Health Resources and Services Administration

Advisory Committee on Heritable Disorders in Newborns and Children

Meeting

9:30 a.m. to 2:00 p.m.

Friday, August 2, 2019

Reported by: Gary Euell

P R E S E N T

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National Society of Genetic Counselors
Amy Gaviglio
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C O N T E N T S

C O N T E N T S - CONTINUED

P R O C E D I N G S

DR. CYNTHIA POWELL: Welcome to Day 2 of the August 2019 Advisory Committee on Heritable Disorders in Newborns and Children. We'll begin the meeting by taking roll call.

DR. CYNTHIA POWELL: Mei Baker?

DR. DR. MEI BAKER: Here.

DR. CYNTHIA POWELL: Susan Berry?

DR. SUSAN BERRY: Here.

DR. CYNTHIA POWELL: Kyle Brothers? Jane Deluca?

DR. JANE DELUCA: Here.

DR. CYNTHIA POWELL: Carla Cuthbert?

DR. CARLA CUTHBERT: Here.

DR. CYNTHIA POWELL: Kellie Kelm?

DR. DR. KELLIE KELM: Here.

DR. CYNTHIA POWELL: Michael Warren?

DR. MICHAEL WARREN: Here.

DR. CYNTHIA POWELL: Melissa Parisi?

DR. MELISSA PARISI: Here.

DR. CYNTHIA POWELL: Annamarie Saarinen?

MS. ANNAMARIE SAARINEN: Here.

DR. CYNTHIA POWELL: Scott Shone?
DR. SCOTT SHONE: Here.
DR. CYNTHIA POWELL: Beth Tarini? Catherine Riley?
DR. CATHARINE RILEY: Here.
DR. CYNTHIA POWELL: For the organizational representatives, Robert Ostrander?
ROBERT OSTRANDER: Here.
DR. CYNTHIA POWELL: Debra Freedenberg?
DEBBIE FREEDENBERG: Here.
DR. CYNTHIA POWELL: Michael Watson?
MICHAEL WATSON: Here.
DR. CYNTHIA POWELL: Steven Ralston? Jed Miller?
JED MILLER: Here.
DR. CYNTHIA POWELL: Susan Tanksley?
SUSAN TANKSLEY: Here.
DR. CYNTHIA POWELL: Chris Kus? Jacqueline Rychnovsky? Jennifer Kwon?
DR. JENNIFER KWON: Here.
DR. CYNTHIA POWELL: Theresa Hart? Natasha Bonhomme?

MS. NATASHA BONHOMME: Here.

DR. CYNTHIA POWELL: Siobhan Dolan?

DR. SIOBHAN DOLAN: Here.

DR. CYNTHIA POWELL: Amy Gaviglio?

MS. AMY GAVIGLIO: Here.

DR. CYNTHIA POWELL: Georgianne Arnold?

DR. GEORGIANNE ARNOLD: Here.

DR. CYNTHIA POWELL: All right. At the, at the April meeting, we heard about some examples of rare disease registries in order to inform the Committee on possibilities for following children with rare disorders identified through newborn screening long term to be able to track their outcomes.

So we're continuing along those lines today and to think about research efforts for conditions currently on the RUSP. Today we're going to hear about an international registry in rare disease research efforts. Dr. Pariser, Director of the Office of Rare Diseases Research at the National Center for Advancing Translational Sciences at the NIH, will share an overview of the

International Rare Disease Research Consortium and the different activities the Consortium is working on.

Our goal with this series of presentations is to determine the role that these registries might play in providing data for evidence reviews, as well as for states for long term follow up.

I'd like to invite Dr. Pariser up to the podium.

DR. ANNE PARISER: Good morning, everyone, and thank you so much to the Committee for inviting me here to talk about the International Rare Diseases Research Consortium, or IRDiRC as its commonly referred to. So IRDiRC, the purpose of IRDiRC was to promote international collaboration and advanced rare diseases research worldwide.

So it was officially established in 2011, but the, the thought for this actually came several years earlier in about 2009 when Francis Collins and Ruxandra Draghia-Akli of the European

Commission had a meeting to, to discuss rare diseases with the recognition that rare diseases weren't getting the research attention or weren't advancing as fast as everyone would like.

So rare diseases, there's about 7,000 or so rare diseases. Nobody knows really for sure, but it's estimated to affect about 8% of the world's population. And because the individual, there's so many disorders and the individual disorders are so low prevalence, the research environment for rare diseases is just naturally, was very divided and siloed and there wasn't a lot of coordination.

So this was an effort to try to change that. So there were a series of meetings from 2009 and eventually in 2011 the first founding meeting was held actually here in Bethesda and IRDiRC was established. So the initial meeting included members from Europe, North America, Asia, Australia, and the Middle East. So it was truly international right from the beginning.

So the initial focus was actually on

developing common scientific and policy frameworks that could be recognized and disseminated to the individual members to try to promote this more collaborative approach and its efficiency. So at that first meeting the, the initial goals that were laid down, or the objectives, was a ten year goal of trying to have 200 new therapies for rare diseases approved by 2020, and this could be anywhere in the world. So it was cumulative, the US, Europe, anywhere, and that there would be a means to diagnose rare diseases or most rare diseases by 2020.

So I think as everybody's aware, science has advanced, just are very rapidly in this time, particularly genomic analysis for many rare diseases which are genetic, most of them, about 80%. And the number of new therapies for rare diseases has really been increasing considerably. So for example, last year was a record orphan approval here in the US and there were about 60 orphan drugs approved. About 40 of those were novel medications last year.

So this has actually far outstripped the initial objectives and this was achieved early, quite a bit early. So new goals then had to be established, which was done in 2017.

So the vision and goals, the second iteration of this, the ten year plan, a very ambitious and far-ranging vision, was to enable all people living with a rare disease to receive an accurate diagnosis, care, and available therapy within one year of coming to medical attention. So this is a very ambitious goal.

So this was divided into three major goals. The first one was that patients who, coming to medical attention who had a known disorder would receive a diagnosis in one year, or if this was an undiagnosed individual where the disease had not yet been recognized, that they would enter some kind of a coordinated diagnostic pipeline.

So lengthy amounts of time to diagnose is very common in rare diseases. It's so common it's referred to as a diagnostic oddity. Commonly

quoted five to eight years to obtain an accurate diagnosis, but with recognition now of a lot of these chronic, slowly progressive disorders, many patients it's actually decades if they ever get a diagnosis at all. So this is actually a very ambitious goal.

Also to achieve 1,000 new therapies for rare diseases, and particularly we're focusing on diseases that currently do not have an approved therapy, and again, this can be anywhere in the world. And to develop methodologies to assess the impacts of the diagnosis and the therapy. So are the therapies that are being developed and approved, are they really making an impact on rare disease patients' lives.

So these, these goals were actually published in *Nature* and *Clinical and Translational Science*. There's actually been several publications. One is looking at the progress that, for the first vision and goals and, and the other was these new vision and goals. So just put the references up there if you would like to take

a look at those.

So those, that's the vision and the goals. So how are we going to get there? So to get to these, try to achieve this vision within the next ten years, IRDiRC then turned to developing a roadmap to try to break this down into the individual pieces, stand up committees, and at times taskforce to try to put this together.

So there was a prolonged -- there was a planning process mostly through 2018 and continuing now into 2019, and trying to especially identify those priority areas that are going to help to advance the goals. The committees, which I'll come back to in a minute, each had to define three to five activities that were critical, that would have timelines and metrics, and then try to consolidate these together to try to reach our goals. The, the roadmap was then put together and then it was shared with the entire IRDiRC consortium, which again went internationally to try to get us all onboard with this similar

vision.

So IRDiRC is, you know, a diverse and large organization. So you have to have structure. You have to have policies. So this is just the general layout of how IRDiRC is put together. So the top box up there is a consortium assembly which, formally referred to as the Executive Committee, which is the governing body of IRDiRC.

So included in that is one member, one person from each IRDiRC member, and then the chair and vice chair of each of these six committees that are listed along the bottom there. There is a small, permanent staff, the scientific secretariat, and actually just about everybody else listed there are volunteers. They're volunteers who give their time in addition to their regular usual rare disease type jobs. And then there are six committees divided into constituent committees and scientific committees.

So on the right the constituent committees includes funders, companies, and

patient advocates. And then on the left, the scientific committees including diagnosis, interdisciplinary, and therapeutics. In 2015 to try to help these committees achieve some of these goals, taskforces were spun off for specific issues which I'll return to in just a minute.

So here's a list of the current IRDiRC co-consortium assemblies members. So it's a long list. I won't go through it all, but I think on, on just even a brief glance, I think the international nature and people literally from all over the world. And a little bit closer to home, here's our NIH and FDA representation. So myself from NCATS and Melissa from Child Health, as well as Adam Hartman and Faye Chen from two other NIH institutes, and Kathy Needleman from the Office of Orphan Products at FDA. But broad representation from around the world.

So here's graphically displaying. The red are those countries that have IRDiRC memberships. So it's, you know, again, quite diverse. And if you look over time starting in

2011 was predominantly focused, membership was predominately focused on funders, trying to get them to coordinate their agencies. But the membership has both grown and diversified over the years and including now companies and patient groups are increasing their representation.

And IRDiRC is, has no regulatory power in any particular area of the world, but what it does do is provide guidance and recommendations that can then be adopted by the individual member organizations for their own research programs or priorities, but they are responsible for enacting this and their own funding.

So this is just a representation of some of the topic areas and I think these are, they're very broadly agreed on. For rare diseases I think everybody recognizes these are, these are kind of the key priority areas that we need to focus on, things like ontologies, diagnostics, biomarkers, registries, natural history studies. These are really the common underpinnings of the needs for rare disease research.

So IRDiRC's committees, now turning to the committees, their mission is to try to, working within their area to identify what are the road blocks and the priorities that we can focus on to address these gaps. And at times spinning off taskforce to focus even more closely on some of the issues.

So what is usually tried to do is, is there a best practice? Are their guidelines, operating procedures that have been done somewhere around the world? Can we, can we adopt these? Can we develop them further and then disseminate to try to bring everybody along rather than keeping this information siloed? And then spread that to the rest of the committee so that they can adopt these roadblocks or priorities, areas.

So here is looking a little deeper at some of the constituent committees. There's three: the funders, patient advocates, and companies, and there's the chair and vice chair listed there. And again, very diverse, very international. And the scientific committee

chairs, same thing. Australia, United States, France, Italy, all over the world.

So just to say a few words, a few more words about these ones. So diagnostics, I think that's, that's obvious, and in this day and age one area they're really focusing on is a genomic analysis and the sharing of information. Foundational or interdisciplinary, those are the crossing-cutting or translational issues. For example registries in natural history studies, but also ontologies, data sharing, and therapeutics.

Again, it's not so much the development of a therapeutic, but what are, for example, the underlying regulatory principles, how can we facilitate clinic trial designs and developing efficient, and recognizing efficiencies in the process that can be adopted by the various members.

And then just a few words on taskforces. So these are taskforces that were established in, started to be established in 2015 with the recognition that there were some areas that needed

a little bit more work. And here's just a few. So diagnostics for example that is led by Gareth Baynam from Western Australia, and he's had a longstanding interest in native populations and the particular needs. So there's an under-represented populations taskforce within there. Also certainly an issue here in the US as well.

Interdisciplinary focusing on things like clinical trial networks that can facilitate rare diseases, and therapeutics committee, for example, the regulations that I mentioned and things like repurposing that may be of interest to some rare diseases.

And one spin off of IRDiRC is as people are, were looking for best practices or models that could be followed, it turns out there are some of these resources in various agencies or members. So what they did, it was, developed a process of IRDiRC-recognized resource. So this would be a designee, designation that would highlight this resource of being of good quality and potential utility to a lot of members. And

then those resources are posted up on the website to, again, try to disseminate what is already there that people can leverage and use.

So there are currently 22 IRDiRC recognized resources and a broad range of categories. Here's the entire list right here. Things like guidelines, databases, and tools. And the one to the bottom left corner there just as an example, this is actually the NCATS toolkit for patient-focused therapy development, which is on our website at NCATS, and it's got this little box with the IRDiRC's recognized resource and the checkmark is, is a sign of, I guess, international quality. So that's just one example.

So just to -- my final point here is what IRDiRC is really trying to do is not just introduce efficiency into the process and improve a little bit on what we're doing now, but to truly transform the research environment for rare diseases. So really look for a paradigm shift. And we categorized this, make radically more efficient and effective paradigms, and what keeps

coming up over and over is a common factor for all of this is, is the ability and processes to share, sharing knowledge, our data, our infrastructure, expertise, and, and viewpoints as well.

With the goal of, again, reaching this very ambitious vision by 2027, but also to improve the, the research and the lives of patients with rare diseases. So here's some contact information. Please contact me any time if you have any questions and I, I think there's time for questions.

DR. CYNTHIA POWELL: Thank you very much, Dr. Pariser. Yes, we'll open this up to questions. So operator, if you could open the lines for Committee members and organizational representatives on the conference line. Committee members, please remember to state your name.

DR. KYLE BROTHERS: This is Kyle Brothers. I'm a Committee member. I really, really enjoyed your talk. I've been working this area and was really not aware of what your group has been doing. So I really appreciate your

coming to us and talking about it.

I specifically wanted to ask about therapeutics and how you're thinking about things that are not medications. So whether it be more sort of dietary modifications, physical therapy, educational interventions, all of that category of things that happens outside of doctors' offices, where does that fit into this effort, if at all?

DR. ANNE PARISER: So what they've been predominately focusing on are therapeutics, either drugs, biologics, or devises, and not so much on patient care, is what you've mentioned. And that may fall more under the patient constituent committee that is, is bringing up, again, how to improve people's lives and all of the things that, that go on there.

But the therapeutics committee right now is predominately focusing on ways -- most, most rare disease research is international. It's multinational because you need to get your, your numbers up. So a lot of these cross-border collaborations are heavily regulated, as well as

differences in policies between the member states. So that's where a lot of the effort has been focused right now, but your point is very well taken and I will take that back to the next meeting.

DR. CYNTHIA POWELL: Melissa?

DR. MELISSA PARISI: Thank you, Anne, for that very nice presentation. I'm wondering if there are opportunities to partner in the newborn screening space that we haven't considered thus far, particularly given the international nature of newborn screening and certainly the policies and procedures that we have here in the United States, represent one model for considering conditions to be added to the recommended panel.

