical items, symptoms for example, are specific to the disease categories.

So where are we now ten years later? It began in 2005, and it's 2015. We've screened over 5 million babies in California. We've diagnosed 1,500 metabolic disorders. That's just the metabolic disorders alone. And we've collected over 5,200 annual patient summaries on those kids.

So this chart is a little busy, but as you can see in the lower right hand corner is the 5,208 annual patient summaries we've received, shown by the age of the child. And the -- on the axis on the left is the disorders, just, I think we have 19 disorders listed in this graph.

So you can see we have -- we are, in fact, collecting lots of data about each of these disorders. And you can see by the end of year five, we had 668 reports covering a variety of the disorders listed.

So I wanted to talk just a little bit

about how the data's been used. We have developed some very interesting partnerships with clinical researchers in the state and outside of the state as well.

One of the earlier collaborations, it was mentioned earlier, Cindy Hinton's, the four state collaborative study as it's referred. So we did use our long-term follow-up data in California.

And working with the other states we were able to describe a select group of metabolic disorders and what happened to those kids. Part of the Western States Regional Genetics Collaborative -- we -- California's part of that group.

And Lawrence Merritt led a project. It was a multi-state project to look at VLCADD and essentially looking at the short and long-term outcomes of kids with that diagnosis.

Natalie Gallant and Christine Lamb out of UCLA have each published papers on SCADD and 3-MCC. Danieli Salinas is very active currently in using our data to do genotype/phenotype studies

around cystic fibrosis. And she's been very busy.

And then we have the U19 grant where there's a center out of UCSF. It's my understanding that they're going to also be looking at some genotype/phenotype outcomes for the tandem mass spec disorders.

So in each of these cases, we've -- these researchers have used our data as really a starting point. It's not that we're collecting all of the details needed for a clinical study, but we certainly can characterize individuals in ways that I'll describe in a few minutes.

And it really does serve as kind of a base for doing more detailed clinical studies. But for us, we use it for program evaluation, and we ask what are thought of as these higher level public health type questions.

Essentially, what percentage of children are still in care through age five? What percent become lost to follow-up, and what are the reasons why? How many of the children eventually develop disorder related complications?

How many die and for what reasons? How many eventually develop developmental delay? I mean after all, that's what we're trying to prevent through the screening program. How many have high rates of emergency department visits and inpatient hospitalizations?

And which children are really using the metabolic center services at a high rate, which we would think would indicate maybe that they're having some challenges? But maybe they're actually just healthy, and the centers are doing a great job maintaining their health status.

So we, one thing I wanted to share, there's some new data that we've looked at. And we decided to focus on access to care as kind of a first focus. And we wanted to know what percentage of children with the RUSP primary metabolic disorders remain in care between the ages of age one and five.

So we have the ten years of data, which basically covers two, five -- two cohorts of five years. During a ten year period we've screened

over 2,500 newborns -- were screened during this period and 448 of the RUSP primary metabolic disorders were diagnosed.

So here's some, just a first look at the data. So of the 448 kids that were diagnosed with one of those primary RUSP disorders, metabolic disorders, 56 percent were still in active care by the age of five.

And you can see each year we're -- there's, you know, that number declines, and we wanted to look at well, what's really going on here. Can we get some insight into what's going on and why the kids are dropping out of care?

So, let's see. So in addition to being, and we know how many are in active care, but we wanted to look at how many were reported to us by the centers as being lost to follow-up. How many, where parents actually do, they refuse follow-up.

Sometimes the treatment is deemed no longer necessary by the clinicians. Patients move out of the state, and unfortunately, some children

die. So we wanted to see what's going on over the five years.

And you can see that in each of the five years, as far as the lost to follow-up, there seems to be about 5 or 6 percent of kids become what the centers classify as lost to follow-up.

And that's pretty consistent across all the years. And this is not shown in a slide, but we're starting to look at the reasons for lost to follow-up, and one interesting finding was that 73 percent of the lost to follow-up cases had had no reported health problems in the year prior.

So it may be that these are really healthy kids, and for whatever reasons the parents are just dropping out of care. And we've also been looking at the characteristics of those parents that seem to be associated with their children essentially being labeled as lost to follow-up.

So there's more work that we're doing there. And you can see a small percentage of parents refuse follow-up, and you see the largest group is in the first year of life.

And other interesting findings where we found there were 15 deaths reported to us, and 70 percent of the deaths, eleven out of the 15 occurred in the first year of life, which is not completely surprising.

So here we have a comparison of the one year and five year active follow-up status by select disorders, and this is really interesting to me. Perhaps most interesting is the PKU.

You can see by the end of the first year of life, 98 percent or nearly all of the kids that were diagnosed with PKU were in active care. And at the end of five years, 90 percent of them were still in care.

And then you could see between that it bounces around a bit. We know that about 56 percent overall were in active care at the end of the fifth year, but this shows it by specific diseases.

Other interesting things to note in the kind of in the group that you consider high on the active follow-up was galactosemia, another, these

are the original newborn screening diseases, PKU and galactosemia, going back many, many years.

So anyway, next slide I wanted to look at how good is our data. How many annual patient summaries are we actually missing among the group that would be expected? And this shows that we don't have too much a problem.

Although, we're working with our centers to find out more about why they're missing, essentially giving us these reports. But you can see that 10 percent of the reports were missing in year two, 8 percent in year eight, and the number of expected reports drops over the time frame.

So, in terms of next steps, we will continue to explore why patients are becoming lost to follow-up. We're going to, one of our ideas was to use GIS mapping systems and look at distance that families have to travel to clinics. Maybe that's a contributing issue.

We're going to do a detailed analysis of specific disorders that I showed, looking at symptoms and developmental status treatments and

services provided.

We also will be looking at insurance status. And we may go back and revisit all this data in a few years to see if there's an impact as a result of the Affordable Care Act on service utilization.

So in conclusion, in California, the long-term follow-up data has been very helpful for us in getting an assessment of the impact of the screen program and how well parents and families have been able to access care.

It's been a valuable resource for clinical collaborations and certainly for program evaluation. We have a challenge with some missing data, but it doesn't seem to be a big problem.

Our data system doesn't collect a lot of highly detailed clinical information, but we work with our partners so that they can collect that information.

Cost of data is a challenge. We're paying, and I don't know how often -- we'll see what the budgets are looking like. Will we be able to

provide those incentives in the future, especially with the late onset disorders? Our ALD screening is scheduled to go once a year through age 21.

How is this all going to be work? It's going to be challenging, especially when we have to collaborate with multiple specialty care centers, particularly with ALD with neurologists and endocrinology.

So this is my final slide, a disclaimer that I've come here on my own time because I feel so passionate about this topic and that the views that I've expressed are not necessarily the views of the Department of Public Health. So thank you very much.

CHAIR BOCCHINI: Thank you, Lisa. Your passion is pretty obvious, so that's great. Thank you. So let's open. Joan?

MS. SCOTT: Joan Scott, HRSA. Thank you, Lisa. That was really a wonderful overview. I have one question about your process. I'm sure we'll -- in the group discussion, talk a lot more in detail.

But I have one question about the process. In one of your early slides you said that parents who are found to have a child who is affected are invited to participate in the long-term follow-up. Is it really under informed consent or --

DR. FEUCHTBAUM: No. This is, parents aren't specifically invited. We just, this is part of our program evaluation that is -- we're allowed, as written into state regulations, we are allowed to collect data from our contracted centers for program evaluation and research purposes.

So we always, it's done, we're basically, we've been exempt from, the California Human Subjects Committee has given us an exemption essentially to evaluate our own data. So, and we already, you know, we run the screening program, so we have the identifiers.

MS. SCOTT: Right.

DR. FEUCHTBAUM: But of course what we care about is data in the aggregate.

MS. SCOTT: Right.

DR. FEUCHTBAUM: And, but it's not a consented process. We are considering maybe with ALD that perhaps given that it's a really, we don't know how far we're going to have to go out that we may even want to experiment with consenting parents and engaging them in a more active way in long-term follow-up.

But this current system is going to continue the way it is. It's, again, it's a partnership with the follow-up centers in California.

MS. SCOTT: Thank you.

CHAIR BOCCHINI: I got Cathy, and then I got Tiina.

MEMBER WICKLUND: Thank you, Lisa. It was a great presentation. I had a quick question just about the five year length of time and just the decisions.

I'm sure cost is a factor, but the decisions about going five years. And then it sounds like for ALD you're going 21 years you said.

DR. FEUCHTBAUM: Well, yes. I mean

originally we're not dealing with --

MEMBER WICKLUND: And the pros and cons.

DR. FEUCHTBAUM: -- late onset decisions. And the thought back -- way back in 2002 to '05 when we were thinking about putting this system together was that we tracked the kids through the time that they start school essentially because then we thought well, then the school system kicks in.

There's a departmental, developmental disabilities, and they should be collecting data on these kids. In fact, we've looked into trying to partner with those centers as a data source, and if we can do some data linkage then maybe we could actually, not that we'll be collecting the data, but we can, through basically linking to other data systems, we could maybe track how the kids are doing once they enter the school age.

MEMBER WICKLUND: So have you found that they are tracking that data?

DR. FEUCHTBAUM: Well, we haven't

looked at it yet.

MEMBER WICKLUND: Okay.

DR. FEUCHTBAUM: One of our research scientists that unfortunately is no longer with us, but she had established some kind of agreement to get that data.

But she actually never was able to get, you know, actually start working on the project. But it is something that would be really interesting and worthwhile to see if we can do some long-term tracking by just linking to other data systems in the state.

CHAIR BOCCHINI: Tiina?

DR. URV: Quick question. With the funding being limited, how aggressively are you able to track down the parents in the sense of is it just a letter and if it comes back change of address, or do you phone or do you go on Google to try to find them or anything?

DR. FEUCHTBAUM: Okay.

DR. URV: What are you able to do?

DR. FEUCHTBAUM: Well, the burden is on

the metabolic center to provide the data. We don't actually have any contact with families or parents directly. It's completely done through the computer system.

So the system does allow a transfer of care, so if a center knows that a child is moving from say Northern California to Southern California, they will actually make the transfer of the child and notify the new center that the family's moving down south.

And they enter it into our computer system as a transferred care. And it's just all done basically by the computer. And so, but what's been interesting is for this presentation I wanted to know how many of the kids that got transferred indicated as transferred to another location in the state actually showed up the next year in the long-term follow-up system.

And I was actually pleasantly surprised. 70 percent of the kids that were noted in the system as transferred from one center to another, that new center reported them as active,

in care at the new location. So that system does appear to be able to work.

In a big state like California, there is, as you saw, a lot of movement. Well, actually I showed movement out of state. That's where we really lose touch, when families move out of state.

But if they stay within California, they're really hooked into this network of care. And everyone's hooked into the long-term follow-up system.

CHAIR BOCCHINI: Next is Steve.

MEMBER MCDONOUGH: Thank you for your excellent presentation. A couple questions. One, have you had any discussions regarding a point of care testing, newborn hearing screening and congenital heart disease long-term follow-up?

And then the other question is, how do you find it? Is it part of your newborn bloodspot that funds your program? Is it state funds, federal funds? Do you have opportunity to get additional funding and expand, go beyond age five?

DR. FEUCHTBAUM: Particularly for

hearing and congenital heart disease screening?

MEMBER MCDONOUGH: Yes, in the long-term follow-up.

MEMBER MCDONOUGH: Well, I know that in many states the newborn screening program has picked up the responsibility for monitoring the implementation of those two other point of care services.

In California, that has not happened, in fact. We are really, our genetic disease screening program is basically kind of following up on the more traditional diseases, laboratory-based diagnosis.

And there is a hearing screening program and a CCHD screening program, but it's not run by us. And it's actually run by a completely different department.

And I've been, over the years, encouraging one of the staff or a physician who's actually in charge of the congenital heart disease screening program to actually work with this committee so that he's not feeling like an

outsider.

But it is run by a completely different department. And I don't know that much about how that program's, in fact, operating on the ground. I -- We haven't had a lot of communications with them. So, it doesn't make sense, but that's the way it is.

CHAIR BOCCHINI: I have Jeff and then Don.

MEMBER BOTKIN: So Jeff Botkin. Thank you for your presentation. There was some observations, at least a number of years ago, that suggested that there was a really broad spectrum of treatment approaches to individual conditions, so -- and perhaps due to the difficulties in developing large scale comparative research protocols to sort of figure out what really does work best.

Is your system able to make those sorts of comparisons to try to guide clinical care for outcomes for these kids?

DR. FEUCHTBAUM: Well, that was

certainly one of the intentions was able -- you know, to gather the evidence. We do collect, again, it's not in great detail, but we know what kind of treatments the kids are receiving.

And we also ask whether the family is essentially adhering to the treatment regimen. And so with some simple data, we were hoping to at least be able to make some kind of broad generalizations.

And we, in fact, will be looking at the data. I'm just really thrilled to say that I just was able to put together a team of epidemiologists that are just devoted to looking at newborn screening outcomes, evaluations.

So for the first time, it's not just me at the program trying to, you know, work the data. But I have a team of people that, again, this is on the agenda for things to look at because we are collecting a lot of data.

And I don't want the data to be kind of a black box that goes in and never comes out. So those are the kinds of things we will absolutely

be looking at in the next year. We're going to really mine the data and see what kind of useful information we can get out of it. So that would be forthcoming.

CHAIR BOCCHINI: Don.

MEMBER BAILEY: Hi. Don Bailey again. Thanks for a great presentation. Are you collecting data on families? I know you talked about family adherence to recommendations. Are you collecting data on satisfaction with the services or adaptation to having a child with a disability or any data on --

DR. FEUCHTBAUM: Well, again, that would be a wonderful project that I'd love to do, but we don't have any contact with families. We are simply working through the specialty care centers, and they are the ones that will tell us if say, there's an issue with adherence to care.

Do patients, are they -- there's different types of questions that are asked say in the hemoglobinopathy clinics. There's issues about families missing appointments.

And we collect that kind of information. So they're really essentially, whether you're missing appointments and not adhering to care, they're essentially markers for families that are really struggling to provide the proper care.

And so we don't work directly with families, and with some of the new grant opportunities that have come out, particularly some of the long-term, the natural history project that has just been announced, we're actually considering maybe doing something a little bit more creative where we can connect with families directly. But we haven't done that to date.

CHAIR BOCCHINI: Carol Greene? Oh, Dietrich?

MEMBER MATERN: Dietrich Matern. Thank you for the presentation. I hope you find money to continue it and fill the gaps. I have a question about the children that died. Do you know whether they died of the screening conditions or complications at all or were those NICU children

that basically like ---- well, they were NICU children?

DR. FEUCHTBAUM: Well, I don't know the answer to your question. We really do need to do a more detailed analysis of the deaths and the reasons why the deaths occurred and were the children in the NIC.

Did they ever go home, or was it really just a child who was sick at birth and never essentially left the hospital? So we should be able to get the answers to those kinds of questions.

That alone would be maybe just one, that could be a manuscript in and of itself, is just looking at the mortality and morbidity associated with those deaths.

CHAIR BOCCHINI: So Carol, I'm going to give you the last question. Then we'll move on.

DR. GREENE: Thank you. It was spectacular and enormous opportunities and lots of work, and I want to go back to the very first slide and to say that with all the recognition of the incredible value that this gives us to look at

what's been going on, going back to Cindy's and Amy's presentation, fundamentally long-term follow-up comprises the assurance and provision of quality chronic disease management, condition specific treatment, age appropriate preventive care throughout the lifespan of the individuals identified with a condition included in newborn screening.

That's the definition of this committee. That's the definition of long-term follow-up. And I respectfully request that we all keep in mind that this is long-term tracking and that when we say long-term follow-up and we hear such a spectacular good job being done and so much more work needed, we tend to focus on long-term follow-up and forget about long-term follow-up means first you treat them. Then you do the outcomes evaluation.

DR. FEUCHTBAUM: Well, the treatment is something that unfolds over the years. Treatments change. In fact, disease diagnoses we find change.

DR. GREENE: That's part --

DR. FEUCHTBAUM: We thought it was this, and now it's that. And again, so we're actually tracking that, the change in the diagnosis. And that's another interesting topic. So many interesting things to study, but --

DR. GREENE: Completely agree, and that's probably where some of the fall off is, is galactosemia, but maybe it was just DG. But I just really want to focus the committee's attention that this spectacular presentation doesn't use the definition of long-term follow-up that we have established by the committee.

DR. FEUCHTBAUM: Right. Well, in fact, under the why we do it is essentially the definition taken from the Kemper paper. So we completely are on the same page.

And I wanted, you were talking about galactosemia. I just want to point out primary congenital hypothyroidism, how many are transient? How many doctors are really testing those kids at three years of age to determine if it's transient?

So we find that data out through our data collection. We'll find how many convert to transient if the data is presented to us.

CHAIR BOCCHINI: All right. Again, thank you, Lisa, for a great presentation.

DR. FEUCHTBAUM: Thank you.

CHAIR BOCCHINI: Let's next bring up Dr. Susan Berry. Dr. Berry is Professor of Pediatrics and Genetics, Cell Biology and Development at the University of Minnesota.

She's Director of Division of Genetics and Metabolism in the Department of Pediatrics. Like many genetics professionals, she sees adults and children with heritable conditions of all kinds.

She has a particular interest in providing management for persons with inborn errors of metabolism and has a longstanding interest in improvement in their care through early diagnosis and treatment.

Her research focuses on evaluation of long-term outcomes after newborn bloodspot

screening. So Sue, we're going to turn this next over to you.

DR. BERRY: Well, thank you for the opportunity to share a little bit about -- what I wanted to try and do today was talk a little bit about where the project that my most involvement has been and why it got there because it kind of mirrors some of the information that you've been hearing from others about the process.

So I'm really more about, today about the process than our data. I'm sort of jealous that I didn't put all my data in because Lisa did such a fabulous job with hers.

We've all been echoing this, but I bring this almost every time I present this because it's so important to us as clinicians. I'm speaking to you as a clinician.

We initiated this project because we wanted to know if we were doing what we wanted to do in caring for the children that were sent to us after newborn screening.

I think the point that we are all

grappling with today is that this is not just a test. It's a process. It's not an event. It's a long commitment on -- to an individual that's identified by these conditions. And it's the whole scope of this.

It doesn't tell us who's going to do what job. It just says that as a community we owe people this overall response. The definition by the committee really reflects that.

So we started our project at a time when newborn screening was really expanding. This committee is more familiar than almost anybody else about how newborn screening's mission expanded quite radically with the addition of tandem mass spectrometry.

The point that came from that was that all children should be treated equally, that everyone should have access to the same level of screening. We've maintained that to some degree but not perfectly.

The purpose of this is to improve outcomes and save lives. That's what we're trying

to do. We're not trying to give the best test. We're not trying to get the most money. We're trying to make things better for the children that are identified.

And so, it's only as effective as what we do with it. And that's why projects like Lisa's are so important and why I hope I'll make the case that ours is that also.

But the point is that this has to be a collaboration. It's only one set of data, and it's about these kids. And whoever takes ownership or the responsibility of stewardship for it is a different thing, but it's only one set of people we're trying to answer questions about and that's the kids we're identifying.

And so we have to collaborate. Short-term has to share with long-term, has to share with families, has to share with everybody. We all have to, that's the goal.

So we have to share that data. So it's really important that we have the opportunity to present in forums like this and to do more with the

work as we go forward.

I'm going to tell you a little about how our project came about and what we wanted to do, and this is, thank you HRSA for the regional genetics collaboratives because it really brought clinicians together in our region in ways that we hadn't worked together before.

And we thought it would be just great if we could all treat somebody the same way and do a better job. And so we all had experience, but there wasn't much evidence.

The problems with these are that all of these conditions are rare, even things that are common. They are all in children, so doing research in children is non-trivial because they're held to a higher standard of protection.

It was hard to justify testing accepted treatments because they seemed to work, but there's no data to substantiate that. And then also, who's going to pay? That's always a question, so I just throw it out there. Who's going to pay? Because that'll be something that has to be addressed.

So our original proposal was we were going to get everybody together, and we were going to treat MCADD deficiency the same way. It was common enough, so we thought we'd have a lot of kids.

We all thought we knew that the most important thing was to keep them from fasting, but there were other elements that everybody disagreed on and still do.

Carnitine treatment, use it or not? Corn starch at night, use it or not? Modified diet, should you? These are all things where everybody knows the right answer to it when you ask them, but they're not the same answers. Just putting it out there. That's what evidence is about.

So we thought that we'd, so Bob Steiner wrote a nice editorial. Now it's more than ten years ago, about how we were going to develop evidence-based medicine for management in inborn errors of metabolism.

And one of the things was we had to have

collaboration. We needed support to make this happen, federal and state. We needed to teach people what evidence based medicine was. We had to make sure we were all talking the same language, and we had to publish. We had to publish the information we get.

So our group has evolved over time, but it's the same people. We had our region four genetics collaborative long-term follow-up workgroup. We were fortunate to compete for funding for the Priority 2 projects which were long-term follow-up projects.

So we came, we like our little names, so we were R4P2 for a while. And it was cute. Wasn't it? It sounds really a good name, but then we were able -- when NIH put out their first series of natural history grants, we competed and successfully won one of those, and we became the Inborn Errors of Metabolism Collaborative.

But it's all the same group of people. Right now it's, I lose track because there's people coming in and out, but it's about 25 centers that

are trying to gather information about long-term follow-up.

So the early evolution of this was we've decided to have a MCADD registry. We wanted to have our uniform protocol. I'm going back into the history, so that's why I have some of these old slides that have old logos.

We didn't have natural history, so we wanted a natural history. We had lots of clinicians and successful strategies. Oops. Let me back up one. We wanted to gather uniform data.

That was the secret to it. We wanted to all answer the same questions at the same time with the same language. We figured if we gathered information, and you asked about this, the clinical practice differences, we really hoped to be able to capture those.

So we were kind of agnostic in saying this treatment or that treatment was the right treatment. We just said, are you doing this. Then tell us about it. Are you giving carnitine? How much are you giving? Are people taking it?

So we thought maybe we could compare different outcomes with it. So, because we couldn't do a treatment in front of -- for a follow-up protocol we took the treatment plans.

We took advantage of the things that we've heard about the Oregon database, the CORN studies, all of these things to create the questions we wanted.

We identified elements that we thought were essential and that should be done uniformly, and then we identified elements that were anecdotal and then could ultimately be subject to randomization. Although, we weren't going to try to randomize from this. We were just collecting information.

So we decided, if we could, to create an information system to do this. We started because you can't do everything at once. God knows we try, but we can't.

So we started with MCADD, and we developed what we thought would be a demographic database and condition specific data elements. So

this is 2005, '06, '07.

We created our sense of what the issues for short and long-term follow-up would be, and then we agreed how we would add additional disorders.

We tried to build this in a modular fashion so that once we had MCADD, we had sort of a model, fatty acid oxidation disorder, for example. We had the demographics, and then we added an aminoacidopathy and built aminoacidopathies from that. So we were trying to do it that way.

We wanted to have it accessible and easy to maintain, so we initiated our plans with a web based system, and we bought a -- we got licenses off the shelf for sort of a quality assurance program so that we could make this happen. And that was actually pretty effective.

The trick, the thing that we did that's different than what California does, and it's both an advantage and a disadvantage, is that we decided ours was going to require prospective informed

consent from the beginning. That was our choice.

We had family members that were sitting with us in these committees, and they said, you know, we need to know. And we want to participate. We want you to tell us you're doing it.

And so we do not have the denominator that California's project has because ours only, people only get enrolled if they say yes. So it may or may not be a complete ascertainment. It's a good thing and a bad thing, but it is what it is.

So we thought that would be useful, particularly because we wanted to be able to go back to families and say, we have something new we want to try. Do you want to be part of that? And this allows us to build that opportunity.

So we do have direct contact with the families because our clinicians enroll the families. They're both treating physicians as well as a part of our research team, always has its own problems.

I'm not going to, this is not to make you read all of these. This is to show you kind

of what we were thinking of, and this is partly because this is something we thought really hard about.

And we were really grateful for the support to be able to have the chance to do this. And these are the kinds of questions we wanted to ask.

Everybody had demographics, but we wanted to get things like pregnancy history and how long it was until somebody got to see a treating physician. And when did we start treating as opposed to when did they see somebody? Those are two different things.