And I just, given the broad breadth of expertise in the rare diseases space that IRDiRC represents, that there might be some opportunities to develop some sort of partnerships or at least some exchange of ideas and information with folks that are part of IRDiRC that may be involved in newborn screening as well?

DR. ANNE PARISER: Yeah. There, there absolutely are and that's an issue that the diagnostics committee has been looking at. I know that Europe, I'm sure you know this better than I do, Europe has made a lot of, a lot of progress in that area and there's been a lot of discussion about, you know, cross-border study and early diagnosis and registries. So is there an opportunity to, to leverage that? There probably is. So I'd urge you actually to get in touch with Gareth. I know that this is a topic of significant interest to him.

DR. CYNTHIA POWELL: Mei Baker?

DR. MEI BAKER: If I heard you correctly, you mentioned that right now it's emphasized on genomic data and I was just curious what's, why you decide because in the mainstream now you have a genome typing and omic together. So I'm just curious why it's, it's because the difficulties with my --

DR. ANNE PARISER: Yeah, no. I was just speaking very broadly. Genomic analysis or omics

approaches to diagnosis, most rare diseases are Mendelian. So called single gene disorders. So that's where an awful lot of the interest is right now. But it's certainly not the whole story by any means. But, yes, any of those approaches are valuable.

DR. MEI BAKER: Thank you. And another question is because this is the international collaboration, so you have so many stakeholder in that. I just curious of how you, in terms I don't know how you collect data and do you, because I heard a lot of terms for the duration and unified ID stuff. And all this involved HIPAA and the consent, can you comment on that?

DR. ANNE PARISER: Right. So IRDiRC itself is not collecting any of these data. That falls to the members and, and often regional authorities or the members that have the ability to stand up these, these repositories. It's more about trying to come up with best practices or even awareness sometimes that these, these tools or these repositories exist and then encouraging

other areas to either collaborate with them formally, or to increase their interaction, or to access data that may already be there. One fairly common situation for rare diseases because often we have very few researchers for a particular disease and they may be very geographically disbursed, is a disease expert may be very far-flung and they may not be aware of what's going on somewhere else or what other, what else exists for some of these rare diseases.

So we don't want to have five registries for a rare disease. We'd like to have one. Is there some way to make these interoperable? But the difficulties that you note, bio-banking across borders, for example, challenging, very challenging. So what kind of strategies can we come up with to make the most of what's already there. Are there any questions from the organizational representatives?

DR. CYNTHIA POWELL: I have a question. This is Cynthia Powell from the Committee. In terms of your goal of individuals receiving a

diagnosis in a year if the disorder is known, could you talk a little bit about how you're approaching that both, you know, in the US, as well as what's being done internationally?

DR. ANNE PARISER: Yeah. That's a great, great question. So the therapies I think is, is proceeding at really an accelerating, just accelerating speed and we're seeing just a lot of new drugs and breakthroughs and targets to aim at in understanding the molecular underpinning. Diagnosis has been a real challenge and we have not really seen as much movement in that, that area.

So, you know, things like newborn screening, can we broaden these things or can we use other techniques? Nobody walks around with 7,000 diseases in their head. Are there ways to leverage article intelligence? Medical records, these networks are repositories that already exist. So these are things that a lot of people are looking at in a lot of different ways. And we too at NIH, this is really a big issue for us as

well.

But we're really trying to turn our attention there. Without a diagnosis, you can't start the research. You can't get people treated. If there's a therapy out there and we're not finding these people, that's really, really a tragedy. So we need to do better and it's a goal. Not there yet.

DR. ROBERT OSTRANDER: Bob Ostrander, America Academy of Family Physicians. As I was looking at your initial concept of how this ought to go, that someone who isn't diagnosed within a year gets funneled into a coordinated international system for diagnosis. As a family doc in a small town in private practice, I look at the other end of this process and realized that when this has come up, and although rare diseases are rare individually, they are not rare in, in conglomeration, and, you know, primary care doctors going to know that in the back of their head, but don’t have a good approach to, to dealing with a patient with a difficult to

diagnose process, I don’t think.

And in any case, I got thinking of the front end and it's just awful chaos in my experience. You know, it's a visit to me. A visit to me. A visit to a subspecialist who says I can't find anything wrong; go back to your family doctor. A visit to me, to a different specialist, back to me, to a center in a bigger city, back to me. And it's awful. I wonder if you have or if you have considered doing some journey mapping with patients and patient groups?

We're doing it right now with, involved in a project on SCID. It's, and we're doing that now to find out partly what, what the care experience is. But partly as a way of identifying what doesn't work, and better yet, what does work, who had a good journey. And if we can find the common elements of what a good journey is, maybe that could help us develop a basic process that we can share with people at the frontlines like me and my colleagues.

DR. ANNE PARISER: Yeah. I, I think you

just gave pretty much the perfect description of what people go through and they get referred all over the place until they finally end up at a specialist who may have seen this before. And that can take just years and multiple testing, redundant testing, and it's very, it's terrible for patients and their families.

So we're trying to look at this a number of ways, and journey mapping, yes, and, and it's becoming more accessible to do that now, especially here in the US where people, you know, we don’t have one cohesive insurance company, for example. And people, I think the average is they switch insurance companies every two to three years. So trying to get a good look at one patient's journey is difficult.

And it's getting a little bit easier now, though, with the electronic records and these larger health systems, is can you look at people pinging, pinging around the system and can we use that to identify people earlier. I mean you wouldn’t necessarily have to say, well, this

person has disease X, but they can start, we can start recognizing a pattern. This person may be a high risk for a rare disease just looking at that pattern. Can we, can we identify them? Can we accelerate them earlier?

So there's all kinds of things being looked at now. One of the common things we've heard, talked to a number of IT companies looking at exactly this kind of data mining approach, is if there's a disease, for example, that has a new therapy, they develop algorithms around this because diagnostic codes is, is another biggie. It's just a lot of our patients are actually silent in the database and they're very hard to find.

But could you find any typical symptoms or patterns of symptoms, then use that, lay it on the medical record and try to find people who may have this disease? So that's, that's one approach. So this a real growth, growth area, but do we have the magic formula yet? Not yet, but we're working on it.

DR. CYNTHIA POWELL: I have another question. This is Cynthia Powell from the Committee. So genomic sequencing is certainly a way to identify a diagnosis in some cases in individuals with undiagnosed conditions. People can get into an undiagnosed disease network clinic if, if they're accepted. But still on a clinical basis a lot of insurance companies are not covering genomic sequencing, and certainly most Medicaid programs, I don’t believe, so far are covering it. So I wonder if there's any efforts under way that you know of to, to kind of promote that?

DR. ANNE PARISER: Yes, yes, there are. And especially in children. I mean thankfully most children are healthy, but when you start seeing these high utilizers or undiagnosed children especially, it's getting easier now to make a case to an insurance company to go to a quicker genomic analysis, but, you know, it's not, not perfect.

And again with the fragmented system.

But there are some academic centers that have looked at this in high risk populations, for example, Stephen Kingsmore at Rady in San Diego, the University of California, they've started going to rapid genomic analysis in the NICU. So obviously this is an enriched population. But as we start to build more of a, a database behind this showing the utility, can, can we get to that faster?

But the other thing I think, as you mentioned, genomic analysis alone, the diagnostic yield in the best hands may be about 15%. So it's got to be combined with the clinical efforts as well.

DR. CYNTHIA POWELL: Jennifer?

DR. JENNIFER KWON: Jennifer Kwon, Child Neurology Society. Thank you so much for the talk. And I've actually been looking at your website and the resources are excellent. So thank you very much for that. I notice that on your roster of members, member societies and supporters, there are about 50 odd organizations,

and I'm noticing the lack of some of the organizations that I'm more familiar with when I think of rare disease, rare diseases resources.

And so I'm wondering what the growth is like of recruiting additional rare disease organizations including ones, like there's a muscular dystrophy organization, but it's from Europe and not so much from the, the US. And so that was one question.

And the second question is a follow up to the question about genomics. So I recently moved from Northeast to the Midwest and I would say that the barriers to getting genomic diagnostic testing are, are quite substantial. So I think there's a lot of geographic variability and I'm sure that applies internationally as well.

And, and so one may, one way to maybe even the playing field of rare disease diagnostics -- because I agree with you, it's with diagnostics that we can funnel these patients to appropriate treatments. One way to even the playing field might be to just shine a light on how easy or

difficult it may be in different systems to get this testing done.

DR. ANNE PARISER: Yeah. I mean those are excellent points. So here is a representation of the membership that is increasing. And I think as I said before, it's basically a volunteer organization. So if anybody is interesting in joining and devoting their time, we are usually very glad to have you. So please just, you know, approach one of us and we're always accepting new, new members.

There is a fair time commitment, but, you know, it's also, it's just been very exciting and interesting and rewarding to learn about all the things that people are doing and trying to bring them back to the member organizations.

Genomic analysis for, here in the US for insurance companies, as I'm sure you're well aware, is you have to make some kind of a cost effectiveness argument. So it's getting easier as we have successes, and particularly if there's any possibility of a directed therapy. So what we are

looking at right now back at NIH is the cost of rare disease, which is very hard to map.

It's hard to find the patients because they're often silent and these databases are hard to find. And then trying to estimate what the true cost of a rare diseases is. So I don’t know what that exact number is, but a few diseases we've looked at the cost and the cost is high. These patients are sick, high utilizers, high hospitalizations, and lower age cohort.

So if you can make an economic argument that knowing what that disease is or holding out the possibility for a therapy when you have a target, that can be persuasive. So it's becoming easier. We're, we're not there yet. And a lot of variability. Health insurer to health insurer, region to region, if you're at an academic medical center or out in the community, there are differences and, and we do see the same thing in our member states.

Europe in particular with, most of them have national health systems. So it will vary

country to country, but often it can be a little easier to make that argument. Although not across the board.

DR. CYNTHIA POWELL: Sue Berry?

DR. SUSAN BERRY: I'm delighted to know of such an international coalition. So thank you very much for this. The question I have is those of us -- I mean this is somewhat, to some degree framed in a research context, but increasingly as those of us on the frontline are doing this on a clinical basis, I may in a good given clinic day order three or four exosomes. And I get results back and I know about them, but no one else does.

Certainly the company that performed the laboratory testing would know about it, but is there any real effort to correlate or to collect some of this information that those of us just in the trenches are what I refer to as really cool cases, just getting all of the information that we end up finding and we're the ones who have the phenotypes, not anybody else. So any thoughts about that?

DR. ANNE PARISER: Yeah. So there are disease specific registries and natural histories that almost always collect genomic information in this day and age. So if one exists, that's one good place to put them. There are also, NHGRI has some. Some of the NIH institutes have genomic data repositories where you can put this information.

DR. SUSAN BERRY: But that means that the clinician has to go the extra step and effort to identify and find places like that. It would be fantastic if there was some way where we could, nothing else, just send something in and say this is a great case or something. I don't know. I'm over simplifying, of course, but, you know, the additional effort to identify a rare disease database is not always feasible.

DR. CYNTHIA POWELL: Melissa?

DR. MELISSA PARISI: Melissa Parisi. So just to follow up to your comment, Sue, I don't know the details, but I wonder if Matchmaker Exchange and some of those resources might prove

to be sort of a clearinghouse for these interesting cases. And I know that at least in the past there have been some testing companies, genomics testing companies, that have been fairly enthusiastic I think about, yeah, about putting the data in and making some of those matches.

So it's not perfect and it's not comprehensive, but I think it's a starting place, particularly for some rare disease patients who may wonder is there anyone like me out there. So, but I don't know. Does anybody want to say more about that or --

DR. SUSAN BERRY: I would say the most common place for families to make connections that, my experience is through Facebook. They put something in Facebook and they find other families, and that is by far the most likely way that families connect, not through things that we --

DR. ANNE PARISER: Yeah, that's absolutely true. Yeah. They're actually quite well organized on social media, but if you want to

explore this further, please, you know, give me a call and we can brainstorm around this because you're absolutely right. It is burdensome. So are there, are there better ways to do this? I'm sure there are. But, you know, this is a real interest area for us. So, you know, feel free to get in touch and we can talk further.

DR. CYNTHIA POWELL: Yeah, this is Cynthia Powell from the Committee. I would put a plug in for GeneMatcher that, or Matchmaker that I had a case the other day of, that was reported out as a VUS after whole exosome sequencing and because there was no known condition associated with the gene. And, you know, I put it up on there and within an hour, you know, I was contacted by somebody from Germany who also had a case, and they've identified another case from Israel. And very similar phenotypes, so it definitely looks real. So it was very, very helpful.

Any other questions? All right. Thank you very much, Dr. Pariser. Really appreciate

your presentation.

DR. CYNTHIA POWELL: All right. We're now going to move on to Implementation of RUSP Conditions Report by Dr. Kemper. Over the last decade, six conditions have been added to the RUSP. The Committee has had many discussions about wanting to know about the impact on states, the public health, and healthcare systems, and individuals living with these conditions.

To inform the Committee about the implementation issues facing newborn screening programs, the following key factors are being evaluated: NBS program organization and authorization screening methods, short-term follow up, long-term follow up, anticipated resources and costs, projected timeline for adoption.

This evaluation will inform the Committee and help to identify the resources needed, impacts, and costs, including opportunity costs, that can affect a State's ability to implement screening. Also to estimate how long it will take for State newborn screening programs to add a

particular condition to their screening panel.

I'll turn it over now to Dr. Kemper who will present the information he and his team have gathered so far. After this presentation there will be time for questions and Committee discussion. Dr. Kemper?

DR. ALEX KEMPER: So thank you very much and thank you for the opportunity to present again today. It was actually a little daunting to listen to you read out all the things that we hope to get from this, but I do think that looking back in time and, and seeing how things have gone since the recommendation was made to add something to the RUSP will lead to a lot of important lessons.

I also want to thank everyone again for the robust discussion around values and a number of people came up to me after the meeting as well. So I really appreciate everyone's engagement.

Finally, before I go ahead and get started, of course I'd like to acknowledge the work of K.K. Lam and Ashley Lennox. So I think many of you have met and, and know. And now we

also have Margie Ream who, as part of our team and she's helped a lot with tracking down articles and interpreting them and stuff like that. So I want to give credit to the, the folks that have been involved with this.

So where we are looking at SCIDs, CCHD, Pompe disease, MPS1, and X-linked adrenoleukodystrophy to look at what's happened since they were added to the RUSP between 2010 and 2017. And then to develop methods that can be used prospectively as things go on to the RUSP, as well as trying to learn lessons that, that we can about how to make the, the, the process smoother.