So don't read all of these. It's just to give you an idea that we thought a lot about it in terms of trying to get things like sociologic things.

Everybody keeps on saying, well, did you ask this? Did you ask that? We had to ask the poor clinicians to be able to answer as much as they could without going absolutely nuts. So no, we don't have a lot of answers that now we maybe could

want. But it is what it is.

Again, we were looking, we tried to gather newborn screening data. That's harder to do than it thinks when you have to type it in by hand. That's a problem, so we're going to have to think about systems where we can make this more facile.

We, from the beginning, wanted to collect genotypes. Again, it depends on whether somebody gets it paid for because this data collection effort was not designed to pay for getting anything but the data entry. It doesn't pay you to get genotypes done.

We wanted to know about whether people were getting counseling, whether they were getting follow-up plans, whether they had sick day plans. These are things that clinicians need to know about taking care of patients.

And we wanted to know if they were alive. We wanted to know if they -- we were keeping up. We want to know if they were growing. We wanted to know how much they were going to the

emergency room.

These are some of the things. It's not surprising because as this moved on, we sat at the table with folks like Lisa and tried to make sure that we had some harmony in the kinds of things we wanted to know. So these are not surprising that some of these things overlap.

We really want to know about the developmental outcomes for our children. This was very important to us. We want to know if they have insurance. We want to know if they're using community care.

We want to know if they have healthcare referrals. We want to know what medicines they get, what nutrition they have. So all of these things were stuff we wanted to know.

The way we set it up is you had intake information when you enrolled them, and then they come back for each visit and we answer questions about them at each visit. So we also know about the density of care because there's a new form filled out for every time they visit.

So this is just a history just so you know date wise. We developed and worked on our long-term follow-up in the early phases of regional genetics collaborative and began to add centers when we had a Priority 2 project where we engaged other regional collaboratives to participate.

When we received NIH funding in 2011, we started with 13 NIH-funded centers, but subsequently added another 15 or so centers that were primarily funded by HRSA.

But anybody can come to us and say I'd like to gather this data, and we say okay. Do you have an IRB? So that's another thing. We'll have to think a little bit about how IRBs handle.

And so central IRBs are probably going to be a much more useful strategy for things like this because it's a lot of work even to get what is this expedited project, through multiple IRBs.

And then you get some, what do you call it, there's some entropy for what the consent looks like. So we -- people have already talked about this. I don't want to dwell.

I just want to emphasize the degree of collaboration that we had from clinicians all over the country to take this to the next step in creating the Longitudinal Pediatric Data Resource, which was a scale up of the data collection elements we had to incorporate more expert opinion and to really kind of reconcile some of the questions that we all have as clinicians.

So we adopted the Longitudinal Pediatric Data Resource after collaborating and creating it, and that's how we're collecting our information, using the REDCap data system instead of our off the shelf product at this point.

Our goals from all along have been to improve knowledge about the clinical history and to gather evidence about effective management. We're clinicians. We want to do a better job taking care of the kids.

So I've already talked about this, but just to remind you since it's got prospective informed consent, it's a bit of a sample of convenience. We gather this on web based program,

and this is just to kind of show you the accumulation of cases.

At this point, we're very close to 2000 enrolled subjects. Our largest dataset is children of phenylketonuria. We didn't start adding those until about 2007. We waited because they were industry databases, but everybody says, but we're not part of that. So I said okay. We'll do it.

And so that's our largest dataset. This really reflects to some degree the numbers of these cases in the centers. There's a lot more, PKU is a relatively common disorder, so we have lots of kids with PKU in the dataset.

MCADD turns out to be a very common disorder as well, and we started with it. So it's our second largest. We have really significant numbers of kids with VLCADD, nearly 100, which doesn't sound like much, but for a rare disease that's a crazy number.

So we're really happy about how this has grown. Again, not trying to look at everybody.

You can go over the slide and go what are all those things, but the other two big bars are galactosemia and biotinidase deficiency, just so you know.

All right. So what are we doing now, just to give you an idea? At this point, the Longitudinal Pediatric Data Resource, when we put this together, had nearly 2300 unique data elements.

We've filled over half a million data fields with our subjects. That's a lot. I don't want to go into more detail about it than that, but we also have datasets for special occasions, such as pregnancy, dialysis and transplant. So we're capturing information about those if we can.

So people know, because we had an NIH grant and five years is up, we've also hoped to begin to move this forward and have chosen a program project grant is one strategy for that.

The three projects we wanted to work on were essentially to continue our data and management collection activities to really emphasize the neurocognitive outcomes by focusing

on that as a project of its own and then to look at the subclinical disorders, the ones that everybody goes well, I don't want to screen for that, things like SCADD and DG and 3-MCC deficiency where everybody says, well maybe we don't need to screen for them anyway. Well, how do you know? Well, we hope to find out.

So the other thing we did was add a family core because we think that's critical to all the care plans that we want to create. We have some publications in process.

And again, I'm not trying to make you read these all. It's just to let you know we're trying to publish. And that's our public website. I'm just going to quickly talk about what this brings to me.

And now I'm going to get a little editorial, which is what we're doing now. Our original intent when we did this was to include conditions where you had early treatment and it made a difference. That was kind of where we started.

And that's true now for these new ones, but not so much. But some of the old ones actually we didn't know that either. We want to add conditions with effective treatments, and for some, yes and some no for that, but that was also true for our old ones.

We don't know that much about the treatment. So at first I was all up in arms when I started to think this out. And I said, really you know, these new disorders are only different in a couple ways.

So what's different? Well, the timing of therapies is somewhat different. People aren't really certain about when you might want to do infusion or when you need to start thinking about doing a transplant on X-lined ALD.

The effectiveness of therapies are less well established. The cost of therapies are spectacularly different. The timing of onset of the manifestations is very different. What's the real big difference? Well, the onset variations of the conditions.

See, I can animate, but it didn't work too well. Oh well. The point here is that this is an 800 pound gorilla. We've got a timing differential.

Lisa already alluded to that for the X-linked ALD, and that's true for all the disorders. And this changes, if you will, the locus of control.

And that's one of the discussions I think we need to have as a group is since we're all talking about the same kids and we all have a responsibility to them, how do we share that responsibility appropriately so it gets taken care of.

Where do we go? Well, we've added conditions that are late onset and have poorly characterized long-term interventions. We have limited knowledge of the timing and utility of early interventions.

We have no current infrastructure for long, long-term follow-up. We just don't have that. It just doesn't exist for really true

long-term follow-up through the lifespan. We don't have that.

And we have the added fill up of having conditions added by legislative mandate without an evidence review, yet we have a responsibility to those children as much as we do for the ones that were on the recommended uniform screening panel.

If we're identifying it, and it's being done by screening, we owe them follow-up. So we're not doing this. We can't get the elephant back in the barn. We have that responsibility no matter what.

So we have advances in knowledge that have to take place, and we have a balance. We have public health research, which is a responsibility to the population and the general good.

What does public health do? Newborn screening is a public health measure, but on behalf of the children that are identified, we have individual responsibilities.

And the clinicians who care for them have those. There's a relationship between you

and that person, that family and that child. You have a responsibility for those improved outcomes. So we have to find a way to acknowledge both of those things.

So my final words, we signed up for a bigger, more permanent job, but we always that. We just didn't do a very fulfilled job of it. It just really emphasizes once again our responsibility for the longer long-term follow-up. I don't know if there's a term we can use for longer long-term follow-up because we have a longer commitment.

Keeping up with people identified with long-term disorders will require a complex infrastructure. No matter who you assign that task to, someone's going to have to do it and we're going to have to do a better job. We owe the families this. We owe the families. We owe ourselves advancements in knowledge.

And so I'm hoping that we'll have some really constructive thought about how we can accomplish it. Like Lisa, I'm pretty passionate about this, so I know that all of you are as well.

Just to acknowledge by co-PI, Cindy Cameron, who's an inspired organizer and leader and cheerleader for all of this and the group at MPHI, the Michigan Public Health Institute, that helps us administer this activity and all the collaborating centers and the MBS chair and special thanks to them for all their hard work. And that's what I have for you.

CHAIR BOCCHINI: Sue, thank you very much, appreciate it.

(Applause.)

CHAIR BOCCHINI: An excellent presentation, and thank you for framing some of the questions for going forward. Thanks.

DR. BERRY: I didn't know if that was my job, but I did it anyway. Sorry.

CHAIR BOCCHINI: That's all right. All right. Quickly from the panel, Dr. Botkin?

MEMBER BOTKIN: So Jeff Botkin. Thanks for all the important work you've done over the years.

Two questions. Do you have a sense at

this point about whether your data and the California data can be combined in an effective way to answer some of these questions? And then secondly, if money were available, would it be necessary for other collaboratives to do something similar, or is it adequate for one collaborative to do a nice job and perhaps with California and a few states?

In other words, does everybody need to do this, or is it adequate to answer these questions to only have some people engaged in this?

DR. BERRY: Yes. That's two important questions. With regard to the marrying of the data, I looked over it, Mike, because one of the things that we've really had as a dream in the MBS chair is to be able to map the data from California to add to the longitudinal dataset.

So that is something that's very important, and we would really like to accomplish it. We're still working on the data exchange activities.

DR. URV: Yes. I actually emailed Amy

Brower and asked her that same question because Amy is our guru that maps all the different variables. And there is mapping that's possible.

DR. BERRY: There is mapping -- yes.

DR. URV: Some of the California stuff is at a higher level than this, like a 20,000 -- this is Tiina Urv, at the 20,000 foot level. And some of this work is a little more detailed, but you are able to map. And there's been some --

DR. BERRY: Yes. There's another important project going on --

DR. URV: -- work.

DR. BERRY: -- in the MCC to create a public health dataset, if you will, which is a subset of the elements in the LPDR, to target them at public health.

It overlaps very nicely with the question California asks, and the idea would be to map so that public health could use it in a far more denominator higher view. And then clinicians could be involved at the more detail-oriented strategy.

Now you asked whether one collaborative -- we aren't just one collaborative because that's just our seven states and we have others. I think for large and well-represented disorders you probably could get away with it. Although I would say, we are not ethnically distributed correctly to get the fullest scope of information. We need southwestern states. We need Texas. We need California. We need places where we have different populations because we think the outcomes could well be different when distributed differently depending on not just socioeconomic but other factors.

And the other thing is, for rare disorders, we don't even have -- we have 41. All of the primary/secondary disorders on the panel, we have datasets for them. Several of them sit empty now. To get data about rare, rare diseases, we're all going to -- we're going to have to collaborate even more effectively.

CHAIR BOCCHINI: Mike and then Bob.

DR. WATSON: Yes, I'd only add two

things. One is data storage is incredibly expensive with this magnitude of data, so we do ask questions about how much statistical power do we need to answer questions and stop collecting data where we can.

We'll have to -- the long-term data will reside in the EMRs, and eventually we'll figure out how to talk through those systems into databases to ask the questions we need to, but we're not quite there yet. They really bill well though, for the EMR systems. The other is --

DR. BERRY: It's really billing systems, not EMR.

DR. WATSON: Yes, really, sadly. The other point is that we have begun to talk to the states about interfacing into these long-term follow-up efforts.

We've been discussing it with 22 states now, and over the next few months there will be five states that will initiate pilot studies, fairly narrow studies of one or two conditions just to see how they could fit into the LPDR system of data

collection that we've been building.

So we'll hopefully be starting to tease out those five over the next month or so and begin to get some long-term follow-up going within the state systems as well.

DR. BERRY: Ideally, if you'd do that you'd be able to create it in such a way so that if a state did that initial data collection with the subset and then that individual was also engaged in our research project to open a conduit and not have to do things twice.

DR. WATSON: Yes.

DR. BERRY: That was always the vision. Whether it'll be realized is harder to note.

DR. WATSON: And it's one of the nice things about the IBMC studies is that they work -- and several of the institutions do work very closely with their states.

They may not be even among those states we're directly talking to now, but they're probably states that we should be looking at to integrate into this more state-based system because

obviously they can -- you'll have long-term data that can help them over time.

DR. BERRY: Yes. Some of our states actually have the Department of Health person as part of their IRB, and that person has direct access to their state's data and can download it. It's just not -- it's a denominator problem.

CHAIR BOCCHINI: Bob, I'm going to give you the last question here. Well, Dietrich. Bob and then Dietrich, and then we'll move on to the next presentation.

DR. OSTRANDER: Robert Ostrander, Academy of Family Physicians. I want to just share an observation and tie together Lisa's talk and Sue's talk, which was terrific, and Carol's question.

I think, Sue, your talk pointed out something we should be aware of as we're looking at trying to improve the long-term follow-up schema outlined in the initial article, and that is that we're not building a long-term follow-up system from scratch. We have a long-term follow-up

system in place whether it's good, bad or indifferent.

And if we're going to improve long-term follow-up and carry out some of the visions that we had in the Kemper paper and so on, we need to bear in mind there are systems in place already.

And if there are systems in place, the approach to changing and improvement requires good measurement at the front end, first of all to identify if there's a problem or not and not assume there's one, second of all, to decide where the problem is, third of all -- and I really applaud Lisa's ability to collect information at about the right level of granularity -- you have to decide which areas you want to intervene on, and then you need to be able to do an intervention and then test it.

So I disagree a little bit with Carol that tracking is not really what we were talking about because I think when the system is in place tracking and measurement has to be first step. And I think in my years with this group, I'm seeing that

approach start to gel, and I really am impressed with it because I think a lot of times we've jumped to action without measurement ahead of time.

And I really think that what you've both presented is going to be a great foundation for interventions that will be measurable and will be able to be carried out in a small enough and focused enough way that we can get something done and see things that matter.

DR. BERRY: Thank you.

CHAIR BOCCHINI: Dietrich?

MEMBER MATERN: Dietrich Matern. Great presentation, great points, thank you Sue.

When it comes to the next additions -- two additions like lysosomal storage disorders. There are registries out there already, and I wondered, are there any discussions ongoing with those and how those could be combined and made accessible?

DR. BERRY: So that's a point of difficulty. Many clinicians neither participate in that nor want their data handled and controlled

by an industry.

So there are already NIH-funded long-term follow-up projects or at least newborn screening history projects that are looking at some of those disorders. And they've been working actively with the MBS chair and to develop congruent datasets for those conditions that would be deployable in the LPDR.

Our group, the folks -- the clinicians in our group who live in states where they're already screening for some of those want to add those. So I think you -- we would like to find ways to reconcile the data from the registries. I think that would be foolish not to do so.

But I think we will move forward with collecting data about those disorders irrespective of that because not everybody participates in the registries. So it's more ways to get more data.

MEMBER MATERN: Just another comment about this. These registries are for patients that are diagnosed and have the disease, whereas in newborn screening now going forward we find

these patients that are of uncertain significance.

And so I think if there was a way for this group or patient advocates to kind of get these registries to be more open so that we can actually compare diagnostic results, be it genotypes or enzyme activities in newborn screening, et cetera, I think it would be extremely helpful for their programs to go into screening.

DR. BERRY: Couldn't agree with you more. More data supports those children. Absolutely. Mike, maybe, I know has worked very hard on this point.

DR. WATSON: Yes. It's a bit of a financial disconnect. The registries for the four LSDs that Genzyme maintains, they operate a system that costs about $15 million a year and has way more FTEs associated with it than we do in the NBSTRN. So we haven't been able to actually figure out how to integrate.

What we're looking at is just mapping. Is it possible to share data so that when a clinician or the states are entering data into a

registry, can we map across those so that they do it once and we exchange data? It can go into the LPDR and then into the registry or vice versa. Though I'd obviously prefer NBSTRN before the private sector data first.

CHAIR BOCCHINI: Kathy, one quick comment. Then we're going to move to the next presentation.

MEMBER WICKLUND: I hope it's quick. Well, it's a question. Can you guys comment a little bit more about public-private partnerships and thinking about how that could work if funding is so difficult from grant funding to keep this going? I'm sure you guys have considered partnering with PhRMA or -- and what your thoughts on the positives and negatives of that.

DR. WATSON: We've thought about it.

DR. BERRY: We've thought about it, too. Part of it has to do with control.

DR. WATSON: These registries go back decades. I mean this is not a new registry for the LSD. Some of these go back 20 years, I think. So

there's a retrospective aspect to it that's extremely expensive to get a handle on. And they've gone through probably two or three iterations of their data systems that further complicate trying to integrate everything.

But no, public-private partnerships are probably the best way to try to get at this. And hopefully we'll reach the point with NBSTRN where we have enough volume to be able to encourage that relationship.

DR. BERRY: Yes. I think you need an honest broker in that setting. You need to be able to make sure the data's freely accessible to researchers. So, and understandably, industry has a proprietary interest in their data. So we have to find a way to reconcile that differential, in my view.

CHAIR BOCCHINI: All right. Thank you again, Sue, for a great presentation. Let's bring Ms. Christine Brown forward. Christine Brown is the Executive Director of the National PKU Alliance, a nonprofit organization working to

improve the lives of individuals with PKU and to pursue a cure.

Through her leadership efforts since 2009, the Alliance has emerged as a leader in advocating at the national public policy level for access to lifelong treatment for PKU and other inborn errors of metabolism, launching a robust research and fellowship program to accelerate the next generation of therapies and creating comprehensive systems of support for assistance to both families and adults living with PKU.

So Christine, thank you for being here.

MS. BROWN: Thank you for the invitation. So I'm here to give you a parent perspective on long-term follow-up and perhaps a larger view and to share a little bit of our personal story as well as our experience at the National PKU Alliance.

So first I'm going to start with a question. So how many of you have pictures like this at home, either of you or your wife? Everybody has those pictures of when your child was

first born.

And so these are pictures of my two children with PKU when they were born. Connor was born in August of 2005, and Kellen was born in August of 2007.

And so I have to ask you, when you think about those pictures and you think back to those days when your children were born, what kinds of questions did you ask yourself that first day when you held that child in your arms? Did you think, you know, does this child look like me? Does it look like Grandpa? Whose nose does he or she have? What sort of ears? Did they get Uncle So-and-So's ears?

You probably also asked some other perhaps more philosophical questions, like what is this child going to grow up to look like, to be? How is this child going to make its mark on the world?

And I asked all those questions when Connor and Kellen were born, but I also asked some additional questions. When our oldest child was

born, who is now a teenager, in this picture he's very young. When our child without PKU was born, I never asked, will he look normal. Can he go to school? Will he need special accommodations at school? Can he play sports? Can he travel to foreign countries? Can he go to college? Can he get a good job? Can he get a good job that requires him to take clients out to dinner? Can he get married? Can he have kids of his own?

And maybe you did ask some of those questions as well, but instead of can, you probably thought will. Right? Will he play sports? Will he go to college? When you have a child that's born with an inborn error of metabolism through newborn screening, those wills turn into cans.

So I think when you're looking at long-term follow-up, you're looking at data collection, you're seeing the numbers with PKU. It's like oh, PKU, this is a success story of newborn screening. Right? I mean we have now been screening for PKU in our country for more than 50 years. Asbjorn Folling discovered PKU back in

the '30s.

We estimate that there's about 15,500 Americans living with PKU in our country right now. Of those, we estimate that about 8000 of them are being treated for their PKU. They're in a clinic relationship, but almost half of them are lost to follow-up. And so the question is why?

Well, back in the 1970s when there was really no long-term follow-up at all, the medical community believed that by the time these PKU children reaches ages 7 or 8 that their brain was fully developed. And so there was no detrimental effect to have these children discontinue their PKU treatment.

So this is Dr. Koch who for many of us in our community is really a hero. And so again, I am not a medical professional, but when I think about PKU and I think about long-term follow-up, the first long-term follow-up projects that really occurred in PKU were with the collaborative studies that Dr. Koch led.

The first one, the national

collaborative study back in 1976 to 1984 and then also the maternal PKU pregnancy outcomes study. And what he found and what his team found through those first long-term follow-up activities was that when you took these kids off of diet, off of therapy at age 7 or 8, they had a loss of IQ. They had a decline in their school performance. Many of them developed psychosocial issues, depression, phobias, schizophrenia, epilepsy, tremors, paresis and then of course we have maternal PKU syndrome.

So it was really these early initiatives and long-term follow-up projects that led to the recommendation in PKU that dietary therapy is for life. But in the meantime, because there had been no long-term follow-up, we lost at least two generations of adults.

The adults on this screen are lucky. They were able to get back on diet, but Kay in the purple shirt who lives in Wisconsin, she has a walker. She has some physical challenges. Frank actually lives with his sister Marcine in Nevada,

so he's unable to live on his own.

And Debbie is doing really, really well, but she also has some neurocognitive issues. And I hear from Debbie about three or four times a week, and she emails me about her softball games and what her mom is doing and what her dog is doing, but we lost at least two generations of PKU patients.

So I think until maybe seven or eight years ago or ten years ago, I really feel that there was this prevailing culture or belief in our medical community that PKU was solved. Right? We screen for them. Every state screens for PKU. We put these kids on diet. They're fine. Let's move on to the next thing. Let's move on to the next inborn error of metabolism. Let's move on to other research, other diseases, et cetera.

And so even with those collaborative studies that happened, they ended. And so there was actually little long-term follow-up, again, within our community. And so I think that this has obviously changed in the last seven to ten years

as more data has been collected, as people began to get more interested in research.

And at the National PKU Alliance, we've only been around since 2009, but I think that what we've learned in the last seven years has really surprised us. And this past summer we decided to do a survey of our patients. And really, the purpose of the survey was to look at patient-focused drug development.

So as an organization we thought, we really think that the PKU community wants new treatments. People on our board believe that new treatments are important, but we really never asked the community if that was important.

So we were very scientific. We did SurveyMonkey. We put information out on our social media pages and to our patient database within our organization to really get an idea in terms of what patients wanted in new treatments. We had 625 respondents. 53 percent of those were parents, and 47 percent were adults, so pretty good range of experiences.

And I have to say that what we found out was really, really interesting. And I think again in my non-scientific manner, the people that responded to our survey, these are engaged patients. Right? They self-selected to click on that link.

These are patients that are aware of the National PKU Alliance. They attend our meetings. They're involved in our advocacy work, in our educational programs. I mean 86 percent of them reported having visited a metabolic clinic to receive PKU care in the last year. Only 8 percent had said they hadn't visited a clinic in more than two years. And almost 62 percent said that they had drawn their blood in the last month to monitor phe levels.

So these are good patients. These are engaged patients. They know what they need to do. They know they need to be on treatment. They have support around them. And what's really interesting is that even though people really knew what they needed to manage their PKU effectively,

challenges were evident in terms of the current therapy.

So this is a graph that shows the number of children and what they reported their blood phenylalanine levels to be. So this says PKU patients under the age of 18. Now you all might think, well this looks pretty good. 68 percent of children had their blood phenylalanine levels within the recommended range.

What really surprised me is that 25 percent of them didn't. And PKU is, I think, the easiest to manage when these kids are little. Perhaps this isn't as surprising to clinicians in the room, almost 62 percent of adults reported that their blood phenylalanine levels were above the recommended range.

And so again I go back. I remember still when Connor was born in 2005 I was told, hey, we screened for PKU. He's going to be fine. We're going to put him on dietary therapy. He will grow up, and he will be just fine. We have an effective treatment. And we do have an effective treatment,

but what we're finding, I think, through research and data and long-term follow-up is that actually while this treatment is effective, it's not optimal.

In the survey, 91 percent of patients said that new treatments were important. That goes to show that something is there in terms of why the current treatment is not optimal, and what is it that these patients are suffering from, or what is it that they want in terms of new treatments?

So this table shows we did a forced ranking and said what are the most important things that you want to alleviate. Or what are the most important results that you want to see when considering new treatments for PKU?

Obviously it makes sense, 87.5 percent said a drop in blood phe concentrations was very important to them. And then after that it's some of the things that we've seen because of long-term follow-up activities that have occurred.

People want new treatments where it

increases ultimately their attention span and ability to focus. They want to see improvement in their executive function skills, such as the ability to plan, organize and prioritize. They want new treatments that address the issues of depression, anxiety or ups and downs in overall mood, treatments that help increase their processing speed, increase in energy, memory, et cetera.

And it's interesting because I think that this really tees up nicely to what we're finding now in terms of the research out there and as more data is collected on long-term follow-up in PKU. We now know that dietary therapy doesn't control phe levels within the recommended range for many, and that that becomes more difficult as our patients age.