And I'm going to go over from a high level some of what we learned and where we go. So I'll be talking about our methods. I'll be talking about implementation of those specific conditions. I'm not going to read them again, but I did put up the year that they were added to the RUSP.

I, we, we've learned some interesting things about barriers and facilitators of adding a

new condition. Most of them are not going to be surprising, but it's still I think worthwhile looking at it. And then we'll talk about our next steps moving forward.

So again, we're looking at what, what happened within the newborn screening program and the public health implications, and also what we can learn about the clinical impact of adding those conditions onto the RUSP. And we're going to look at the full range of evidence that we can find. So published literature, grey literature. We're working very closely with NewSTEPs and APHL more broadly around their new disorders work. And then also state programs.

All this work is still ongoing and so I'm going to give you really sort of a high level look at what we've learned so far. And, you know, I guess one of my spoiler alerts, one of the things that I want you to think about as we, we go along, is the amount of new published evidence that we've been able to find. Regarding the impact of adding these conditions to newborn screening probably

isn't as big as what we were hoping to find.

But I think it also speaks to the issue that it takes oftentimes a long time, both, you know, you need to identify cases and then also find out what happened to those cases. So in a way, it's not surprising that there's not a lot. But it, it does take a while and I'm going to point out one, what I thought was a creative way to look at impact as well.

So I hope that gets everyone excited. So again, we, we're interested in looking at condition-specific factors, as well as sort of lessons that can be learned throughout. And focusing again on newborn screening program issues. So I'm just going to move past so we can dig into some of the ones in particular.

As I go through these things, and again, remember this is a work in progress, if anybody has a specific question that they need clarification or they think that there's a, you know, a little road that we should pursue further, you know, please interrupt me and let me know.

So let's start with Severe Combined Immune Deficiency which was initially evaluated way back in September of 2007. It was not initially added to the RUSP in part because more studies were, were needed including the need to identify prospectively at least in one case of an infant with SCID. By January 2010, the second nomination package came in with the, the complete information. And by May, the Secretary added SCID to the RUSP.

So where are we? This is a, a very colorful map and I'll just give everyone a chance to look at it. This comes from our friends at NewSTEP and is accurate out to May of 2019. You can see here that for the 51 programs, we're able to implement SCID within less than a year. However, in gray it, it took 40% or 21 out of the 51 newborn screening programs to implement it.

So the average time from when the Secretary added the condition to the RUSP to when it was actually implemented was 4.3 years with, with quite a, a, a big range. These maps always

look funny to me 'cause it looks like Alaska and Hawaii are little islands near Texas. But I, I apologize.

So in terms of challenging, challenges to implementing SCID screening, well, this was the first use of a molecular test. And so it required a lot of work on the newborn screening program side of things. There was variations in targets of screening.

So in terms of what exactly, you know, is it just T cell lymphopenia versus more traditional immuno, SCID was the target. Pre-term infants had a higher re-test rate compared to full term infants. And so this required some work within laboratories to find the sweet spot for screening. Now that I say that, I appreciate that's probably not a word that's used in the laboratory environment, but hopefully you know what I mean.

And there's variation in incidents by race and ethnicity, which also created, you know, issues with, with figuring out, you know, what the thresholds are for testing.

In terms of things that, that facilitated the process, well, certainly there's a lot of advocacy work as well as collaboration amongst federal, state, and nonprofit organizations. There is national technical assistance activities including from the CDC. There was funded SCID newborn screening projects and then kits that, according to the lab folk we talked, were relatively straightforward to use and they help establish uniformity.

So I'm going to, I'm going to move on now and talk about CCHD. This is a condition that was initially nominated in 2010. There was some back and forth with the Secretary clarifying the evidence. And by September 2011, CCHD was added to the RUSP. So here is a similar map to what you saw before and the average time to implement CCHD newborn screening after it was added to the RUSP was 2.6 years.

However, there's a lot of nuance in terms of how individual states decided to implement CCHD screening because unlike the other conditions that

we're talking about, it's a point of care newborn screening tests in certain terms of, you know, who's responsible and how reporting worked and that kind of thing. There was a great deal of variability.

So as I just mentioned in terms of challenges, it was a point of care test. So when you move things out of the newborn screening lab, things become more complicated than when they are on the dry blood spot. There's variability in the approach to how screening was required and the, the specific rules around this, things were decentralized. And of course because there's differences in hospital's birthing centers, home, variable reporting requirements, and then there was also some differences in the screening algorithm.

So it's not that unusual for newborn screening tests to work a little bit different from state to state, but here in terms of the cutoff or whether or not there was requirement for an upper extremity and a lower extremity, those

kinds of things really did vary. And then there are very special challenges related to things that could cause false positives. So if you're born at a high altitude where the oxygen tension is lower, that could lead to a higher false positive rate. And so those things are, are still in the process of being worked out.

And then screening in the NICU also created a lot of challenges and there's a lot of worry. And I think some of it still exists about babies who may spend a little bit of time in the NICU and then are transferred to the full term nursery in terms of missing out on the opportunity for screening.

So things that facilitated CCHD screening, as before, there was a lot of advocates that were involved in the process. With, with that involvement there was some nice educational material that was developed. Some states were able to use their birth defect registries as a way to understand the impact of, of the screening. And then there is some work that it developed

around telemedicine, especially for remote echocardiography.

So I'm going to, and I'm going to go into -- once I'm done, I should have mentioned this before, is that once I'm done talking about the individual conditions, talking about some of the things we've learned from the, from published reports, but I just want to give this high level again about the timing of, of implementation and some general themes about barriers and facilitators.

So let's talk about Pompe disease. That was initially nominated in 2006 and there was some back and forth. It was renominated in 2012. In January 2014 the Secretary requested additional information and it was by March of 2015 that Pompe disease was added to the RUSP. So here is a map. You'll notice this is the first time that we're seeing white, which is states that are, that are either not screening or not in the process of pursuing screening.

The blue states are those that are

screening. The green ones, actually only one green one, New Mexico, is involved with some pilot study work. And then the yellow states are somewhere in the process of pursuing implementation. Again, this is from May 2019. It's a fast moving field. So I apologize if you're, if your state has flipped to a, a different color. Among those who have implemented screening, the average time to do so after it was added to the RUSP was a little bit over two years.

Let's now talk about MPS1. This was initially nominated back in May of 2012. In February of 2015 things moved to evidence review, and by 2016, that's when the, February 2016, that's when the Secretary added MPS1 to the RUSP. So this state uses the same colors as before and you can see that there's a lot of white in terms of states not actively or even in the process of pursing MPS1 screening.

The blue ones have universal screening. And now we have two states, North Carolina and New Mexico, that are involved with pilot studies, and

the yellow ones are somewhere along the process of pursuing screening.

The, for those that have adopted screening, the average time has been about 1.6 years after it was added to the RUSP. Everybody with me so far? Okay. This isn't creating as much attention as value, so, which is probably a good thing, I guess, for me.

So in terms of challenges to implementing Pompe disease and MPS1 screening, and I put these together because they're really, the issues are, are similar. Having commercially available -- the commercially available tests we've been told are more difficult to use. There's been some challenge around getting reference material.

One of the big problems is pseudodeficiency, which really varies by subpopulation as well. There's the issue of diagnostic uncertainty after a positive screen in terms of the challenge of figuring out if something's pseudodeficiency or not, or early onset case versus a late onset case. And of

course there's the challenge of identifying late onset forms in terms of not only communicating that to the families, but having systems to track those individuals.

In terms of facilitators, well, these lysosomal storage disorders can be multiplexed, which makes things more efficient. There are tools that can be used to reduce false-positives like CLIR. There are pilot studies that have been done to help facilitate where the cutoffs are. And then really sort of harkening back to the talk before mine, there're are databases out there with mutations and some expected clinical characteristics that can help with identifying the expected course for a child after a positive screen.

All right. Now any, everyone with me so far? Okay. Now let's talk about X-linked adrenoleukodystrophy. This was initially nominated in 2012 and like the other conditions, there was some back and forth before things went through the evidence review process. And it was

in February 2016 that X-linked adrenoleuko-dystrophy was added to the RUSP.

So here is our map using the same colors as before. Again, I'll just highlight that the blue ones are doing it. The green ones are presumed pilot studies. The yellow are somewhere along the line of pursuing implementation. And the states that are in white are not screening or actively pursuing that right now.

And among those that are doing it, the average time to implementation has been about 1.6 years after addition to the RUSP. Again, these numbers are going to change once these other states come on. You can see how many states are in white.

So in terms of the challenges of implementing X-ALD, there have been some laboratory challenges in terms of FDA approval for certain reagents, and then some, the liquid chromatography tandem mass spec columns weren't available that that's used in the process of screening. There's diagnostic challenges with X-

linked adrenoleukodystrophy like the other ones. There's the issue of follow up. Remember, it can be some years before a child might need intervention.

There's a challenge of cascade testing. So identifying a case and then working up the other family members to see if somebody might, somebody else might have adrenoleukodystrophy. And then the incidents that's been reported so far is somewhat higher than expected based on the evidence review. So about 1 in 5,000, which has been reported in Minnesota versus the 1 in nearly 17,000 that we expected from the evidence review. Again, in a sense, the changing epidemiology as people start screening isn't entirely surprising.

In terms of things that have facilitated x-linked adrenoleukodystrophy screening, there's been, you know, tweaks to the follow-up algorithm to make the process smoother. There's a potential for multiplexing Pompe disease. This is -- we shouldn't have that in there. That was from before. But there are registry databases for x-

linked adrenoleukodystrophy.

So let's take a step back and just think about some of the common barriers and facilitators. So in, in terms of common challenges to new disorder implementation, and this harkens back to a lot of the stuff that we talked about yesterday with costs and the modeling and that sort of thing, but the need to hire and train new personnel. Issues of procurement and getting the equipment in place, updating the LIMS system, the Laboratory Information Management System, having databases out there to be able to interpret variants. And then the issue of developing follow up programs and clinical management programs.

In terms of things that can make the process smoother, peer resource networks across the newborn screening programs. Certainly pilot funding or implementation funding never hurts, right? So we know that that's helped in the past, having working groups developing protocols. Next generation sequencing for second tier testing,

having that more available can make the process easier.

And then, and this is where some of the advocacy groups, I think, have been particularly helpful as well, is in terms of coming up with common legislative approaches, model legislation so newborn screening programs can adopt these conditions in a, in a, in a similar way without having to go back and start from scratch. Everybody with me? Yeah? Okay.

So in terms of the legislation, there, you know, one of the interesting challenges is that there's variations in how the, the process works with some states needing new legislation for each condition, some states needing separate legislation to get funding to be able to pay for the adoption of the tests.

And then the, going through the whole budget process and figuring out fee increases and that kind of thing, which is highly variable, can certainly slow things down. And that's why the, you know, the more that states can work together,

that advocacy groups can help with model legislation, the sort of easier that process goes.

We, we did hear from people that we interviewed about the, the benefits of blanket legislation as a facilitator of newborn screening. So I'll just highlight three states. This is not meant to be exhaustive. There's probably other stuff out there that we're not aware about, aware of, but there is this California Senate Bill 1095 that mandates screening for any disease recommended on the RUSP with an implementation deadline of two years from RUSP addition. And the state's required to put forth funding for that. So that sounds pretty good.

There's Florida SB 1124 from June of 2017 which states that a Florida Advisory Council must review any condition added to the RUSP within one year of, of its addition to the RUSP, and that conditions approved by this Florida Advisory Council must be implemented within 18 months. So it sticks this council in place where California goes directly from the RUSP.

And then in North Carolina there's legislation from 2018 that grants State's Department of Health and Human Services discretion around newborn screening expansion. I'd be interested to, to hear members of the Advisory Committee if they have any comments on those so if they know of other legislation that we should look at.

We are in the process of interviewing newborn screening programs at the state level regarding issues of implementation, a lot of the things that we've already talked about. And we're specifically looking at early adopters and late adopters to understand how things came about. And I, we have this list of states that we're going to be looking at and the, the conditions that they're screening for here. I won't belabor that point.

But I want to switch gears now and talk about what we've learned from our look at the literature. So this is not final. I'm going to show about a million numbers. I don’t want to get -- for the purpose of the talk, I don’t think

there's a lot of value. Using that word a lot today. But to, to dig into each specific finding. I want to keep this at a high level just so you can get a sense of what's out there.

So we've identified these four studies regarding SCID screening that have reported test accuracy and their overall experience including what's happened with babies in the NICU versus babies who are not in the NICU. You can -- I'll just leave it here for a minute. So if you want to take a look at it to get a sense of the variability. Okay. I'm going to move on.

So in terms of some of the, the specific things I like to highlight, there was one study that looked at 11 screening programs and combined the newborn screening data from them. And this was what was reported in that, screening between 2010 and 2013 of slightly over three million programs. And what's nice is that this study really describes the outcomes of the babies that were identified, the 52 babies with SCID. This, this study also nicely summarizes some of the

incidental findings.

Let's move over to CCHD. We identified this, it was, yeah, six studies of, of screening, and you can see they reported test accuracy and the number of cases that were identified. You know, it's interesting to see there's, you know, things are really all over the map in terms of sensitivity and specificity and that kind of thing. A lot of it depends when you read individual studies what exactly, what population they were looking at and how they were classifying individuals.

So I did want to highlight one study that I thought was particularly creative. Scott Gross, Scott back there was, was one of the coauthors on those. And it was really policy analysis looking at whether or not states had policies regarding newborn screening for CCHD versus those who didn’t and did a complex difference-in-difference analysis.

So they looked at differences in outcomes in states that had policies compared to those who

didn't. So those states that don't have policies around CCHD screening essentially provide a control group. Because, you know, there's all sorts of other things that are going on. So being able to have this comparative group to understand the impact is, is really helpful. And I think it's a good example of the kind of creative work that can be done to understand the impact of screening without necessarily having to go to the individual level to understand, you know, what was this baby's screening results and that kind of thing.

I don't mean to imply that that level of work isn't important, but I think it's a nice way to point out that, that using existing datasets you can be creative to get a sense of, of what the impact of a policy level recommendation is. And there was about a one-third reduction in death due to CCHD following newborn screening implementation. Certainly if the Committee wants, we can have Scott comment further on his study once I'm done going through these slides.