We're also showing through research that there's actually differences in the white and gray matter in the brain of people with PKU, well-controlled people in PKU versus the white and gray matter of their non-PKU siblings. Research

and I think some of the long-term follow-up data is showing that even in well-controlled children, there's still a slight decrease in IQ. There's issues with executive function, processing speed and emotional regulation, again, when compared to their siblings and also a higher incidence of anxiety, ADHD and depression in the PKU community versus the general population.

And so it makes sense, when you look back at that table and what people want, it lines up nicely with some of what the research is showing us.

So this was taken a few years ago. This is Connor and Kellen in from of the tandem mass spectrometer at our screening lab in Wisconsin. And saving babies' lives does not end with the newborn screen. It is just the beginning.

And I know that a lot of this is very difficult in terms of data elements and what you collect and how you collect and what you look at and how you look at it, but it's really the long-term follow-up and how you're measuring

outcomes and what you're seeing those outcomes to be that's the most important.

And I do hope that as new conditions are added to the RUSP that you don't make the mistake that happened in PKU where we lost at least two generations of adults.

Have that long-term follow-up in place so when you see other issues arise, it can be addressed. It can be further researched in the medical community, and you don't have that delay like you did in PKU. Any questions?

CHAIR BOCCHINI: Thank you very much for doing this. You've given us the most important perspective related to newborn screening, so thank you. So other questions from the committee? Jeff Botkin?

MEMBER BOTKIN: I wondered what your -- whether you have feedback what the nature of the concern is these days about the children of adult women who have PKU and whether there's long-term follow-up and data these days about any impairments that those kids are experiencing.

MS. BROWN: There's been -- there's a project that we did fund at the Alliance looking at children that were born of adult women with PKU. Some of that research is showing that even those that were well-controlled, there's still some issues in terms of head size, some developmental delays.

Within maternal PKU itself, I still think that is a huge issue in our country. We run an emergency assistance program for adult women with PKU who are pregnant who can't get access to medical foods while they're pregnant.

And through that application process, a number of those women, this is maybe the second, third or fourth time that they've been pregnant. And the outcomes before have not been good because their phenylalanine levels were too high.

I'm not aware of at this point any national statistics which show how often still maternal PKU syndrome is occurring.

CHAIR BOCCHINI: Carol?

DR. GREENE: I'll add my thanks and

also add that I would be interested to know how many of -- and it looks like you did ask in freeform, but did not report in the paper -- how many people are having trouble keeping levels in control because of trouble with access to formula?

And I know you have another paper about that, and that was more of a rhetorical question --

MS. BROWN: Right.

CHAIR BOCCHINI: -- because what I really wanted to add is that, again, the long-term follow-up data outcome is important, but we're actually still losing -- not a whole generation, but we are still losing people exactly as we did in the '70s and '80s, not because we don't know but because they don't have insurance that covers.

I mean they have insurance. Everybody's got insurance these days, but we can't get the treatment. So we're still losing people, and from the point of view of a clinician -- and I think the parents and families would agree -- that for me is a fundamental issue of long-term

follow-up.

MS. BROWN: Absolutely, and usually when I talk before this committee I'm always talking about medical foods reimbursement. And again, I think, you know, I want my children to have every opportunity available to them just like you all want that for your children.

And Connor, the guy in the badger shirt on this picture, he couldn't decide a couple years ago if he wanted to become President of the United States or Pope. And I basically -- well first of all, he's also pretty popular with the girls. And I said well, to become Pope you have to be priest first. And he's like, okay. I'm like, well if you're a priest you can't kiss girls. You can't get married. He looked at me. He's like, well Mom, as Pope I can change that. Right?

And I say to him though, like he would have better chance of being Pope right now because he can't be President. You know why he can't be President? Because the federal employee health benefit plans only cover medical foods up until the

age of 21. He wouldn't have his care. I'm sure he could get his care in Italy. He can't get his care right here in Washington, D.C. So Pope it is.

CHAIR BOCCHINI: Cathy and then Don.

MEMBER WICKLUND: I want to thank you for your presentation. And I also just want to like emphasize I think the point you're trying to make, which is we talk about like there's treatment and there's formula, but it's like not fun. Right?

I was like a camp counselor for PKU for like five years in Texas, and I had the adolescents. I had the teenage -- it's hard to believe. I know. And I think the idea that we think like oh, it's a diet, da da da.

And I think trying to change that attitude that they are looking for some other treatment besides what we have currently available. Right? I mean that's kind of what you're --

MS. BROWN: Absolutely. And that's again that's why --

MEMBER WICKLUND: -- talking about.

MS. BROWN: -- long-term follow-up is so important. I mean as Sue said in her presentation, advancement in knowledge is what long-term follow-up is about. And that's what we need. And that's what we're finding in PKU now.

Yes, every day I'm fortunate I live in the country where I do where we had newborn screening and it caught this. And my kids will never be severely intellectually disabled like the children before them that weren't screened or if they were born in China or some other place.

But at the same time, with some of the data that we're seeing, I want them to be 100 percent. 75 percent isn't good enough for me.

MEMBER BAILEY: Don Bailey. Thank you also for the presentation. I think the lived experiences of people with screened conditions and their families is just really so very important.

So in your sample you had, over half of them were parents or caregivers. It sounded like the data that you were presenting was primarily from the people who actually had PKU themselves.

And did you ask the parents and caregivers a different set of questions?

MS. BROWN: No. Everyone was asked the same sort of questions, and I do have some of those responses broken down. I guess what was interesting to me, too, was I really thought going into this that those people that had high phenylalanine levels or said that their treatment was very challenging, that those would be ones who were most interested in new treatments.

And even though they were, the highest percentage was actually of parents of children who maintained good control. They wanted more new treatments even than adults that were struggling.

CHAIR BOCCHINI: Bob? Okay.

DR. OSTRANDER: I appreciate it. Thanks. I'm Robert Ostrander, Academy of Family Physicians. I think what would be interesting for us going forward as we look into these more subtle neurocognitive behavioral health issues to try to tease apart the contribution of the substrate related to the condition itself and the

contribution of nurture, that is, how these kids' early childhood is different.

As a parent, I guess, of a child like this you have to be more concerned. You have to helicopter a little bit more than you would otherwise, and obviously they have to step up and do certain things, get their fingers pricked and all these kind of things.

It's certainly very clear that early childhood exposure to those kinds of things increases long-term substrate at those domains that relate to anxiety and mood and concentration and so on. And again, it's not our place to solve that here, but I think it's worth remembering that the substrate is modified not just by the disease but by the disease experience in people.

And before I close, my little boy wanted to be either a general or CEO of McDonald's. That was his two choices. I mean he'd probably skip the lead-in stuff. He didn't want to flip burgers, and he did not want to be a private.

MS. BROWN: Very nice.

CHAIR BOCCHINI: All right. With that, I think it's time for us to take a short break. We're going to take our 15 minute break, and then we're going to bring the speakers back up front and continue the discussion and see if we can come forth with some additional comments from all.

Thank you. So we'll be back at 11:25 sharp.

(Whereupon, the above-entitled matter went off the record at 11:12 a.m. and resumed at 11:32 a.m.)

CHAIR BOCCHINI: So first, can I get the three speakers back up to take seats in the chairs up front. Okay. Thank you. We're missing a couple of key people. Sue. We've got everybody. Okay.

All right. Thank you all. Let's -- we have our speakers in place. I just wanted to introduce everyone to Catherine Spong. Catherine is now going to sit in for NIH. She's the Acting Director of NICHD. So welcome.

So Amy, are you still on the line?

DR. BROWER: Yes, I am.

CHAIR BOCCHINI: Okay.

MS. SARKAR: Cindy Hinton?

CHAIR BOCCHINI: Cindy, are you there as well?

DR. HINTON: I am, but I'm muted.

CHAIR BOCCHINI: Okay. All right. Sounds like you fixed that.

DR. HINTON: Oh, okay.

CHAIR BOCCHINI: So now we'd like to just continue the discussion, and I think we've had excellent presentations to give us some background information, some of the key issues, and a number of key points have already been discussed are open for further discussion. And so let's go ahead and see if we can continue this discussion and use the expertise of the -- of our panel. Joan?

MS. SCOTT: So let's see, how do I want to phrase this? So what are the points of -- in looking at a big systems approach, and where does public health end and the clinical systems touch what we're doing and locus of responsibilities?

And this is a broad question, I think, for everybody. Where -- what are the potential data systems that we should be also looking at and attempting to build sort of the bigger system that can answer the questions that we have about our kids, but we could ask about other kids as well who have special complex needs?

Do you want to start?

DR. BERRY: I'll try. This is Sue Berry. This is, that's the -- that's my elephant and my gorilla. And actually I had a whale in one presentation where I made the whale come in because that's the big question.

And I guess what I'd say is -- and I'm not that techy -- honestly we need to really be very creative and thoughtful about ways to create linkages because again, this is all -- the kids with special healthcare needs are often these kids but kids like them.

So I think we need common languages. We need ways to share the information. We need fair and comprehensive access to the data so that

the people who really need it to use to think about things have access to it. We need to be able to pay for storing it. We need to be able to support entering it. It's expensive. It takes time, and that's really a tough piece of it.

So to the degree that we can automate ways of gathering that information, as Mike alluded to, with things like electronic records, we ought to be really exploring those things actively. These are big questions, and those are big global answers, but those are some of the things that have come to mind in my personal consideration of it. Lisa?

DR. FEUCHTBAUM: I think that's all important. With some of the work with did around hemoglobinopathies with the RuSH and FRESH projects, which many of you may know about, we did some very interesting, creative linkages and were able to develop profiles of the population of people living with sickle cell disease in California, not just newborns, but across the age span. So that was a successful project. It has

its limitations, and so it's not perfect. And it's hard to get those linkages.

Technically, it's a challenge to make sure you've got the right people connected to the right people and deduplicate them at the individual level. So that's a way of going.

In terms of some of the new disorders on the horizon, I've had thoughts about this idea of partnering with primary care providers, and we've been experimenting with that with a HRSA grant that we have around primary congenital hypothyroidism.

And it's again, each of -- engaging primary care providers seems to be a natural way to go using REDCap for data entry. But again, how do you make it a successful system, provide incentives for providers to get onto the computer and report the lab results. That's the system that also could be done in a consented environment, so that works nicely.

So working, I think, thinking creatively, maybe working directly with families

is really ultimately the way to go. Really partner with the families in the way that some of those registries do but as public health programs begin to consider ways to partner with families, again, pediatricians and then all the data linkages that exist within the system already. So it's not one easy answer to your question, Joan.

MS. BROWN: I would just add that I think it's important that patients have access to that data and what the results are because it helps us answer some of those quality of life issues that we had when we first held that newborn in our arms and that front in center. Any data that's going to help us look at the future picture of our child and what he or she may be challenged with or may not be challenged with is only going to help increase ultimately the quality of our kids' lives.

CHAIR BOCCHINI: So I have Cathy and then Don.

MEMBER WICKLUND: This is just a follow-up question probably on Joan's question and might be unrealistic, but has there been

discussions in working with like EDWs or HI -- you know, health information exchanges in different states? I know that's, or existing EDWs and --

DR. FEUCHTBAUM: Well, it's been -- yes, there's certainly a lot of talk about doing those things, and we're trying to do some very fundamental things in California, just reporting out results of newborn screening electronically.

So we're trying to do some very fundamental tasks right now using electronic health information exchanges. It is very challenging to set up these systems. So we're doing really the fundamental work, but in terms of collecting complex data using HL7 messaging systems that Alan has referred to and presented to this committee in the past on, it's challenging.

It's a lot. For me, it seems like a long way off that you're going to be able to collect that level of detail electronically.

DR. BERRY: As much as anything, it depends on having a place to put it and a way to transmit it. I mean we've done some stone knives

and bear skins kind of things like creating common Epic templates because most of our groups are in Epic, and so we created a common template. The data enters into it, but it turns out you need to have a back piece to that that you populate and then create. You have to actually do it in reverse. You have to fill in the data and then create a note from it.

That being said, obviously that seems like a straightforward thing to do, yet it hasn't happened. So all of us would like to see that happen, of course, because why do things twice ever, which we do all the time.

The other thing I would say is that I know that others have created strategies for trying to have families be able to participate in entering data. I think that those data elements are quite complementary to the ones that are gathered by clinicians. You're not going to get the same perspective, but you're definitely going to get complementary perspectives that are really critical.

So I would urge that when we plan these things that we always make sure that families are engaged so that we're answering the questions they want to know the answers to, beyond what we want to know the answers to. Sometimes they're the same, and sometimes they're not.

DR. BROWER: This is Amy Brower. I think I mentioned in my presentation briefly the data linkage project that one of the RCs did, the Heartland. And the idea there was to sort of a survey of public health and to see what kinds of information they routinely collect.

Like some kids are on Medicaid/Medicare. They already collect information on are they in care? Have they gotten their immunizations? Are they getting medical food? Things like that, so we're trying to see if there's already systems in place within public health that we could harvest the data and answer some of the questions.

DR. HINTON: And this is Cindy Hinton, and I will add in something that's even broader than

that, and this is going back to what Joan had asked about what are some of these broad systems changes.

One of the things that Christine brought up is how will my son do in school? What about a job? And I think these are data systems that we've had real challenges accessing and get that kind of follow-up.

I think it's a public health issue. I think one of the reasons why we're working on this is, how will that child with PKU do in school. And that's a hard data set to get access to. And I think it's a key outcome that people are interested in.

So, no easy solutions to that, but I put that out there. There are other outcomes that go beyond the clinical outcomes that are going to help those kids do well in school or do well in jobs.

But then having access to data or having that kind of follow-up to show that people are doing well or what needs to be done to help them to do better, that's part of the whole system approach as well.

CHAIR BOCCHINI: So I've got Don, Jeff, Steve and then Carol and Mike. And then we're going to have a microphone set up so that people from the rest of the room can go up to the mic. And we'll, yes, so that we can hear and all. Let's go through the committee members first.

MEMBER BAILEY: Obviously no one's interested in this topic really, so --

CHAIR BOCCHINI: Yes. Bad choice.

MEMBER BAILEY: Don Bailey, a member of the committee. So I'm pretty sure I know the answer to this question, but I'm going to ask it anyway because I think it's important. I was looking at the screen.

We're the Advisory Committee on Heritable Disorders in Newborns and Children. And so obviously a number of the disorders have some consequences for families, cascade testing of other family members, maybe people being identified that never expected certain things.

And certainly as we have conditions where there's carrier status being detected, like

CF or some of the other conditions. So my guess is that this is research that is going to require interactions with families to truly understand this.

But kind of the cascade effect of some of these conditions in families to me is an important gap in our literature, an important gap in the newborn screening cube because I think we focus immediately on the baby, a little bit on the immediate family. But there's a much broader community, a family community that I think is very important here.

DR. BERRY: This is Sue Berry. I couldn't agree more, but one of the things that's a little odd about this is since they're recessive disorders, while there is some cascade, it's not as profound a reach as it's going to be as we add X-ALD, which is going to really substantively change some of the paradigms of how we need to facilitate exchange of information for families after newborn screening.

Because right now we, you have kid, and

it's one in four and two thirds for the siblings and have a nice day. And that's, I'm slightly being flip, but the minute you add something where there's multi-generational impact, it's going to really bring a whole new level of responsibility and care. And that's going to continue to accelerate our need for that kind of interaction.

That being said, there is impact. We have young people growing up who have these disorders who want to get married and then have babies. And who's going to make sure that their spouses get tested?

We just had a family where a spouse was a heterozygote for the disorder that the person had. If we hadn't tested, well, it would've been screened.

But still, it would've been an unpleasant surprise. So I mean we have longer responsibilities. So it does have a cascade effect through time as well through people.

DR. FEUCHTBAUM: Well, we do offer for sickle cell and the hemoglobinopathies in general.

And cystic fibrosis in particular we do offer follow-up counseling for people determined to have basically carrier status.

And the uptake hasn't been huge, and so it makes you wonder why when we have a program in place to pay for follow-up counseling, trait or carrier counseling. What's going on?

Is it people are going onto the Internet and getting the answers to their questions addressed? So we don't really know, and it really goes to the larger issue of providing genetic services really in a larger, you know, making genetic services a priority and how to integrate genetic services into general practice of medicine so that these conversations are had and the knowledge is out there and readily available to provide to families.

And we don't know how well that's happening, but that would be a great project I would think.

CHAIR BOCCHINI: Jeff?

MEMBER BOTKIN: So Jeff Botkin. I

think your presentations just are a good reminder that we spend a lot of time about bringing new conditions onto the RUSP, but there are a lot of issues obviously for the conditions we've been screening for 50 years still.

And that's not to say that the committee hasn't done a lot of good work, and this has been a longstanding area of interest for the committee. But I guess I'm interested in whether you have any specific recommendations for the committee at this point based on the work that you're doing today.

Is there something that you see the Advisory Committee ought to be doing in this domain?

DR. BERRY: I am sort of talking while I'm thinking. This is Sue Berry. So I would say that we did, as I observe it, the committee has known that this was a responsibility for a long time because they do have a full subcommittee that's devoted to this activity.

And that subcommittee, when you heard the things that Amy described, they've done a lot

of substantive work to identify sort of what the frameworks are, what we should be thinking about as a system.

So I think we're actually, got a good start. Yes, Bob mentioned there are some things that aren't broken, so we don't need to fix them. And some of those things we do have, but what we really haven't talked about at all is practical and thoughtful ways to actualize some of that activity.

It's not the committee's responsibility to do that action, but in analogy to the public health impact for the new disorders, we haven't ever done a larger impact assessment of longer-term follow-up.

And so I think that's one of the things that we may want to think about. Again, this is at a very high level. What are the systems that need to be in place, and how do you accomplish those systems so that you can fulfill this responsibility that we basically took on by screening.

The things we owe, I mean we identify it and then we don't give them their stupid

hydroxocobalamin injections, for God's sake. I mean, people, let's do this. Let's take care of these folks. So, you could say that over and over. How do you make sure it really happens for these families?

DR. FEUCHTBAUM: Well, an issue that is reemerging, especially with some of the work around the common rule and those discussions is there seems to be, I don't know if I want to call it a lack of trust but there's a need to recognize public health as really the honest broker of the data that's out there.

And we just come upon barriers all the time that seem to have a lot to do with trust and even families feeling that big government should stay out of my private business. And I don't want my data shared. I don't want my specimen shared.

And sometimes it just takes a discussion with those families, and they say oh, you guys are actually really doing something important. And I've completely had a turnaround in my view because I have conversations with

parents fairly frequently when they call to complain when they hear that, for example, we're storing the blood specimens of their children.

But just having that conversation really turns people around. People are distrustful of government, and if there were some way for the committee to promulgate policies or programs to encourage more discussion between the public and the public health genetics folks about why all this is important and why they do need to trust us and that we are really trying to serve the interest of the public.

And we're not trying to do anything nefarious or evil beyond the scenes. And so maybe it's just policies that would promote more dialogue and discussion in an open way about how advances in genetics could positively impact people's lives.

So if there's a way to make that happen, that would be great.

MS. BROWN: I also think that there continues to be a disconnect in terms of, newborn

screening in and of itself is covered by health insurance companies, by the Affordable Care Act, et cetera.

So there's an importance and there's a responsibility there. But then again, when it comes to access to treatment to treat these conditions that you've screened for, there's not that same follow through or commitment to these children to ensure that they have access to the treatment that they need to alleviate the most serious consequences of the condition that they have.

And that's my second point; I know that there's been several times where it's been pointed out that the committee looks at this through age 21.

And that's been brought up, well, PKU in my kids doesn't go away at age 21. I mean I'm hoping that with the long-term follow-up, right, that you're collecting data.

You can't throw these kids out at age 21. We don't know what happens. I mean, is there

an increased risk of other issues and other things happening? So while I understand that the main focus is on infants and children, I've never known an infant who doesn't grow up and become an adult.

CHAIR BOCCHINI: Steve?

MEMBER MCDONOUGH: Dr. Botkin basically asked the question I had. What do you want this committee to do in the next year, year and a half on long-term follow-up? Any recommendations you would like us to make to the Secretary or to states?

DR. BERRY: So I think from the clinicians' point of view, since we're going to talk about what's happening on the short-term, what can we do now, I'd like us to see if we can encourage the participation in projects like the one that NCC is trying to put together where we get data at a 10,000 foot level so that we can have other states get anywhere close to what California and New England have done.

Not everybody's going to be able to do that, but if we could even get a baby step towards

having more uniform information available from states, it would be a tremendous advancement.

So finding ways to get that framework moving forward, and states would be, I think, really powerful. And that's hard because every state does what it can do, and that's tough. 11:55:27

DR. FEUCHTBAUM: Yes, and just to build off of Christine's comment, the availability of medical foods just keeps on coming round and round the same issue.

Even our committee, our subcommittee did a report on that, and I don't know if your group is able to really make a strong recommendation that medical foods can be mandated through insurance coverage.

I know it sounds maybe naive for me to say it, but I don't think that's been dealt with properly in the Affordable Care Act. And it's not considered an essential coverage item, and so I think there's a real fundamental problem there.

And you're going to screen for

disorders, you have to have the treatments in children up to 21, and of course beyond 21 seems obvious. So that seems like if we can make more progress in that area, that would be huge.

DR. HINTON: And this is Cindy Hinton. Going back to what Sue had mentioned in the discussion, data sets like the Genzyme dataset, I mean this has just come up recently here with a colleague that I work with wanting to know what is in the Genzyme set.

Is it worthwhile for us to pursue an activity when Genzyme's already collecting data? As we look forward with the rare conditions, I don't know what kind of role the Advisory Committee could play in helping broker discussions.

But I think that's going to be a really important issue for the committee and the newborn screening community and outcomes to look at datasets like that. And so I just throw that out there as well.

CHAIR BOCCHINI: So obviously we're going to have continued work and discussion with

this over the next couple of meetings and then perhaps some recommendations from the long-term follow-up committee to address some of these issues. So I think that was a good question.

So, in the interest in time, what I have here is Carol, Mike, Debbie, Natasha and then Anne at the microphone. And then that will, we'll need to stop so that we can go to the next segment for those individuals who wanted to make public comments to the committee.

So we can end in enough time for people to get ready for the different subcommittee and workgroup meetings that are going to follow. So let's go to Carol.

DR. GREENE: Thank you. Carol Greene, Society for Inherited Metabolic Disorders. And I originally raised my hand when Joan asked a very interesting question, and that's what I want to say something about.

But I also do want to say that the conversation moved on from there, and I think that possibly what I'm hearing from the panel is that

there's more than one avenue we need to be looking at.

So we need to be collecting more data to be sure that anything that we change is evidence-based but at the same time, and I think the, Cindy Hinton and Amy Brower's presentations summarize that there's actually already been quite a lot of data.

And there are some things that we do know, like problem with access to therapy. And so we really need, I think, to be working on what do we do about, what do we do with the data we've already got as well as how do we get more and better data in the future, which is where I raised my hand originally.

And that is, I understand there are huge technical challenges. And I think one of the things to think about and that there should be ways to do is to tag data. When you bring things together, I think that there are huge differences in what's collected.

There are different denominators, so

Christine Brown pointed out that the survey that they have are from the people who are engaged. And so if you could ask the people who are lost to follow-up why were they lost, you'd get different answers.

So I think we have to, if you ask parents around satisfaction, you're going to get really different answers than what some doctor or nurse thinks that they think.

And you also might get different, somebody might say my child has PKU, and in fact, it was an abnormal newborn screen for thyroid disease, but somebody called it the PKU.

So I think we have to pay a lot of attention to the N and the quality of the data. And to do that as we merge things, I think we have to tag where the data came from, what were the assumptions, what are the limitations and that we have to be really, really clear when we're reporting about which subsets of what data.

CHAIR BOCCHINI: Okay. Mike?

DR. WATSON: So only a couple of

things. The questions about educational outcomes are going to be important in a lot of these chronic diseases, so I think getting a better understanding of how FERPA constrains getting that kind of information, the Federal Educational Rights and Privacy Act or something like that.

I think it's important to understand that because there are some huge impediments to getting access to certain kinds of information. And then it's probably worth going back and just getting a lay of the land now.