This is a slide similar to the ones that I've shown before around Pompe disease screening including the rates. Again, as we move closer to the full study, we're going to be able to do this graphically and put it in a way that's more easily digestible. One of the things, though, and I alluded to this before, and actually Dr. Riley and I talked about this last night, or yesterday afternoon, was that one of the things that's striking is the relative small number of studies. But I, you know, hope that, that more similar studies are going to be coming out soon. And I would certainly encourage those who have access to the data to, to do so.

So the, this is a slide around screening accuracy. This is a slide that, that highlights what happened as a result of screening in terms of the cases that were identified, not surprising given that the, you know, it's a relatively new screen that programs are doing. The numbers in terms of identified cases is small.

Here is a similar slide for MPS1. Again,

I'm not going to read through the whole thing, but I can leave it up there for a second until it looks like people are glazing over or they avert their eyes. This is like when you're sitting in a restaurant, you got to close the menu to get the waiter to come. I'll wait until some people aren't looking and then I'll know to go on.

And these, again, are what we've been able to find in terms of outcomes. And again, the numbers are small. So it's hard at this point for us to have a, you know, less than about the overall importance to public health for screening for these conditions. And here are the studies for adrenoleukodystrophy including the, what we've been able to get out of here thus far is the, the key thing is the positive predictive value.

And move on. And this is what's happened as a result of the cases that were identified. Again, we're really talking about a small number of positive screens. So in the North Carolina report there were 12 and in the Minnesota report there were 14. Again, I don’t mean to imply that

this, that there's no other data out there. I suspect that there's unpublished data that we'll be able to get access to.

So let me stop it there and open up to questions.

DR. CYNTHIA POWELL: Operator, please open the lines for Committee members and organizational representatives on the conference line. Any questions from Committee members? Beth?

DR. BETH TARINI: Thank you, Alex, for summarizing that trove of data. I, the one thing that struck me as I went through the document before the meeting was the apparent lack of population based data in that many of the studies, but I didn't read it word-for-word, seemed to be pilots and health systems, small groups as you alluded to, I think, biased populations. Is that your sense when you look at these, this data?

DR. ALEX KEMPER: Yeah. I mean there's variables, right, or some are, you know, more state level data in terms of reporting out the

number of positives and the diagnostic workup and stuff like that. I, I generally agree with what you're saying. I'm just being a little bit cautious because we're still in the process and I suspect that there's probably a lot of unpublished data that newborn screening programs have. But it's, you know, it's, it's a concern.

DR. BETH TARINI: That's an excellent lead-in to my next question, which is we as a Committee are, we've talked a lot I think in the last five year about the pilots, trying to get more data on the front end so we know, know more when we're reviewing these conditions about what actually the impact could be predicting it forward.

In this case it seems we, and I use the collective we of the room, and the programs, have the ability to access this data more directly than we do, for instance, doing pilot studies on the front end for some of these potential disorders. So is there a way to leverage the infrastructure we have with APHL, for instance, with our other

partners at HRSA to actually help the programs?

And I'm not saying we need every program because quite honestly if you do like two or three that are the size of small countries, like California, New York, etc., Texas, we could have a better understanding immediately, relatively immediately post of what, post implementation of what is the effect of our screening decisions in the real world.

And I just have this sense that we've not leveraged data that we have the ability to leverage. So I just open that up that to the Committee --

DR. ALEX KEMPER: Yeah. So I think there are two levels and I'm looking at maybe I'll call Jelili up too 'cause he can talk about like what NewSTEPs can access and their, their tie-in to that. And then the second thing is, I mean we've talked, you know, as a group a lot about what things -- when a newborn screening program accepts funding to do an implementation pilot study should there be, you know, a prescriptive list of things

that they should provide at the end of the day --

DR. BETH TARINI: A deliverable.

DR. ALEX KEMPER: I mean just, you know, if there should be some sort of database that things get put into it. And I, I don't want to speak for the NIH or, you know, where, where the thinking is with that, but I mean I know that a great deal of thought has gone into what the expectation should be from the program when they accept funding in terms of sharing their experience, but I'll let Jelili talk about what NewSTEPs is accessed in.

MR. JELILI OJODU: Jelili with APHL. As you all know, the data that we collect in NewSTEPs is actually voluntary; however, as noted by Alex, when we provide funds to states for implementation of any one of these new conditions, one of the things that we try to stipulate is that, in fact we get data beyond the, the voluntary data that they provide to us.

So we do have and we've gotten a fair amount of data at least from the states that are

doing, or screening new conditions or we've provided implementation funds to lately. As Alex showed, a good amount of that data is not being published yet, but I think it will take a little bit of time before we'll be, we'll be able to show more.

DR. BETH TARINI: So I agree being a consumer of peer review with the value of peer review, but could there be a mechanism for this Committee --grey data was used in the SMA, could there be a mechanism for this Committee to review that data as the peer review sort of first step --

MR. JELILI OJODU: Which data?

DR. BETH TARINI: The data you're talking about that's not yet published that APHL has.

MR. JELILI OJODU: I don't know. I don’t think so.

DR. BETH TARINI: Because it's not there?

MR. JELILI OJODU: Because it's, we're still accumulating it, yes, one, and two.

DR. BETH TARINI: So it's not peer review. It's not that it's not in a peer review;

it's that it's still being accumulated and nothing analyzed?

MR. JELILI OJODU: Correct.

DR. BETH TARINI: That's all.

DR. CYNTHIA POWELL: Dr. Warren?

DR. MICHAEL WARREN: Thank you, Dr. Kemper. Always informative presentations. One comment I wanted to share before a couple of questions is I think it's always good to stop and pause, and you highlighted a couple things from a population health impact. Ninety-two percent survival among infants who screened for SCID and were connected with treatment, 33% reduction for kids identified with CCHD, reduction in mortality compared to states that weren't implementation screening.

So I think as we think about the work of this Committee, ultimately you need to improve population help. It's good to step back and, and look at those successes and celebrate that.

The questions I had, one, as you talked about the challenges to new disorder

implementation, I'm always interested in what are the things that we can do to support states. And so do you have a sense among those challenges, are they more weighted towards -- some of them were things like personnel and procurement versus others around plans of care. So some of those are more state specific. Some might be amenable to a more federal support.

Do you have a sense of the weighting of those? Like are there tremendous opportunities if we thought differently about supporting that at the federal level or is this more state or --

DR. ALEX KEMPER: That's such a great question. And that's one of the things I hope to learn from when we do our interviews with the newborn screening programs. It, we went into this project really hoping to be able to figure out like, you know, what are the levers. What are things that can be changed, right? Because there's some stuff that just, it's just the nature of the program and it just takes a while to go through.

I suspect that there's things that we're not thinking about that this Committee or that other federal agencies, other parts of HHS could do to help expedite the process, and I think they're probably lessons too from the, that we could get from the advocacy groups in terms of things that they were able to do to get things moving quickly.

So I, I would love to be able to tell you that, oh, if we did this, this, and that it would make a big difference, but that's something that we just need to wait 'til we do the newborn screening program interviews. But it's something that we hope to get for you.

DR. MICHAEL WARREN: Great. It is interesting looking across if I compare the maps like the less than one year, one to two years. There's not always a lot of consistency. I mean there's just so much variability. It's not like certain states have really challenging policies and it's always difficult for them. The colors change.

The second question I had was, is you talked about some of the legislation and, and some of the legislation is very specific about then the state will fund. Do you have a sense from what you're looking at, are folks doing that through like general state funds? Are they using their state NCH funds? Are they putting that in, into the payer's hands? Do you have a sense?

DR. ALEX KEMPER: I really, that's, that's a good idea. We should ask about that in terms of the, the flow. You know, one of the things that's great about presenting this kind of stuff is as -- you know, I'm a general pediatrician. So I don't oftentimes think about these, you know, very difficult policy things regarding how funds go. So we can certainly tee that up, but it's not something that I'd even thought about to be honest.

DR. CYNTHIA POWELL: Melissa Parisi?

DR. MELISSA PARISI: Melissa Parisi, NIH. So one of the things that we've tried to do, particularly more recently when funding pilot

studies for new conditions through a grant program that, that we are supporting, is to actually require some of these metrics, as I guess you want to call them, for screening efficiency and utility, and try to be very systematic about that.

And one of the useful resources that we've used to try to identify what are the valuable metrics, and right now we're asking for pretty much everything, but really came from a pilot paper that I know Dr. Watson discussed at the last meeting. And I think -- I don't know what its status is. I don't know. It hasn't been published yet, I don't believe, maybe under review, which really tried to lay out what some of the considerations were for pilot screening and what are the metrics that may be valuable for assessing the, the actual value, and whether you're being efficacious in your screening attempts.

DR. ALEX KEMPER: Yeah, and I just really want to commend you for that because I, I think it's going to help us like gain lessons out of

this whole thing. Just to expand on this, Dr. Parisi and I, if you remember this conversation like a year ago, about my idea which I sadly have let whither on the vine, but should maybe look at again, which is for lots of different kinds of studies there's standards for how, how things are reported out.

So for example if you do a randomized control trial, there's this thing called the concert form which is highly prescriptive about how you present, how patients were recruited and what happened to them and whether or not there was an intention to treat analysis and that kind of thing. And it makes everything very transparent.

One of the problems when you look at the results of the screening studies is that people use language a little bit differently or whether or not they include, you know, certain findings or not as a positive screen, or as a true positive versus a false positive, if it was something that they might not have targeted. And so it becomes very difficult when you look at the data to

understand what was the overall impact of it.

And I, I still think that as a future opportunity to develop a standardized way to report outcomes of newborn screening studies, would, would help move the field forward.

DR. MELISSA PARISI: Can I just respond to that? Again, this is Melissa Parisi. I think that's a great idea and I think that those of us who are funding some of the pilot work should agree on the metrics that we request and the outcomes, and of course how those are defined. I mean we all know about, you know, false positive, false negative, and positive predicted value, etc, but, you know, we should really sit down and say here's, here's, here are the data that we would like to see collected and reported out in a uniform way.

DR. CYNTHIA POWELL: Mei Baker?

DR. MEI BAKER: I have a specific question actually. The slide 199 talks about challenging implementing SCID screening, you list variation in incident by race, ethnicity becomes

challenging. Could you explain a little bit more?

DR. ALEX KEMPER: Oh, we were just, and I got to find, find the particular slide, but we were just, because the screening results can differ based on subpopulations, just trying to understand that. Is that, which slide were you talking about? Now I got to --

DR. DR. MEI BAKER: One ninety-nine.

DR. ALEX KEMPER: I don’t have the slide numbers on here.

DR. MEI BAKER: Because the TREC assay, it's the function marker, right? I do notice like in Wisconsin we have planned community and Amish, they have a more high incidence, actually screen them actually little bit easy because they find a mutation we can use genetic. So I just trying to understand this.

DR. ALEX KEMPER: Yeah, I think we were just alluding to that fact that there's variation by subpopulation.

DR. CYNTHIA POWELL: Deb Freedenberg on the phone, do you have a question?

DR. DEBBIE FREEDENBERG: I do. Alex, thank you for that great summary. I just have two quick comments and a question. One is that when a state implements a state-wide screen, that the data is going to change as the implementation occurs because you continue to refine your algorithms, your follow up, and like for instance with CCHD, you know, we, toolkits or whatever recommendations, but then it was recognized that NICU populations needed some more guidance. So those numbers continue to evolve as you do that.

And then one of the other questions that I had is that sometimes on some of the funding opportunities there's a requirement that the state actually implement the screening within a prescribed timeframe, and that may not be possible for the state to agree to. And so that's kind of a barrier for participation in some of those, bringing up some of the new conditions, and I was wondering if you had any thoughts about that.

DR. ALEX KEMPER: Well, so my, my thoughts are, number one, in terms of the work

with the newborn screening programs to continue to refine their processes and also just reflecting changes in our understanding of the epidemiology, that's 100% true. And that's actually why it's so hard to talk about outcomes in screening programs here. So I'm glad you made that point.

In terms of the funding requirements for when to begin screening, you know, that's a question for the funders. So I'll say if anybody has anything to say about that. Although I, I wonder -- I understand that that may exclude some programs from participating, but it might also be a good hook to move people forward.

But as someone who's never actually funded these other than, I guess, paying my taxes, I can't comment on that. I don’t know if anybody else wants to --

DR. CYNTHIA POWELL: Anybody want to comment?

DR. ALEX KEMPER: Nobody's jumping to comment, so, but --

DR. CYNTHIA POWELL: Amy.

DR. ALEX KEMPER: Oh, Amy, Amy Gaviglio.

MS. AMY GAVIGLIO: Hi, Alex. Thank you for the, the good background. And certainly I appreciate the need to glaze over all the tables for the purpose of this talk, but I do think if, if we are going to kind of truly ask ourselves whether screening for this conditions was a good idea or how it is going, it'll, we'll kind of have to stop and delve into those a little bit more.

I mean certainly looking at some of the, the tables that show almost a 30 to 1 pseudodeficiency to disease impact, I'm wondering if there is going to be work to talk with programs about what is that impact on not only the medical system of, of having all these pseudodeficiencies, having all these carriers, but also to the public health program and the time it takes to call that out. So that's my first question.

DR. ALEX KEMPER: Yeah, so 100% yes.

MS. AMY GAVIGLIO: Okay, perfect. And then I, I feel a bit the need to say this; although I defer to Dr. Scott Gross on his paper,

that while that, while that CCHD paper is, is very interesting in terms of that reduction in mortality, I think it's important to point out that it is a result of the policy in and of itself, the legislation and the rule and not actually the implementation of a screening program.

Which I think is an important distinction to make because to know that just having that policy, having something in law legislation in and of itself apparently brought enough awareness to CCHD to reduce mortality kind of regardless of how you chose to implement the program.

DR. CYNTHIA POWELL: Beth Tarini? No. Jennifer?

DR. JENNIFER KWON: Jennifer Kwon, Child Neurology Society, and I'm going to piggyback on that last comment. I, I think the papers -- actually I thought the way you presented it was riveting and I really enjoyed it. And I think the papers, though, are very, they're just very early in the process. And so I think to, to Beth's

comment about -- I really, I think we need to look at those rates of pseudodeficiency and late onset cases and we are going to need to have more data to do that.

And it would be nice if it didn't feel like this data were siloed within individual states. If we, we can look at in aggregate to get more of that population perspective.

DR. ALEX KEMPER: I thank you for that.

DR. CYNTHIA POWELL: Okay. Thank you, Alex.