The National Library of Medicine went after newborn screening back in 2008 and '09, put together an entire coding manual that gave uniformity to the communication of information from newborn screening programs, results of tests with standardized languages, and they can communicate across the states and provide that information in a standardized way to providers.

The Newborn Screening Translational Research Network works with the National Library of Medicine. So as we develop our data elements

in projects like Sue's and the other grantees, we're able to take those to them because ultimately, they fund things like SNOMED and LOINC that are the programs that establish the way EMRs are going to collect data, what is the information. How is that information standardized?

So ultimately EMR vendors have to accept those standards, and they become part of their systems. So I think getting a better understanding of where we are in being able, in having developed some standards for either data or for the systems that can be applied to newborn screening because it is the IOMs chasm between public health and private care providers.

I mean that's one of the bigger chasms identified was that data sharing across those kinds of entities.

So I think just getting a better lay of the land as to where we are now on creating this kind of an infrastructure and the compatible data standards under them would be useful to think about where you go next.

CHAIR BOCCHINI: Thank you. Next I have Debbie Badawi.

DR. BADAWI: This is Debbie Badawi from MCHP. This is going back to Joan's question, I guess, about the division of responsibility or roles in long-term follow-up.

And this is overly simplistic, but it seems we have kind of two categories of long-term follow-up. One is the clinical follow-up to make sure we don't lose generations of young adult kids and young adults because we're not aware of the proper treatment.

And to me, that's kind of separate from the role of this committee, which is looking at more the public health impact in terms of are kids getting the care that they need, whatever we know right now is the care, which we realize may change in the future. Are they getting the care they need?

And I think partnering with Title 5, Children with Special Healthcare Needs, would bring together resources from a couple of different

sectors because the kids in general, kids with special healthcare needs obviously are facing the same types of barriers to care, inadequate insurance, care coordination, geography, all of those things that are barriers for families to getting care. So that's just something I want to put out there.

CHAIR BOCCHINI: Thank you. All right. Next I have Natasha.

MS. BONHOMME: Okay. Thank you. Natasha Bonhomme from Genetic Alliance. First, I want to say this is a really great presentation. I'm glad that we were able to spend the morning really diving deep from a range of different perspectives on it. So thanks to organizers and presenters on that.

One thing I wanted to pick up on is talking about the facilitation of kind of discussion. I think that it is really important for, particularly conditions that are being considered for the RUSP or advocacy organizations who are looking at newborn screening, either

condition specific or as a whole, that these gaps still exist.

And I think that there's a lot of this discussion that happens within the long-term follow-up community, but it isn't necessarily getting out there. And I think that's hard because we always want to talk about how successful newborn screening is.

And its newborn screening is really successful, and we have these areas that we really want to be able to improve on and build upon. So I think that's something to consider, and I don't necessarily know how we would go about doing this.

But as there are discussions about different pieces of newborn screening and new conditions coming up, really thinking about, even if we don't necessarily know for sure what will long-term follow-up look like for this condition, these are the questions we really need to start asking, and to have that conversation be between researchers, clinicians and the families as you all were presenting.

Let me see, I'm trying to follow my notes here a little bit. Oh, I guess one thing that I guess would be the question is have there been examples of any of that, that you guys know, done well where we have really talked about with as conditions have been added, and you can talk about that whether that's RUSP or at the state level or panel, whichever way that you have all seen where there have been opportunities to have those discussions of really make sure you, this group, have done XYZ.

I know that's something that at Genetic Alliance we've tried to do when new groups are building registries, to say it's really great you're capturing this data.

Make sure you're capturing it in a way that down the line when you hand it off to someone, they can use it. I'm just trying to think. Are there anything we can point to, or maybe that's something that we need to think more about and maybe sketch out a little bit?

DR. FEUCHTBAUM: Well, I can just

address a little bit what some of the development work we're doing in California around bringing up an ALD screening program has really forced us to think a little differently because normally we've had certain, metabolic centers follow kids with metabolic diseases.

And hemoglobin centers do hemoglobin and endocrine does endocrine centers, so that everybody's been siloed to a certain extent within their disease category.

But ALD has forced us to start thinking differently because we know that a large percent of the kids with ALD, even before they have the neurological systems, they're going to have symptoms of Addison's disease. So it's an endocrine disorder.

So we realize well, gee, we're going to have to really partner with the endocrinologist even in the short-term, that those are going to be the issues that are going to present earlier than the neurological conditions.

And, of course, we need to partner with

the neurologist. And we need to partner with the primary care docs because those kids are going to need an MRI every year. It's been suggested.

And we don't know when the symptoms are going to show up. They may not show up until the person is 48 years old. Again, there are so many. The disease presents it in different times in so many different ways.

So that's been a challenge for us. And as we've designed our data system, we put a lot of thought into having conversations with all the specialists and even a primary care doctor to make sure we're asking the right questions on the form.

Again, not getting too detailed, not too high level, kind of finding that just right balance to getting what they consider to be useful information to evaluate the impact of an ALD screening program. And so ALD's been our first challenge, and we've been trying to have those broader conversations.

DR. BERRY: I would say no, generally. No one does that. They add things, and then we have

no plan. And that's pretty much where we've been all along, and the clinicians have a responsibility because they see the families.

The public health follow-up programs do their very best to be respectful and to get that information in meaningful ways, but they don't have the resources for it.

And as Debbie correctly points out, is it the newborn screening programs' problem? And we say public health globally, but when the rubber hits the road, who pays for it?

Is it the newborn screening program? Is it Title 5, da da da? How do we make sure that we marshal the resources that are probably there to be able to ask those questions more meaningfully?

So I would say one of the things I've thought about as we talked about the public health impact statements when we do the adding things, that what we ought to be adding to that impact is this question.

Not only, are we going to be able to

implement the test? But then, are we going to be able to do the things we owe the families afterwards so that they get what they need from the newborn screening?

So that would be one thing, I think, that this committee could entertain very carefully, which is as they add conditions, thinking very thoughtfully about what the implications on the longer term basis are.

DR. COMEAU: Thank you. Is it on? Anne Comeau from Massachusetts. So I think that the committee has already done quite a bit by bringing forward presentations such as you've heard today and previously about how people are collecting data and collecting data through services that they provide.

I think what the committee can do is to perhaps emphasize both a staging and quality. I see staging as being the kinds of public health data that California and Massachusetts collect and others try to collect and others do collect, which is the overarching we've identified these

children, and we need to know are they still in care.

And in general, how are they doing? Have any of them died? Very superficial, and of course the clinicians have to do their clinical services. And when they can collect specific data, of course if one wants to marry that.

But the one thing that when Joan says how do we do that, and how do we pay for that? Clearly, I don't, it's not my sense that we need to collect detailed data on every single child.

I don't think anyone has that sense, but boy do we need good case definitions. If we don't have good case definitions, if we don't use good case definitions, five or ten years from now, all we're going to have is a bunch of data about some kids who died, some kids who did well.

And we don't know why because, I mean even within PKU, we know Classic PKU. We know Hyperphe. People just inherently are going to do differently without treatment, and you layer treatment on top of that.

If we want to include clinical outcomes, we have to be comparing apples to apples, and I know, I mean, this is one of my mantras. But I think if the committee can bring back the, we love all the efforts that everyone's doing.

But when it comes to having data that is going to be really move improvements of clinical outcomes forward, the data that we want to analyze has to be quality data. And we have to have a way to do some of that detailed work, all of that detailed work on some of the cases really well. Thank you.

CHAIR BOCCHINI: Thank you, Anne. Well, I want to thank all the panelists for their presentations. It's been an excellent discussion. And I want to thank everybody for their comments and the ideas that have been brought forward.

So we really appreciate that. I think we started off on a new path here to kind of see where the gaps are and how to deal with those. So thank you all very much.

I want to now go to the public comment section. We have three individuals who have signed up for public comment. I think if they will come to the microphone that we set up here to the right.

The first is Jon Miller, President of the Network of Tyrosinemia Advocates. And each speaker has been allotted four minutes for presentation. So, Mr. Miller, thank you.

MR. MILLER: Thank you for having me everybody. It's an honor. I'm humbled to be here. I'm coming to you as the President and Founder of the Network of Tyrosinemia Advocates. We cover tyrosinemia type 1, 2 and 3. As you all know, tyrosinemia type 1 is much more common.

If I may share my story, a very quick CliffsNotes version of it is that my son was born in 2009, and he was given a newborn screening panel in the state of New Jersey. And the newborn screening panel failed us.

He was given a clean bill of health. We were sent home. Enjoy your lives. You have a

great little boy. He started getting sick. You guys know the rest of the story. Fortunately, he was caught, and he's alive. And he's doing well with treatment.

But it was not without a massive fight with three hospitals, two transfers and somebody getting in a car on Thanksgiving eve transferring NTBC, which is the medication, from Nashville to Philadelphia where he was ultimately diagnosed and treated.

It was not without side effects, and it was not without some permanent damage that we have to take care of forever. I used that fuel to create my organization, and I couldn't understand why I was the only one who had been failed by this system until I started getting members.

Oh, thank you, until I started getting members and realizing that the members had very similar stories. My son is not the only one who was misdiagnosed or not diagnosed. I have a handful of families who tell me stories just like mine, that did not end well.

I have one family that is one their third child with tyrosinemia type 1. The first two were not caught on the newborn screening, and they both died. I have a family in Ohio. Their daughter died. They didn't diagnose her until 10 months.

I have another family. It goes on. Okay. The point I'm trying to make is that there was a void in the panel in that you would test tyrosinemia for tyrosine as your primary marker. It has been recommended by this panel that we use succinylacetone as the primary marker.

The reason I'm standing at this podium is to remind you all or inform you if you don't know, that the great states of Connecticut, Delaware, Maryland, Georgia, Illinois and Oklahoma, as of about three weeks when I last updated this, are not performing your recommendations.

As those states do that, we are running the risk of losing more children or damaging more children before they could be treated. It's unacceptable.

It's insulting to this panel, and it's dangerous essentially because what happens is if you don't, if you test for tyrosine only, and you send the families home and then the kid gets sick 12 weeks later and they go to clinic, a regular clinic not a specialized metabolic clinic, the doctors look.

What is the first thing they do? They look at the newborn screening, and they go well, can't be tyrosinemia. And sometimes months can go by. Weeks can go by. I know in our time of evolution, that time is getting shorter, and we're making great strides.

So with any hope, those clinicians can pick up on those false negatives. But we can't rely on that. If you test for succinylacetone on the newborn screening as a primary marker, you will pick up dramatically more of the cases.

What your numbers and your statistics don't show, excuse me, I'm assuming they don't show, is the amount of kids who died not from a late diagnoses but were never caught, have died of

unknown liver disease or unknown problems.

And there could be tyrosinemia kids in that as well as other situations, so my proposal to this committee is could you please reach out to the states that are not currently in compliance with your recommendations and ask them to update their machines to get on the right systems and get everything going so that we don't have to do this.

This is my mission for 2016. I've promised my membership that by the end of 2016, all states will be doing this. And I don't see any reason that we collectively cannot make that happen. So thank you very much.

CHAIR BOCCHINI: Thank you for your comments. They're very pertinent, and we'd be happy to work with you on that.

MR. MILLER: Thank you. If anybody needs me, I'm available, and I'll be more than willing to do anything you want me to do.

CHAIR BOCCHINI: Okay. Thank you. Next we have Annie Kennedy, Senior Vice President, Legislation of Public Policy of the Parent Project

Muscular Dystrophy.

MS. KENNEDY: Hi, and good afternoon. Thank you for allowing me to present here today. I printed my comments so I didn't go over my four minutes. As you all know, Duchenne muscular dystrophy is one of the most common fatal genetic disorders diagnosed in childhood, affecting approximately one in every 5000 live male births.

Because Duchenne is a gene found on the X chromosome, it affects primarily boys. However, carriers can manifest symptoms that range in variability from mild muscle cramping to cardiomyopathy to young girls with the class Duchenne phenotype.

Duchenne results in progressive muscle loss of strength and is caused by a mutation in the gene that encodes for dystrophin. Because dystrophin is absent, the muscle cells are very easily damaged.