DR. ALEX KEMPER: Thank you.

DR. CYNTHIA POWELL: So we're going to move on next with a discussion of linking data resources by Ashleigh Ragsdale. The Committee's interested in hearing about how states are linking data from various databases to improve newborn screening activities.

Ashleigh Ragsdale is with us today and will present an overview of the current landscape in newborn screening regarding linking data and databases and how state newborn screening programs

interface with other state agencies, hospitals, repositories, the national databases. She will also share where things may be headed in the future.

I'd like to welcome, welcome her. And she is a newborn screening epidemiologist for the Washington State Department of Health and serves as the co-chair of the Association of Public Health Laboratories, Health Information, and Technology Workgroup. Hopefully this overview presentation will be followed by a panel in November highlighting different experiences from, from various states.

MS. ASHLEIGH RAGSDALE: Thank you. And thank you to the Committee for having interest in data interoperability for newborn screening programs. I'm going to try and keep it kind of high level for everybody and not get into some of the more detailed specific topics.

So I want to start by just going over what interoperability is, why it's important for newborn screening, what it looks like today, and

what we hope that it could look like in the future, and then just address a few of the barriers that we have to implementing interoperability.

So I'm going to start off just by defining interoperability. We, we have a lot of terms that we throw around in health information technology, so I want to make sure we clarify a few things for you all. So interoperability is the exchange of data between computer systems or software that leads to the use of the information that is exchanged. So this is a really overarching term used to talk about data exchange.

So interfacing is another word that you'll hear today and that is the act of two or more electronic devices interacting or communicating to exchange information. So when my cell phone sends somebody else a cell phone text messages, our phones are then interfacing.

And so when you look at the differences between the two, interoperability is encompassing the entire exchange process which includes

interfacing, and then also includes the use of that data that you're exchanging. Interfacing is the actual act of doing the exchange.

And then something else you'll hear today is data integration and that involves combining data residing in different sources and providing users with a unified view. So data interfacing, or data integration, excuse me, could be taking a spreadsheet from one database and uploading it into another database to combine that data and use it for a purpose. So just keep those terms in mind as we go through this.

There's also a lot of components involved in interoperability. You have to have databases. They need to have a connection and a, and a data route, and then some of the issues that we find a lot are the issues around data standards, vocabulary standards, as well as syntactic standards.

So if you've ever heard the terms of link codes, that's a data standard or a SNOMED code, and then we, you hear something like HL7 or XML.

That's a data syntactic standard. And so those are things we have to use in order to make sure that our databases can talk to either other in a common language, much like a translation type of situation.

So in newborn screening we actually, we actually have interoperability already within our newborn screening programs. We just don’t tend to think of it that way. So when you have your laboratory information system that's used to do the testing and houses all of that laboratory data, and then that data is transferred into your case management system that's used by your follow-up program, that's a truly interoperable system where that data is being exchanged from the laboratory to case management. Sometimes it's one system. Sometimes it's two systems talking to each other.

But we can really expand on this type of a data exchange for newborn screening programs and when we think about the whole newborn screening system, there are a lot of stakeholders involved

in newborn screening and the bidirectional sharing of data between these stakeholders could really have a benefit to newborn screening programs and the public health system as a whole.

And so I'm just going to highlight a few areas where we could see interoperability benefiting newborn screening. We could ensure that the entities involved, some doctors, laboratorians, nurses, physicians, can have the data so that they provide the best outcomes for these babies with these afflicted conditions and all of it can kind of come together for the appropriate parties to improve those outcomes.

And so just go back one second. So there's just a few of things on here that we haven't really talked about before when we talk about interoperability, things like data repositories, maybe a long-term follow up database, working with the registries that are already within our agencies, so birth defects registries or immunization registries, and there's really big opportunities for combining and sharing

data amongst these areas.

So this comes from the NewSTEPs data repository and this is a screenshot of when programs self-reported use of data integration with their laboratory information system. So I just want to clarify this as data integration, not necessarily interoperability or interfacing. And you can see the most common things that are happening are sharing data with your hearing screening, your CCHD screening, and then your case management screening system. And then the next most common one is vital records. So I want to dive into a couple of these just to give you an example of how these can be beneficial or newborn screening programs.

So one of the goal of newborn screening is to make sure that every baby gets screened and it's really difficult for states to know that they are screening every baby because they don’t know that every baby is born.

And so when you're linking with your vital records, there's two really critical things

that can come out of that. In a real time feed you could identify babies that have missed screening and actually be able to do birth monitoring and outreach to ensure that those babies receive the screening that they might have missed at the hospital when they were born.

And then on the backend you can get a more accurate denominator of the babies that are being born so that when we're doing program statistics and analysis for quality improvement, we have a really, a much better understanding of how our programs are functioning and if we're really reaching the entire population the way that we hope that we are.

And so linking with vital records which are receiving birth certificates, by combining that data together we can get a feel for actually what's happening out in our states at the, at the whole state level.

So when we talk about integrating with vital records, very few states are able to go beyond the data integration factor into

interoperability or even interfacing. Most states are doing some sort of manual process. In Washington it's manual. We're taking an export from our vital records, we manipulate the data, we clean the data, and we do some comparisons with the data that we have in our newborn screening system.

And then you have some states, Minnesota, has been able to develop a fully interfaced data system where that process is more manual at, or sorry, more automatic. So at the push of a button they're actually able to import the data from vital records into their screening system and then match that up with the screening records that they have to identify babies that haven't been screened.

And so interfacing is more reliable just because it's, it's, it gives you more accurate data and it's quicker, which is very important when you're talking about newborn screening. That, that speed is critical.

Another place where there's opportunities

and already cases of interoperability is with our point of care screening. And so what we're seeing with these, with this type of interoperability is demographics and contact information is coming out of a hospital medical record. Your hearing or screening results are coming from your testing equipment, and those are being transferred via HL7, for example, into a newborn screening case management system to be used by the newborn screening staff.

So this is an example of how that looks for when something is full interoperable. And not all states are doing this, but this is where we could go with our point of care testing in particular.

And so just to dive into kind of what that looks like now for newborn screening programs, this is also out of the NewSTEPs repository. You can see that the majority of states are getting their CCHD data either on their newborn screening card or it's coming in some, some other independent method that they're then

entering into a database versus two states that are extracting it from different databases, and then the one state that's actually doing it using a health information exchange, which is a full-on data exchange method that's interoperable.

When we move on to the hearing data, we see the exact same thing. So the majority of states are getting it, some type of, on the newborn screening card or in the mail or in some other way. A few states are exporting that out of their vital records and then there's one state that has that fully interoperable health information exchange process.

Another registry that is beneficial for newborn screening, and this was touched on actually earlier today, is using the birth defects registry to supplement the CCHD screening process. So you can use that to help close our feedback loop with the false negatives for cases that were missed by pulse ox screening. That could provide targeted education to hospitals who might not be doing the screening properly.

So it allows programs to do that, as well as just a better understanding of CCHD in the population as a whole. By working with our birth defects registries, we can have quicker outcomes for when there are failed pulse ox screens. And then by sending our data back to the birth defects registry, they also get that benefit of having them see unreported CCHD cases that weren't, that weren't reported to their registry.

And I was talking with Amy about this yesterday and she helped me identify that there are actually other areas where a birth defects registry could benefit newborn screening. There are cases where we could see comorbidities with the cases or the conditions that are already on the RUSP. So that could help us provide more targeted cutoffs for special populations when we're looking at screening results.

So the next one I want to talk about, and this is the one that we hear a lot about when we talk about health information technology and interoperability, is ETOR. So that's the

Electronic Test Ordering and Reporting. So I just want to talk everybody through this so that we all have an understanding of what this means at a very basic level.

So in a particular hospital they can send us an electronic order for the newborn screening test at the same time they're sending the blood spot to, to our, our laboratory. When it's received in our laboratory, the electronic order with the demographic information is then merged with the card that's been received in our LIM system. The blood spot is moved into specimen sampling and testing. We do all of our testing. And then the demographic results are moved, are merged with our test results for result reporting. And that's also then sent to case follow up if there's the need for that.

Those results are then recorded electronically. So there's a pathway that goes all the way back to the hospital. So when we're talking about ETOR, we're really focusing on the red arrow and the purple arrow. And that's an

electronic process of taking the information from the hospital, sending it to laboratory, and then the results from the laboratory going back to that hospital. So this is what we're talking about when we talk about ETOR.

And so this is the map out of NewSTEPs that shows us where we're at currently across the country for where states are doing these types of processes. So this is the HL7 order. So this is the electronic order, and the states in blue are those that have an electronic order process. And the states in red are those that don't. And those in gray just did not provide data.

So it's kind of a mixed bag. This is actually a lot more blue than we saw a few years ago. So we're making a lot of progress in this, in this area. And then, again, this is the results. So this is sending the message from your laboratory back to the hospital. And the states in blue, again, are those that are doing it. States in red are not.

And you can see there's actually a lot of

similarity. So we're seeing bidirectional messaging in the states that are implementing this, which is the ideal way to, to implement Electronic Test Ordering and Reporting.

So we talked a little bit about a lot of individual types of connections and I had that list of ways that we could do that. And a couple months ago we had an HIT summit in Atlanta and we started to draw the connections between the newborn screening programs and the other databases or agencies or processes that we would want to share data with. And it looked like this. It was a total spider web. So this is graphical representation of that. But you can see that we're making a lot of connections in order to share that data amongst programs and entities.

So I want to talk a little bit about what the ideal state would be. So how do we make that fit into our newborn screening system as we see it now. And what we call this is Xanadu, which is like our ideal state. This is where we want to get. And so the stuff that you see here is just

what's kind of happening in a newborn screening right now. Most of this is electronic. It's, it's data flowing in and out of the program.

And so we could see areas where we can improve that by having a laboratory inventory system. So this could be kit management and includes your expired dates, your specimen bar codes, who you sent those cards to. So there's a lot of functionality that can help with that. And then that's linked in with your LIM system.

And then you have a specimen tracking system that can follow the specimen from the hospital all the way to the laboratory. Just the way we follow our Amazon packages now, we can see where they are, where they picked up, have they been, are they going to be delivered. And that way we actually have a better understanding of specimens that maybe got lost or missed or a courier didn't get.

And so we can have a better real time access to following up on those, on those specimens. And this also helps the hospitals to

fulfill their CAP requirement of ensuring that specimen has been received.

And then I'm going to introduce something called the, the ADT message. So this is an Admission, Discharge, and Transfer message and this is an electronic HL7 message that is used in hospitals all the time for lots of different things. And it's floating around the hospital and it's being generated every time a baby gets born because they're admitted. Every time they transfer to a different floor. Every time they're discharged. There's lots of information in this message.

And so if we could harness that message as a newborn screening program, we could use it for a lot of things, one of them being birth notifications. So a baby was born. We could use them at discharge to provide us with the most current PCP information. So rather than taking the PCP information at the time of specimen collection when maybe parents haven't decided or they're not awake to tell the nurse, we could get

it when the baby's being discharged.

And so there's this rolling ADT field so that we can have this flow of information. You can also -- so you can use that to track your patients and start follow up. We can also use the ADT message for clinical purposes because there's actually a diagnostic test field, or a diagnosis field in the ADT message.

So once an infant is diagnosed with something, we could be getting that message electronically into our databases to provide a diagnosis. This could help us identify missed cases and false negatives and have that feedback loop back into our laboratory and do that quality improvement that we're all really looking to do.

Two other places that we could use electronic exchange of information is for our risk analysis databases. So interfacing with things like CLIR or the CDC to send data to a repository. And then also when we expand molecular testing, we could use it to access variant databases so we could have a bioinformatics pipeline to share raw

data with a centralized bioinformatics pipeline.

And so you could have your analysis done by somebody or you could be using it to get feedback on variants of unknown significance. If that information is updated in the future, they could have that feedback loop back into your system.

So the whole kind of goal of this is to just provide an audit of the newborn screening system to assess whether we're doing what we're supposed to be doing. And particularly for these later onset disorders, we can really harness this technology to close those feedback loops that we, that we need.

So just a few things that I think I already touched on all of these. Just that birth notification. The real time patient follow up info could be really useful for follow up programs, getting treatment information, diagnostic testing status, results. And then if we develop long term follow up measures, you can actually take an ADT measure -- or sorry. An ADT

message and you can set up triggers so that those triggers can be, can be set based on your criteria, and that message will come to you automatically when those triggers are met.

So when we look at this, we're thinking about the system. So when we look at this from the hospital perspective, the current state for the hospitals isn't that great right now because this is what they see. They, these are actually all programs at, at Washington State Department of Health that require or request data to be transferred from a hospital whether that's electronic or paper or in batch files. So the hospitals are making lots of connections and they're sending lots of data to public health, and sometimes they're sending the exact same data.

And so what we want to see from a hospital perspective is how can we bring that back for them so that they only have one connection that they're making and they're only sending one piece of information one time. So we're looking at the, the agency, Xanadu, which would for the

hospital so that they're making one connection to an agency and then within an agency that agency is keeping that data and distributing it amongst their programs.

So for example, that birth notification we were talking about with an ADT message, it comes from the hospital. They make one connection to your agency and then your agency is able to distribute that data to all the programs that need it. Like newborn screening, hearing screening, CCHD screening, immunizations, vital records.

So instead of each of those programs connecting to each other, we're just connecting to one place as well. So this is talking about like a spoke and wheel model, hub and spoke model, so that we can just move data in a more efficient manner.

Taking that even one step further back, we had this public health Xanadu that we came up with and this is a very, very ideal state and requires a lot of support from folks to put this into place. But the idea is then we take that hub

and spoke model even further out and instead of us making a connection to a hospital, the hospital's making a connection to something like a health information exchange hub. And then that, we make the connection to the health and information exchange hub so data's flowing through there.

But then your state and federal partners are connecting to the health information exchange hub. Your Medicaid and Medicare pairs are connecting there. Your hospital EMRs, your diagnostic laboratories. And so data is, is being routed through one connection and it really reduces the workload for agency IT staff, hospital IT staff, all of the players involved in this.

Okay. So recap just some of the benefits real quickly. So identification of false negatives. Identifying babies that may have missed screening, which is something we're always trying to do improvements in data quality, which has lots of benefits for newborn screening programs particularly in that completeness and accuracy of the data.

Improved data security. So removing the mail, faxing, and e-mail public health information that happens right now to have more secure data measures. Define case definitions that we could update, disease status, and changes in diagnoses as we move forward, especially with late onset conditions. And then increased efficiency in staff for both newborn screening, hospitals, submitters, public health staff, kind of the whole system.

So there's some barriers to doing this that we've come across. Agency policy can be a big barrier. They are hesitant to move into new things. Lots of agencies don’t have a lot of informatics infrastructure. So we're looking to help build out informatics infrastructure and having them take that, you know, 100 level view of it instead of just building these connections at a programmatic level, doing it at an agency level.

Program prioritization is always an issue for newborn screening. There's a lot of new disorders being added. There's a lot of work.

There's only so much money. There's only so much time. And so this is something that often gets kind of pushed to the side.

Having the right partners at the table can definitely be difficult to understand that just like newborn screening programs are unique, hospital systems are unique, and hospitals are unique, and they all have different methods and they all have different EMRs. They all have different ways that they're collecting and storing their data. And so there isn't a lot of common data structures out there that we can harness at this time. So we really all have to kind of work on that together.

So there's privacy issues. So sharing of data brings up privacy issues. And then there's also perceived privacy issues. So kind of navigating what is a perceived privacy issue versus what is a legitimate privacy concern.

Funding sources can always be difficult. There are some funding sources out there that states can capitalize on, but there's some issues

around not really knowing how to tap into it. Agencies not really knowing how to capitalize on it. And so needing some guidance on how do we actually utilize this funding to make this happen. That's definitely a barrier.

And then the lack of trained professionals in public health informatics is definitely a barrier at this point. I am the co-chair of the HIT workgroup. I am self-taught. This is not what I went to school for. I have like taken some training courses, but it's just something that kind of happened to me and it's been something I enjoy. I'm not complaining.

But most, and that's how most of our workgroup is. You know, we don’t have a lot of people who went to school for this and this is what they're doing in our newborn screening programs. And sometimes it's not even in the agency yet. And so we're really kind of lacking there.

So why are we telling you this? Because we want help. We want to expand interoperability

for all of the benefits that I listed. And there's some ways we can advance that. We know that we need to encourage our agencies to develop interoperability priorities. We need to develop lab level interoperability plans. So working with our other lab programs is really important as well.

We really need to pursue some of these funding opportunities and have some, you know, develop some plans on how can newborn screening programs really harness that. And then expanding that informatics workforce maybe through training programs or internships. I'm not really sure what that looks like. And then we're here to bring this to you guys and see if you guys have any idea on how you can help us, you know, move this forward.

So thank you and thank you to my workgroup and everybody that helped me with these slides. I appropriated a lot of them from other folks. So, questions?

DR. CYNTHIA POWELL: Thank you, Ms.

Ragsdale. We do have some time for some questions from the Committee and the organizational reps if the operator will please open up the phone lines for Committee members and organizational reps on the phone. And let's see.

OPERATOR: All lines are now open.

DR. CYNTHIA POWELL: Beth?

DR. BETH TARINI: Ashleigh, thank you. That was outstanding. I, and I think having someone who can bridge both worlds is crucial, and also you're emblematic that people can learn to do this even if you weren't programing, you know, since the womb. So thank you.

There was a term or a sentence you used that resonated with me. It said we're busy doing all of these other things. I can't remember the quote exactly. I'm sure they have it. And, and we don't always have enough time to pay attention. Not to pay attention. To, to focus on this. And one of the thoughts, one of the things you had was new, when you said was new disorders.

And I sort of heard this murmuring from,

from others. Can, and I don't know that I have a question more than to open the floor and sort of be the conscience of the Committee to say in some ways we, I really encourage us -- I'm not saying we should not include more disorders. I'm not saying we shouldn't give Alex more work to review, do more evidence reviews.

But if we are so busy doing and less busy focusing on the infrastructure of our house and how well we're doing, we are in some ways doing a disservice I think to the system and to the families.

And so your comment resonated tremendously with me. And so can you speak to your -- I guess can you speak to your experience where you've had to navigate this issue?

MS. ASHLEIGH RAGSDALE: Yes, I can. So we've actually had IAPD funding for a few years in Washington for newborn screening and we've used like 2% of it. Because I don't have the time to do that. I don't have the time to do it because we've been under construction. We've been adding

conditions. We've been adding states. So where there's lots that, there's competing priorities, and when you talk about newborn screening, the main goal is to do the screening itself.

And so we definitely have to, when, when things get tight and when budgets get tight, you drop the things that you can't afford to do anymore and focus on the ones that you can.

And I think we're missing the opportunity to realize that if we put our effort into this, we could actually do the job that we need to do better. So we could actually find efficiencies by kind of putting some upfront work into that. I think it's going to pay off in the long run for programs. But it's definitely a long process. And part of that too is we just don’t have a lot of direction on how to proceed sometimes.

So definitely adding new conditions is, is, has taken my time away from my supposedly dedicated IAPD time to work on things like this. That is for sure. And I know other programs are the same way. Brendan Reilly was invited to do

this talk and he's not here because they're starting ALD next week. So, you know, that's a very small example.

DR. BETH TARINI: It's a very helpful, concrete example of the reality of tradeoffs in the real world.

MS. ASHLEIGH RAGSDALE: Yeah.

DR. BETH TARINI: Unless you can -- I mean if the 2% is, is a 90% something used, then that's a local level decision of that. But if the 98% is being absorbed into something else, I mean these are the real tradeoffs having been the chairwoman of two, of a state committee. These are the real tradeoffs that occur in the real world at the state level that, that are the difference between what we see on the maps -- or that are, that are behind what we see on the maps. My, in my experience.

MS. AMY GAVIGLIO: Yeah. And I just want to add one more thing. I think if we can't begin to really push this for programs, newborn screening's going to get, we're going to get left

behind in this process. Agencies are going to move on without us federal -- you know, the informatics world is moving quickly and if we don’t jump on that train, I think we run the risk of just really, really falling behind the, the curve.

DR. CYNTHIA POWELL: Amy Gaviglio?

MS. AMY GAVIGLIO: Hi, Ashleigh. Thank you so much and I want to apologize ahead of time for asking this question a little bit 'cause it's something I've been thinking about. And to put you on the spot, I'll buy you a glass of wine later.

So you, you mentioned, you know, maybe 10 to 15 different areas of interoperability that a program may, may look into, and Beth rightly pointed out that none of this is done in a vacuum; it's done in the context of having to do a lot of other things.

Has there been work or are there tools available for programs to say here's where my gaps are, here's maybe where some of my efficiencies

are, or my gaps in terms of I have no idea what the denominator in my population is, and then to, to kind of choose their own adventure on which path of interoperability they should go to really get the most return on their mission?

Is that something that maybe this group could help with in terms of saying, you know, we recognize that there's a lot of other things to be done, but here's how you can assess where this type of work will bring you the most bang for the buck as quickly as possible?

MS. ASHLEIGH RAGSDALE: Yeah. I think, I think that's a great idea and what we have talked about is kind of developing a roadmap of you're at, you know, you're at ground zero versus you're, you know, halfway down the road. You know, how can newborn screening programs find themselves on that map so that they can move in the direction that we're trying to get at.

And I think it's an interesting concept to think about it not just in moving towards full interoperability, but also what can, what can

really provide me the most benefit at this time. So I think that could definitely be integrated in that roadmap that we've been talking about.

DR. CYNTHIA POWELL: Joan Scott?

MS. JOAN SCOTT: Joan Scott, HRSA. Thank you for that presentation. It really was excellent. I know enough to be able to say the words interoperability, but not necessarily even in a sentence in the right way. So, so thank you very much. That was extraordinarily helpful. And in, in appreciating the conflict in prioritizing, what you're doing, bringing on new tasks and trying to do this at the same time, and this kind of follows a little bit on what Amy was, I think, asking too. Have there, is, has anybody made a business case about, about revenue loss, FTE time loss, doing these things manually as opposed to, you know, biting the bullet and putting the, you know, the time and effort into getting? Because that sometimes can also help move those processes forward in your organizations.

DR. CYNTHIA POWELL: Did you want to

respond to that? Yeah?

MS. ASHLEIGH RAGSDALE: So in my experience so far, Minnesota has been working on a return on investment for the electronic test ordering and reporting. But go ahead.

DR. JOSEPH SCHNEIDER: Yeah. Joe Schneider, Texas, but also Chief Medical Information Officer at a large organization. At one organization where I was at, we mapped out the process of newborn screening blood spots. We wound up with about 50 different discrete steps. By implementing this sort of system, the, of electronic, making things electronic, we were able to cut that by more than half. So these sorts of analyses are done all the time in the, we call it the CMIO world or the CI, you know, the informatics world.

The problem is that when you compare this to diabetes, heart disease, and other sorts of things like that, this is, this is the appendix of a mosquito. And so as a result, newborn screening remedies the back order.

MS. JOAN SCOTT: Some of those places that has been done, is that generalizable enough that other organizations could take the few folk that have done that?

DR. JOSEPH SCHNEIDER: Probably the, the methodology could be spread, but unfortunately because of the uniqueness of the processes at, sorry, every state, every hospital, every doctor's office, be, it becomes, it is not a cut, it is not a plug and play type thing. But, yeah.

DR. CYNTHIA POWELL: Right. We have -- Scott has a question, then Carla, Jennifer, Melissa, Mei, and then we're going to need to cut discussions so we can get to lunch. Scott Shone on the phone?

DR. SCOTT SHONE: Scott Shone. So actually I just echo everybody else. Just an amazing presentation. Thank you so much for, for, for what you shared today. My, I think my question's pretty quickly, pretty quick in line with what has been said so far.

In terms of infrastructure and support

with the department, you know, over time a lot of agencies have consolidated the IT support, IT staff, IT projects either at the agency level or some have gone so far as at the state level. You know, in your experience in the state, that slide you showed, you know, the number of states who have integrated and have, are working to move their systems towards this goal, how many of them actually have dedicated resources within, say, the newborn screening programs such as yourself, at the public health lab level, or have gone up? Does that -- the diminishing return, does it go up and is it unrelated?

MS. ASHLEIGH RAGSDALE: So I would say that there's, there's very few newborn screening programs that have dedicated health informatics staff. There's more agencies that do have dedicated staff. So as you kind of move away from the program, there are folks at an agency level that can help.

But just to clarify, informatics staff is not IT staff. So it's definitely a different

component, and so, and I think that's one of the problems that we run into when we start to talk about this, is that lots of people think that they need to go to their IT programs and agencies think that IT needs to handle this, but informatics is very, it's much broader than IT. There's a very small IT component that's involved.

So from my experience, there's a lot of work being done with, with ASTHO and some of the broader public health agency groups to bring up informatics stuff. There's even a public health informatics group at APHL to help with that. So that is really growing and that's where I say newborn screening needs to kind of jump on that wagon so we don’t get left behind and we don’t get kind of lost in the mix.

DR. CYNTHIA POWELL: Carla Cuthbert?

DR. CARLA CUTHBERT: So thank you, Ashleigh. That was wonderful. I was at the meeting and, in Atlanta when you guys discussed this and that was really wonderful. I think Scott just asked my question, one of the questions I

wanted to have answered from you. And thank you for your distinction between informatics and IT staff.

And I think that, that's something I also want to sort of understand and tease out a little bit. One of the things that we as a community, some of us in newborn screening and public health have been thinking about, is the impact of, of introducing data science and data analytics into newborn screening and looking towards how introducing data science could help transform our workflow.

And we've had some discussion about this and APHL and CDC have just funded, or at least in the process of funding a few states to be able to get dedicated bioinformatics fellows to be able to work alongside them to understand how some of the routine tasks could be automated and by using some of those, that, that collective experience, to be able to inform the rest of the community about how we can move towards a set of a minimum criteria, as it were, to sort of suggest everybody needs to

be doing at least this. And that way you help relieve some of the stress and some of the challenges associated with, with workforce.

So in that regard, and bearing in mind that you just distinguished between the need for bioinformaticists 'cause they do a separate task, and IT specialists, is, would you consider there to be a separate need for a separate dedicated newborn screening IT specialist, or would you suggest that the, the response or the solution is, of course, much more agency wide?

And of course it needs political will from the Agency. It needs for people to recognize that there is a common Xanadu that they can all work towards and sort of relieve some of the, some of the, I guess the power that they look for something else that is bigger and better. Would you -- would you consider an HIT newborn screening specialist something that would be a short term solution or really it wouldn't really matter? I'm just trying to get a sense from you for that.

MS. ASHLEIGH RAGSDALE: Yeah, so I think

there's lots of ways to think about it. You, and there's, there's many ways to kind of skin the cat, right? So you could definitely have agency level or public health lab level informaticists that are involved. I think one of the things that we run into, in Washington we have a pretty big informatics workgroup compared to other state agencies, but there's a lot of very unique things that happen in a laboratory that they don't necessarily understand.

So you, you need to have some combination of expertise in the program at the programmatic level or at the laboratory level, and then the, the expertise that comes from the training that you get when you're in an informatics program. And so there needs to be that combination.

As far as whether it's short term or long term, I think there's definitely a need for a short term, really kind of a three year type project situation where you could get a program up and running with lots of these processes and then it becomes more of a maintenance and operations.

And then that could definitely be something that's not necessarily newborn screening specific program. It could be more of an agency person that can, can handle that type of situation.

DR. CYNTHIA POWELL: Jennifer Kwon?

DR. JENNIFER KWON: Thanks. Jennifer Kwon, Child Neurology Society. I think the reason that your talk has been so exciting for people is because I think we can see in it a path forward to solving some of these, these problems that seem almost intractable, right, in newborn screening. So for me, my interest is in long term follow up. And so when I saw that diagram, I was thinking, well, I, I want to see the agencies that are beyond that edge. The Medicaid databases, right, the medical records, the schools.

And so, so I feel like we come at this really with very different perspectives and you described this lovely scope, but what I was kind of curious about is I feel like, again, every state is going to be different because their landscape of agencies are going to be so

different. And their way of creating bridges is going to be different. And the questions that they're trying to answer at the end of the day, or at the end of the year, are going to be different.

So for you, what are the specific asks that you have of your database or your linkages? I'm sorry.

MS. ASHLEIGH RAGSDALE: In Washington, like what am I looking for? There's lots of things I would love to see, but I think the, what we really look for is in a broad sense you want, you want a way to kind of track an individual through the newborn screening programs process and beyond. So that birth notification into the screening system, and then that diagnostic feedback loop is really where I think the most bang for your buck could occur.