This progressive muscle weakness leads to serious and fatal medical problems, particularly issues relating to the heart and

lungs. By the time boys are typically diagnosed, between the ages of 3 and 5, irreversible muscle damage has occurred. Young men with Duchenne typically die in their early 20s.

In September of 2014, I had the occasion to come before this committee and tell you that our Duchenne research pipeline was both robust and hopeful. Because of that, PPMD at that time launched a national newborn screening effort in December of 2014.

Today, I'm pleased to stand before you to provide you with a high level update of this effort, which includes a formalized national Duchenne newborn screening steering committee and six related working groups, a Duchenne screening test development project led by PerkinElmer, a project with NBSTRN and collaborations with most federal agencies involved in newborn screening.

In January of 2015, PPMD enlisted the expertise of Dr. Michelle Puryear to help lead our Duchenne newborn screening efforts. With Dr. Puryear's guidance, along with the leadership of

myself and Dr. Jerry Mendell, we convened a national newborn screening steering committee.

Comprised of generous and active experts from both the fields of newborn screening and Duchenne, these individuals represent a broad array of stakeholders, disciplines and agencies.

With the guidance of our steering committee, we conducted an analysis of our current readiness for public health program and for Duchenne newborn screening and began to map out an action plan to address these gaps that have been identified.

Six workgroups were then created to address the priorities that had been identified by the action plan. It's very Madonna up here. With each workgroup led by an established newborn screening effort, in total, more than 50 dedicated professionals have been involved in this effort over the last year.

The workgroup focus areas include an outreach and educational workgroup focused on healthcare professional and patient provider

community outreach.

To the themes we've been talking about this morning, follow-up and clinical care considerations for pre-symptomatically identified infants with Duchenne that will fulfill the gap between our current care considerations and those who identify through newborn screening, laboratory test validation and refinement workgroup, the NBSTRN integration workgroup, bioethical and legal considerations and then the evidence review workgroup.

Additionally, we've been working closely with PerkinElmer on an effort to develop a refined screening test for Duchenne. This committee is familiar with Duchenne newborn screening project, led by Jerry Mendell, from Nationwide Children's Hospital, which included the state's 43 birthing hospitals, screened more than 43 babies, 43,000 babies, and identified seven male babies who were confirmed to have Duchenne.

That Ohio pilot used an enzyme assay for creatine kinase as a first tier screening tool. We

are currently working to further refine the first tier screening for creatine kinase to develop a potential new newborn screening test method for Duchenne.

PerkinElmer is leading this project in partnership with the California Department of Health Newborn Screening Program and will be using newborn screening residual bloodspot specimens from the California Biobank.

We've been working closely with PerkinElmer to coordinate outreach with five Duchenne care centers based in California that have agreed to participate in the project and assist with local IRB processes and patient informed consent from eligible families.

Our Duchenne community is also very fortunate to have many well developed infrastructure and registry resources, including the Duchenne certified care center programs supported by PPMD, the MDA Clinic Network, supported by MDA, MDA's national neuromuscular registry and PPMD's Duchenne Connect Registry,

which has been a part of the PCORI PCORnet network.

Additionally, Duchenne connect data is a part of a global network of Duchenne datasets, many of which have been a part of newborn screening efforts throughout the world. For this reason, PPMD, MDA and NBSTRN established an MOU to explore data integration and applicable resources available through NBSTRN.

Each of these efforts have benefitted from great expertise and generosity of experts and leaders within NIH, HRSA, FDA, CDC, ACMG and the newborn screening community.

While Duchenne muscular dystrophy is still 100 percent fatal, we've demonstrated that immediate identification and early clinical interventions can add years, even decades to an individual's life span.

In the last year, our landscape has changed and advanced even further. In August of 2014, the EU granted marketing authorization for the use of a treatment of a nonsense mutation in Duchenne muscular dystrophy.

It is estimated that a nonsense mutation causes Duchenne in approximately 13 percent of patients, which is about 2000 people living in the U.S. Translarna will be reviewed in the second quarter here in the U.S.

In the coming weeks, in an FDA advisory committee review for Sarepta Therapeutics' Eteplirsen could potentially benefit yet another 13 percent of boys in our Duchenne population whose disease may be modified through the exon-skipping of a targeted exon-51, which would be, again, another 2000 boys living in the U.S. today.

In other words, this is the dawning of a new age for Duchenne muscular dystrophy. In each instance, these therapeutic interventions would be most successful the earlier they are administered, meaning pre-symptomatic identification of children with Duchenne as early as possible is critical.

I'm almost done. And most importantly, we know that providing clinical interventions to children with Duchenne before

they develop muscle weakness improves therapeutic outcomes and can add years to life spans.

But we also know we have an extraordinary amount of work that we must do to transform our existing national Duchenne care and support infrastructure into one that fits into the public health model for newborn screening.

And we're working hard to accomplish this. We are committed to paving a path forward to Duchenne newborn screening in the U.S. and with the bright hope of therapy approvals on the near horizon, we must ensure that once approved, these therapies are available to all eligible families at the earliest moment possible. Thank you.

CHAIR BOCCHINI: Thank you, Ms. Kennedy for that update. Very important information. We appreciate it. Thank you. Next, Mr. Dean Suhr, President of the MLD Foundation. Dean?

MR. SUHR: Dr. Bocchini and committee, thank you. And I did want to seriously thank you. As we've just heard, we know that your job is very,

very difficult. What you do, what you don't do, how you do it is very, very challenging. So thank you for your hard work.

I'm here to report on the RUSP roundtable, which is an MLD foundation initiative, but it is not specific to MLD. We held our second meeting. About 23 people in attendance. It was an all-day meeting yesterday.

And the purpose of the RUSP roundtable, we recognized that a lot of things work through government agencies. We're talking a lot about public health, and obviously this committee is part of a federal agency.

But sometimes things move a little quicker or have different perspective and different insight outside of committee. And we've heard discussion of several animals today, the elephants and the whales and gorillas.

And I'm kind of thinking of a centipede. If a centipede did not have one brain, those feet would be going all different directions. But the reality I think in the newborn screening community

is there are lot of good brains, but all those segments of the centipede aren't necessarily all connected.

And what we hope through the RUSP roundtable is to provide a forum and an opportunity where there's a broad variety of perspectives, from industry, clinicians, academia, ethics, advocacy, technology and on and bring these people together so that we can all learn from each other because the more we know about each other and the limitations and the opportunities that each of us potentially could bring to the table, I believe the more efficient we will be at doing our particular work at the many committees and the labs and the offices that we do our regular work.

So the perspectives were very broad. What we are not is we are not trying to displace another organization. We're not trying to patch something together. We're really much more open and broad in how we're carrying on our discussions.

We discussed yesterday things related to benefit, benefit to the child and particularly

benefit to the families, alternative and secondary paths, technology, what's happening that's creating some of these alternate and secondary paths.

Specifically, there was a long discussion about genomics and genomic sequencing and where that, not just where that could fit in today but where that might fit in, in five or ten years.

And again, we know that a lot of people are talking about that, but we're bringing a broader sense of perspective there. And historically we've talked about viable therapy as a RUSP requirement as well.

We will more formally communicate with the committee with some questions and we will offer ourselves up if there are things that we can do in a more efficient or a different sort of an approach.

We want to be able to do that. An outcome from yesterday's meeting, basically two things. Again, as a roundtable it's not like a committee where you have subgroups and tasks and

everybody has an assignment, but what's happening is we're inspiring people to work together and to launch into little projects that make sense based on new information they have.

And there are a couple of folks that are going to go identify five diseases where genomic sequencing may be the opportunity to be able to screen children.

So not how do we fit genomic sequencing into an existing newborn screening system, but perhaps how can this be an additional testing opportunity for some diseases where they have all of the other pieces in place?

And also we talked also about repurposing and building upon existing toolkits. It's been alluded to today, and we know the issues with state implementation of newborn screening because of a legislative mandate versus federal RUSP recommendations and the tradeoffs.

We just heard about evidence-based review, and we know how that happens here. So we're going to revisit some of that and maybe help

invigorate getting information out to legislators and families and advocacy groups.

Specifically for the committee, one of the questions that we'll be asking of you, which was discussed a bit yesterday, was how would a nomination for a childhood screening be accepted or processed and/or reviewed by the committee.

And again, this is part of thinking a little bit more broadly because of where we may be heading. We know that this is a committee that's done a lot of work at the newborn level and is chartered into the childhood. And obviously we're going to continue to ask how we can help.

Newbornscreening.us is where we're going to post all of the information publically, and we'd be happy to answer questions. Thank you.

CHAIR BOCCHINI: Dean, thank you very much for that update. Let's now move to our next slide set. We just have a couple of things to frame this afternoon's discussion and what we expect to get from the subcommittees.

Next slide, or we got it? Okay. So we

have, as you know, three subcommittees that have been on hiatus, thank you, while we have tackled restructuring issues related to our new charter.

But these three subcommittees are now going to begin meeting again, starting this afternoon, the Laboratory Procedures and Standards Subcommittee, the Education and Training Subcommittee and the Follow-up and Treatment Subcommittee. And here I have listed the chair and co-chair of each of those subcommittees.

Just to remind you, we did a review about four years ago, looking at what the charge would be for each of these committees, subcommittees. And I just want to remind you all of that as you begin your deliberations this afternoon and determine whether this charge is accurate or whether there needs to be some modification as we go forward.

So the Education and Training Subcommittee charge is to review existing education and training resources, identify gaps and make recommendations regarding the following

five groups, health professionals, parents, screening program staff, hospital/birthing facilities staff and the public.

For the Follow-up and Treatment Subcommittee, the charge has been to engage in a multi-step process that identifies barriers to post-screening implementation and short and long-term follow-up, including treatment relevant to newborn screening results, develop recommendations for overcoming identified barriers in order to improve implementation and short and long-term follow-up, including treatment relevant to newborn screening results, and to offer guidance on responsibility for post-screening implementation and short-term/long-term follow-up, including treatment relevant to newborn screening results.

And then the Laboratory Standards and Procedures Subcommittee charge was to define and implement and mechanism for the periodic review and assessment of the conditions included in the uniform panel, infrastructure services needed for

effective and efficient screening of the conditions included on the panel and laboratory procedures utilized for effective and efficient testing of the conditions included on the uniform panel.

So your task this afternoon is to address the needs/gaps within the scope of work of the Advisory Committee that does not duplicate other activities, update the charge if needed and identify issues and topics for subcommittee work, with the end to be a deliverable or a product based on what's chosen, and bring these potential projects to the Advisory Committee tomorrow for discussion.

The chair or co-chair or designee of each subcommittee will present these projects and/or a summary of previous day's discussion tomorrow. The ideas will be collated, and during lunch the Advisory Committee will review them, and after lunch determine which projects in priority would be then given back to the subcommittees for their work.

And the caveat is that it is possible that tomorrow a subcommittee may not be given a specific task. We may need further discussion, et cetera, before some work is being assigned.

So with that, I'm going to turn this to Debi, and she'll remind everybody of the particulars for this afternoon's subcommittee meeting followed by the workgroup committee meetings. Debi?

MS. SARKAR: Thanks, Dr. Bocchini. So just okay, the subcommittee meetings will be open to the public. I can tell you right now where everyone will be meeting after lunch.

The Follow-up and Treatment Subcommittee will be meeting in this room, Room E. The Laboratory Standards and Procedures Subcommittee will be in Room A, and the Education and Training Subcommittee will be in Room B.

Because we have gone over schedule, we are going to adjust the timing of these meetings. So lunch will be from now until 1:30, and the subcommittee meetings will meet from 1:30 to 3:00

p.m., 3:10-ish.

And then after that though, by 3:10, we do need to leave the rooms because the workgroups will be meeting in these rooms. And we'll have signs up.

The workgroups' meetings are closed to the public because they have projects that they're working on, so at 3:10, we're going to ask that we make the shift between subcommittee and workgroup. I think that is it.

(Off microphone comment.)

MS. SARKAR: For the workgroups, I don't have those right now, but our contractors will have signs. And we'll direct people. Okay.

CHAIR BOCCHINI: All right. So that'll conclude this session, and enjoy the afternoon. Have lunch, and then we'll get to work again. So thank you all very much, and we'll see you in toto 9:30 tomorrow morning. Thank you.

(Whereupon, the above-entitled matter went off the record at 12:36 p.m.)

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