And then right now when we're talking about adding these late-onset disorders, you really want the longitudinal access to those patients. And so something that we're talking about in Washington and I think a few other states

are talking about this, is having some sort of master patient index number so that patients in a state have a unique identifier that can be used to make sure that you're pulling the data for the right folks.

And so that's kind of where that conversation has to start. Newborn screening is kind of the beginning of that process. And that's, that's where I say if we don't start to get involved, we could kind of get left behind because we are one of the first things that's happening for those infants in the public health realm.

So for my program when I look at this, I'm looking at electrical test ordering or reporting as my priority number one, birth notification as my priority number two, and the moving on to that follow-up feedback loop as my next steps priority, if that helps.

DR. CYNTHIA POWELL: Melissa Parisi?

DR. MELISSA PARISI: Thanks again for a great presentation. And just to follow on what

Jennifer and you were just talking about, I think that there's an opportunity particularly when looking at the long term follow up aspects to also integrate with some of the research-based tools that are out there, including the Longitudinal Pediatric Data Resource and NBSTRN tools because they're also using and incorporating Global Unique Identifiers, or GUIDs, for all the newborns that are being tracked for some of these newborn screening conditions.

And, you know, you need a unique identifier for each child because people also move and go from one state to another. So you really want to be able to follow them longitudinally and make sure that the data that might have been collected in the state they were born also are coordinated with the data if they move to a different state because these are long term issues and long term challenges.

So again, thank you and I hope that you also include some of the research based tools because I think there may be some opportunities to

be mutually beneficial.

MS. ASHLEIGH RAGSDALE: Absolutely.

DR. CYNTHIA POWELL: Mei Baker?

DR. MEI BAKER: I just quickly everybody, I thank you too. The one thing I bring back to the laboratory practice, because we talk about the efficiency also, and I'm going to say one thing. Our staff the common thing is, we didn't improve our efficiency. We just traded one set of problem to another set of problems. So I'm not so sure our experience is unique because a lot of work needs to be done.

And the system become, when you do the electronic interface, it change, becomes so, so complicated, so, so inflexible and the people say what's the collection time involved, you cannot touch. But then you need this calculator to do the cutoff, whatever. So I think there's a lot of nuance in that. So we need to keep this in mind.

And second is the newborn screening interesting is like can we learn from one entity, transfer that, you know, is our experience. In

Wisconsin you have 200 some submitters. You learned from one system. You implement. When you take that, start over because their system different. They use a different software, everything. So it's a lot of things embedded in it. One will think because this is things, also you relied on the other stakeholders.

We cannot automatically think for this entity, for the hospitals, and also we have midwives that don’t even have a phone. So we need to keep in mind that we need a multiple process in place. So I always look at the backend. What's the alternative? What's the most efficient way to do things? So just need to keep this in mind.

MS. ASHLEIGH RAGSDALE: Absolutely. I think it's really important to keep that in mind and I do think that there are some challenges with electronic test ordering and reporting that we're just now beginning to figure out. But the idea is that if we could get closer and closer to that ideal state, those challenges could be solved by some, some work that's done with our partners as a

whole.

So if we're looking at the global ideal state that those types of challenges that you have in particular with not being able to get something like date of collection on an electronic order, 'cause it's not in the same system as the laboratory, you know, the hospital laboratory system, we would be able to, hospitals need to do this work as well.

And I know that there's some frameworks around, around that that, that's happening kind of outside us. So we just, everything's happening in tandem to get to this place where we hope to be.

DR. CYNTHIA POWELL: Sue Berry?

DR. SUSAN BERRY: Thank you, Ashleigh. It really highlights the utility of interoperability, which is essential to the work that we're going to ultimately do. The Holy Grail for most of us clinicians who are interested in long term follow up is interoperability with EMRs and creating systems by which the data flows automatically into something like LPDR. That can

be with structured notes or automatic data mining mechanisms at some point.

This isn't really public health's job, that piece of it, but it's certainly a piece of the system that we would love to see happening. Can you say anything about what you know about any cooperation from electronic health vendors regarding such interoperability?

MS. ASHLEIGH RAGSDALE: In regards to long term follow up?

DR. SUSAN BERRY: At, at any level of that, but long term preferably, yes.

MS. ASHLEIGH RAGSDALE: Yeah. So as we're engaging hospital systems, we are talking to them. The folks at least in our workgroup when they're talking to them, we're trying to take a more global approach. Right now we're working -- so I think it's Utah and Texas and Florida, they're talking to a specific health care system that spans all those states trying to get them to see us as one entity and them as one entity. So can we make that connection.

So there's definitely some thoughts and work around how can we almost sell this to hospital vendors and say here's, you know -- Dave Jones worked on a common data model for newborn screening. So if we can all agree on common data elements and hospitals can agree on a common process, and their EMR can say that if you give me this common data model, then I can do this in every single one of my hospitals, that's a more efficient way of implementing data exchange than me going to a hospital and Texas going to hospitals and Utah going to hospitals and doing it on a one-off basis.

So we're trying to take a wholistic systematic view as we move forward, which would then translate into that long term follow up piece as well. I just don’t know if anybody's really at that, that place.

DR. SUSAN BERRY: It's all about the vendor agreeing that it's not a one-off activity?

MS. ASHLEIGH RAGSDALE: Right.

DR. SUSAN BERRY: That's part of the way

they should build their system preferably --

MS. ASHLEIGH RAGSDALE: Right.

DR. SUSAN BERRY: -- you know. They say if you have one Epic, if you know Epic you know Epic, that one Epic.

MS. ASHLEIGH RAGSDALE: Exactly.

DR. SUSAN BERRY: And that's not really, not really sustainable as a model on a long term basis for data collection, so.

DR. CYNTHIA POWELL: Thank you again for this very important --

MS. ASHLEIGH RAGSDALE: Thank you.

DR. CYNTHIA POWELL: -- presentation and the topic that certainly generated a lot of interest. We're going to break for lunch and we'll plan to reconvene at 12:45. I'm going to turn it over to Catherine for announcements.

DR. CYNTHIA POWELL: Thank you. And what a great morning. Thank you. So just as a reminder, general reminder, as visitors in the building, you do have access to this room and this main 5th floor area in the cafeteria. And if you

do need to exit, we need to have a, we will have a HRSA staff member as an escort by security 15 minutes prior to coming back from lunch if you need to exit and return.

If you have other needs, please let a HRSA staff member know, and again, we will return promptly the 12:45 and we'll start the afternoon. We have two individuals signed up to give public comment. So thank you.

(LUNCH)

DR. CYNTHIA POWELL: We're going to go through the, the roll. Mei Baker?

DR. MEI BAKER: Here.

DR. CYNTHIA POWELL: Susan Berry.

DR. SUSAN BERRY: Here.

DR. CYNTHIA POWELL: Kyle Brothers.

DR. KYLE BROTHERS: Here.

DR. CYNTHIA POWELL: Jane DeLuca.

DR. JANE DELUCA: Here.

DR. CYNTHIA POWELL: Carla Cuthbert.

DR. CARLA CUTHBERT: Here.

DR. CYNTHIA POWELL: Kellie Kelm.

DR. DR. KELLIE KELM: Here.
DR. CYNTHIA POWELL: Joan Scott.
JOAN SCOTT: Here.
DR. CYNTHIA POWELL: Melissa Parisi.
DR. MELISSA PARISI: Here.
DR. CYNTHIA POWELL: Annamarie Saarinen.
MS. ANNAMARIE SAARINEN: Here.
DR. CYNTHIA POWELL: Scott Shone.
DR. SCOTT SHONE: Here.
DR. CYNTHIA POWELL: Beth Tarini.
DR. BETH TARINI: Here.
DR. CYNTHIA POWELL: Catharine Riley.
DR. CATHARINE RILEY: Here.
DR. CYNTHIA POWELL: And organizational reps. Robert Ostrander.
DR. ROBERT OSTRANDER: Here.
DR. CYNTHIA POWELL: Debra Freedenberg.
DR. DEBRA FREEDENBERG: Here.
DR. CYNTHIA POWELL: Michael Watson.
DR. MICHAEL WATSON: Here.
DR. CYNTHIA POWELL: Steven Ralston. Jed Miller.

DR. JED MILLER: Here.

DR. CYNTHIA POWELL: Susan Tanksley.

DR. SUSAN TANKSLEY: Here.

DR. CYNTHIA POWELL: Chris Kus.

DR. CHRIS KUS: Here by phone.

DR. CYNTHIA POWELL: Jennifer Kwon.

DR. JENNIFER KWON: Here.

DR. CYNTHIA POWELL: Theresa Hart.

MS. THERESA HART: Here.

DR. CYNTHIA POWELL: Natasha Bonhomme.

MS. NATASHA BONHOMME: Here.

DR. CYNTHIA POWELL: Siobhan Dolan. And Amy Gaviglio.

MS. AMY GAVIGLIO: Here.

DR. CYNTHIA POWELL: Georgianne Arnold.

DR. GEORGIANNE ARNOLD: Here.

DR. CYNTHIA POWELL: Okay. Great. So in the announcement for this meeting there was an open call for public comments. Today is the second of two sessions to allow people to give their public comments, and then we have two individuals who signed up to provide comments.

First we'll hear from Brittany Hernandez from the Muscular Dystrophy Association.

MS. BRITTANY HERNANDEZ: Good afternoon. Thank you. My name is Brittany Hernandez. I'm the Senior Director of Policy and Advocacy for the Muscular Dystrophy Association. Thanks for the opportunity to provide public comment. Dr. Powell, again, welcome as chair. We are really excited to have you here.

I'm just going to give a brief rundown of kind of what MDA's been working on related to advancing newborn screening for neuromuscular conditions. As I think the entire Committee knows, our organization is really committed to, to, to advancing newborn screening particularly for the conditions of Pompe, SMA, and Duchenne muscular dystrophy.

We recently launched a new patient registry called MOVR, the Neuromuscular Observational Research Data hub, which is being rolled out in our clinics across the country. We have 150 clinical care, clinics across the country

in our clinical care network.

We think that with the combination of our network and MOVR with its clinician entered data that's coming in, we can easily track newborns who are identified through the neuromotor screening process and help connect them to clinical trials and new treatments. And so that's something that we're really excited to continue to expand and, and roll out as, as a resource for the entire community.

We're also committed to state implementation of conditions that are on the RUSP, SMA and Pompe, and that's, that's obviously an ongoing project for us and we will be happy to share kind of our work on that with this Committee whenever that's appropriate.

We are committed to seeing Duchenne be nominated and, you know, at the appropriate time in the near future. We recently hosted a meeting and partnership with Dr. Watson at ACMG to bring Duchenne stakeholders together for a day to kind of talk about what the landscape looks like, what

the opportunities are, and, and really where, you know, the information is missing. And so that's something that, that MDA, ACMG are, are really interested in, in pushing forward at the appropriate time.

Obviously, you know, education via outreach is really important to families and doctors. So we want to make sure that the docs who are working at our care centers understand, you know, the numerous screening process. They're seeing new infants identified for conditions that really haven't come in at this age before now with SMA on, on the panels. And so we're ensuring that, that our doctors are, are, you know, aware of, of, you know, all the resources available to them and especially with the new treatments that are available for SMA.

We recently also did, you know, external education via a JAMA neurology article or piece that was published by a number of different clinicians including people here in this room, and then Dr. Howell who you all know authored an op-ed

in *Stat News* recently about the passage of the Newborn Screening Saves Lives Reauthorization Act in the House.

I will defer to Becky Abbott from March of Dimes to give an update on that at this time, but MDA was really happy to see things move over there. We were happy to work with Dr. Bocchini on his, on his testimony in front of the House Energy and Commerce Subcommittee on Health in favor of the reauthorization of the bill, or of the law, and are always happy to work with this Committee going forward to promote newborn screening.

If anybody has any questions for me, I'm available after the meeting or as always on e-mail. Thank you.

DR. CYNTHIA POWELL: Thank you, Ms. Hernandez. Next up is Rebecca Abbott to provide an update on Reauthorization of the Newborn Screening Saves Lives Act.

DR. REBECCA ABBOTT: Good afternoon, Dr. Powell and members of the Advisory Committee. Thank you for the opportunity to provide public

comments today. My name is Rebecca Abbott and I'm the Deputy Director of Federal Affairs at the March of Dimes.

In that capacity I have the honor of leading a group of public health provider and patient organizations that are dedicated to advancing our nation's newborn screening system through advocacy at the federal level. For over a year our coalition has focused our efforts of reauthorization of the Newborn Screening Saves Lives Act which expires at the end of September.

During public comments in April, I shared our coalition's work to develop a set of principles to guide reauthorization and hinted at the imminent introduction of the bill in the House of Representatives.

Since that meeting there's been a number of exciting developments. H.R. 2507 was in fact introduced in the House on May 2nd. Our longtime champions, Congresswoman Lucille Roybal-Allard of California, and Mike Simpson of Idaho are again sponsoring the bill along with two new champions,

Congresswoman Jaime Herrera Beutler of Washington State and Katherine Clark of Massachusetts.

The House bill renews newborn screening programs at CDC, HRSA, and NIH for five years; makes small improvements to the statutory text governing those programs; and increases the funding authorized for newborn screening activities at CDC and HRSA.

The bill also extends authorization for this Committee and its work for five additional years. In addition to renewing and improving federal newborn screening programs, H.R. 2507 would commission a report with the National Academies of Sciences on modernizing our nation's newborn screening system. This report will include key policy recommendations to inform Congress, as well as HHS, states, and stakeholders as we look to the next 60 years of newborn screening.

In June the House Energy and Commerce Committee held a legislative hearing on the bill. Dr. Joseph Bocchini was the sole witness

testifying about the bill and the importance of federal efforts for our nation's newborn screening system.

As you would imagine, he offered eloquent testimony and deftly answered questions from lawmakers. In subsequent Energy and Commerce Committee meetings, H.R. 2507 was approved unanimously and reported to the House of Representatives for a vote.

Just last Wednesday, July 24th, the House approved the bill by a voice vote. This passage of the Newborn Screening Saves Lives Reauthorization Act was a major milestone for our efforts, but there is more work to do.

The Senate version of the Newborn Screening Saves Lives Reauthorization Act was introduced on July 18th by our champions, Senators Maggie Hassan of New Hampshire and Cory Gardner of Colorado. The Senate bill S.2158 includes fewer changes to the statutory text than the House bill. Further, the authorization levels for CDC and HRSA programs are less generous than those in the

House.

Our coalition will continue to advocate for the highest funding levels possible for federal newborn screening programs to support and expand the essential work whether it be CDC developing better screening tests for conditions currently on the RUSP or supporting informatics programs as Dr. Cuthbert has discussed, or providing federal funding to states to support faster implementation of new screens, as we've heard about yesterday as well.

We expect the Senate Health Committee to take action on the Senate bill in September with a vote in the full Senate quickly to follow. After that our champions can begin the work to reconcile the differences between the House and Senate bills.

We do anticipate some hurdles along the way including possible amendments on the use of residual dried blood spots in research. However, we are confident that Congress will ultimately pass a reauthorization bill that will ensure the

federal government can continue its important newborn screening and work for an additional five years.

I'm here for -- after the meeting today I'm available to answer any questions about the legislation. Further, our informal coalition is open to patient, provider, and public health organizations. I'm passionate about advancing newborn screening and I'm happy to answer any questions about how to join. Thank you.

DR. CYNTHIA POWELL: Thank you, Ms. Abbott. All right. Next we'll hear from Dr. Baker, who will give us an update. She is the, a Committee member and Chair of the Ad-Hoc Workgroup focused on interpreting newborn screening results.

DR. MEI BAKER: Okay. Yeah. Hi, everybody. Good afternoon. I, I'm here give you a little bit updates and our group met yesterday morning. So here is the group members and we already defined the scope. It's nothing much change there. Just to remind everybody. And the unique situation for this group is we're trying to

utilize like every day newborn screening report to promote risk assessment idea.

And another thing that's a little bit unique, because we don't want to duplicate other education effort has been done and the continuing occur in the second part of the year, so we want to emphasize when newborn screening result is negative, we want to put some language there. We call it interpretation. So remind everybody still have residual risk there. So that's kind unique situation.

So the approach we want to do is report to the Committee. We can draft up report. Also based on the report, we hope to do some publication to dissimulate the knowledge.

So the report structure is a three parts, and again I think if people remember, is nothing new, but we restructured and the certain comments from our workgroup members and make perfect sense. And so we will have a, a small -- I mean small, short introduction and readdress -- oh, I have more later -- introduction. Then we will put a, a

lot of effort to talk about the newborn screening and also the kind of practice and indicate that risk assessment practice. Then we will have a third part discussion and propose some suggestions or recommendations.

So the, the introduction we, we will have a general description, but also emphasize why we talk about report now. It's kind of rationale and people knows the media attention talk about the missed cases, this kind of situation. So we think have some kind of underlying course, so we're trying to address that, yes, because, you know, we talk about success, but we need to be transparent in the implementation, and also the language in terms how we utilize that so people understand it, it really is a risk assessment. And we need to further sometimes given, given the situation may get 100% of the cases.

So, again, because that's the, the issues all there and leading to this we call the unattainable expectations. So we want to address that. So that's it. Part two will be more rich

and so a lot of words here. And so I think really is we're trying to do a lot, a lot of research and have peer review to paper over there help us to really establish a credibility here.

So I think -- I found this, the medical screening definition I think is well said. It's really, this is not new in terms of risk assessment, but we need to be reminded all the time, and from there we want to address some additional unique situations for newborn screening.

We also started with talk about when doing newborn screening test, what potential outcome. So use organic way to induce the proper terminology knowledge. That's our mind. Of, of course we want to really use the opportunity to promote a lot of material out there to talk about newborn screening risk assessment.

And again, just like everything else, but we want to emphasize is when you talk about population screening and the individual situation may not be exact same. So we need to recognize

and learn to accept that too. So that's the majority the same. We want to addressing this session.

Also we want to talk about providing some evidence in terms of how we practice and this slides are part, I mean I provide to the Committee last time really is we talk about cut off threshold and the category, and also when we talk about the newborn screening result, we also have associated recommendation. In general is like do further testing.

So that's help us to understand and this is a little bit more details and I don't want to get all the each category, but one thing I do want to mention that and our group members want to emphasize is newborn screening will help one screen state, and two screen state, with two screen state as sometimes they'll come to, I utilize the term result pending because they are waiting for second, the day to help to better to do the risk assessment.

So part three is based on the previous

sessions and we, going forward we really want to promote and risk assessment in a more clear fashion. As I mentioned earlier embed in the language report so that can remind the real time and constantly, and the almost unconsciously, and with that they can take this practice to communicate with the families.

But as our group members recognize and right so indicated, you know, newborn screening is very complicated. We talk about tests, but also when you, you found the result, it's not just binary relation, right? So this is -- so we will hope address here. And also we do have a newborn screening for certain disorders. With all the comment, we all know today we heard pseudo-deficiency carrier. So we hope we'll have some discussion in section.

So I hope I have captured the discussion, but my fellow workgroup members can help me if I miss anything. And also I want to -- we further discuss about our timeline. So going forward we really trying to get a draft, among ourselves get

a draft done and the first draft that we talk at the end of this month. Then we circulate among ourselves and do the editing, and by middle of October, we hope have the, the draft ready to be included in the briefing, I mean briefing book. And in November we hope we can take to the Committee for the feedback.

Also if you remember previously we have the intention and we have the plan to ask other feedback like APHL, NewSTEPs, and other organization and, too. And we have quite a few in our group and we may have new members, and we also use this opportunity to get all the feedback. And we plan in the February we'll have the final report. And at that time we also will share our plan for the manuscript. So that's what I have. Thank you.

DR. CYNTHIA POWELL: Thank you, Dr. Baker. We have time to take questions from the Committee and organizational representatives if there are any. Operator, please open up the phone lines for the Committee members and organizational

reps on the phone. Yes, Bob?

DR. ROBERT OSTRANDER: Bob Ostrander, AAFP, and I appreciate that I'll be joining the committee shortly. So I won't give you all the, my input, but I think one of the things that we need to make sure we include when we're talking about the fact that it's a screening test and not a diagnostic test, 'cause those are huge issues for the folks at the frontline, especially if you're not in genetics or metabolic diseases, is that this is not a diagnostic test. Negative doesn't mean it shouldn't be in your differential if people have symptoms. Positive doesn't mean that the person has the condition.

But I think somewhere nestled in there is those urgent, an urgent-to-treat conditions that's going to need to be in the teaching about interpreting or in the reports that while you're waiting for the confirmatory test, you must X, Y, and Z, if it's a baby with SCID, if it's MSUD, one of these ultra-urgent diseases, 'cause that kind of goes against what we're -- we're teaching them

don’t call this a diagnosis and act on it until you’ve done a confirmatory test unless it’s a time-critical condition. And then you need to act while you’re doing the diagnosis.

And so that, that needs to be, be brought into this at a, at a, at a fairly early and straightforward level, I think. And I guess I’ll leave it at that for the time-critical conditions. Our ACT sheets have some language that I think is fairly effective for that.

DR. MEI BAKER: Thank you. Actually the workgroup members has been discuss quite extensively and the one suggestion is in the report kind of we use some language and I think the discussion will be continued. The one thing I do want to remind is as a laboratory and we, our, we, when we issue report, we have to follow clear and CAP, and so, but we will find a way and especially, Sue, if you want to have additional comments on that, please.

DR. SUSAN BERRY: So obviously the point you’re raising is critical in the discussion and I

welcome your further input as we continue to develop this. But the responsibility for action from the result is that of the receiving physician, not the, not the delivering laboratory, so.

DR. MEI BAKER: And another thing we're talking is you're talking action sheet. Actually when you ask, talk about that, actually in my mind see how we incorporated all this pieces together. Go ahead.

DR. ROBERT OSTRANDER: I, I wasn't so much talking about the responsibility. It clearly is the clinician. My concern is, is if we overemphasize this message that this is a screening test, not a diagnostic test, that the clinician is going to make the mistake in time-critical conditions and think they're doing what they told, which is wait for a confirmatory test when in those conditions it should not happen.

So, yeah, and we're talking about professional education, but if, but this, this messaging that's going to be coming from us about

the difference between a screening and a diagnostic test has to have that nuance that sometimes you act on screening tests if it's a time-critical condition while you're waiting.

DR. MEI BAKER: Yeah.

DR. ROBERT OSTRANDER: And it's their responsibility for sure, but we need to make sure the messaging is clear.

DR. SUSAN BERRY: Yeah. This is Sue Berry. Yes, I, I agree with you entirely and that nuance is critical to the appropriate characterization of all of this.

DR. CYNTHIA POWELL: Any questions from those on the phone? Okay. Thank you, Dr. Baker. At this time each of the work groups will provide an update of their current activities and summarize their brainstorming sessions from yesterday. Please hold questions until after all three workgroups have presented.

DR. CYNTHIA POWELL: As I mentioned yesterday, this will be the first step in strategizing next steps for the workgroups and we

will come back to this again at the November meeting. And so first up will be Chris Kus who's co-chair for the follow up and treatment workgroup. Chris, are you on the line?

DR. CHRIS KUS: Yes, I'm on the line.

DR. CYNTHIA POWELL: Okay.

DR. CHRIS KUS: Can you hear me?

DR. CYNTHIA POWELL: Go ahead, yes, we can hear you.

DR. CHRIS KUS: Okay. Okay. I'm Chris Kus. I'm the organizational rep for ASTHO and I'm the co-chair of the workgroup, and I'm pitch-hitting for Jeff Brosco who couldn't be here. And I wanted to thank Sue Berry for facilitating in person in the meeting. We had a rich discussion and -- next slide. I guess the delay -- I'm looking for the workgroup slide up there.

DR. CYNTHIA POWELL: We see it.

DR. CHRIS KUS: Okay. Yeah. I will just talk as I think -- okay. There. I see it. What we did is -- this is, this talks about who the member of our workgroup is. We did welcome two

new members, Dr. Arnold and Dr. Kwon, and we had a rich discussion.

The first topic I'll report on is the discussion about the questions about gaps, topics or issues or specific projects. And to highlight that, one of the things we emphasize that there needs to be continued emphasis on long-term follow up so when a, a new condition is introduced, we should be thinking about long-term follow up from the beginning.

There's been concern about a lack of a national network that can coordinate care and collect data in a standardized way. People highlighted the importance of engaging the electronic medical record and the artificial intelligence industry as, as a gap that could support more efficient data collection initiatives. We often talk about the importance of defining who is responsible for long-term follow up and at what stages.

There's always a concern about financial resources for long-term follow up and clarifying

federal, state partnership with regard to resources. We need to learn about access to care after diagnosis and describing the barriers. There's a need to strengthen long-term follow up standardization by developing core outcomes or minimum data set, and this is actually one of the activities that this workgroup wants to work on and is asking for approval from the Committee.

Two of the issues that were brought up is the statement that the Advisory Committee on Heritable Disorders in Newborns and Children, that the point is that not all heritable disorders are newborn-screen related and do we need to talk about children who are identified with a condition outside of newborn screening and long-term follow up for them. And then the importance of communicating the importance of long-term follow up to families.

We then talked about the feedback on the components of the RUSP condition nomination and evidence review. We recommended that the nomination process should consider some discussion

of long-term follow up, a blueprint for long-term follow up that includes both patient follow up and measuring health outcomes.

It may be important to have a discussion of potential barriers to care and we thought it was important that there's a process to discern the merit of the information taking into consideration the resources that are available to condition, to the condition in the nomination process realizing that some conditions may have more resources than others. That's it for me.

DR. CYNTHIA POWELL: All right. Thank you. Next, we'll her from Beth Tarini who is the Chair for The Education and Training workgroup and Jane DeLuca who is the co-chair of Education and Training workgroup.

DR. BETH TARINI: Thank you, Catharine. Okay. So our education training workgroup summary. So here are our members. We have two new members, Steven Ralston who is ACOG. He's an obstetrician. And Jacqueline Rychnovsky, Rychnovsky, who is AWHONN and she's a nurse

practitioner. So our two new folks.

Okay. We just wanted to recap current members' activities. Natasha Bonhomme is involved in a project right now for Baby's First Test, Ask an Expert. She's conducting an analysis of submitted questions to the website and they're going to actually glean the information that's regarded, questions from parents about newborn screening and look at trends. She'll have a follow-up report in November and if you wanted to say a little bit more about that, please do. Sylvia Mann is involved in a HRSA family education program. It's a needs assessment. They're targeting a thousand individuals and right now I think they're clocking in at 800 with a sub-group of 200 people from underrepresented groups, and how people, how do people want their information delivered. So this will be followed up in November as well.

Okay. So for specific projects, right now we've completed our projects. We have our education and communication guides. We're working

towards disseminating these links to this website and we're off cycle. So we're working with the Committee and HRSA on new initiatives and next steps.

So our agenda for the workgroup was brainstorming current gaps in the field topics and issues that the workgroups can help address specific project ideas and provide feedback on the, on the components of the RUSP condition nomination evidence review process.

So it was a very lively discussion, very animated and we have, came up with a few new ideas, tentative ideas though, for projects. So we thought about newborn screening state education programs. First, what do we need to know about the kinds of education and materials from state programs that are out there already existing? So states' program materials may be needing updating, but we don't know if they're effective even at this point.

So what types of measures can we use, what are the best practices in education, what is

the reality of newborn screening education? So we, we're thinking about two different avenues here. If someone is in crisis, what do they need to know if they're coming in to have their baby evaluated and what do providers and parents need as the new disorders will allow? So those are two areas that we came up with which I think are really pertinent.

So again, we're just brainstorming. So these were some of the things that we came up with. This development of multilingual animation newborn screening videos where we might be able to use different languages, and because the animation might be more flexible, to have this to educate parents so it could be accessible for non-English speaking parents.

The California Dreaming is an example of an animation that's being used for that state screening program, but the concerns, of course, are the time that would be needed to create the videos and the expense also involved for, to, to have a professional product available.

There was an idea about linking newborn screening education materials within electronic medical record portals. There actually could be links when someone accessed their portal and we would have it so it would be taken to an education paragraph or pamphlet.

And we had a very interesting discussion about bridging information between OBs and pediatrics about newborn screening because there is a lot happening in OB where carrier screening is being performed and sometimes this does not make its way into newborn screening and we don’t know that testing has actually been performed, carrier testing has been performed, and maybe there’s some way that we can link the two services, if you will.

So these are fragmented and unconnected healthcare systems. So this is something we might be able to address there from an education perspective.

Now comments on the RUSP. So values may not be represented or different perspectives

appreciated in smaller groups, and we actually talked a bit about the citizens' jury 'cause we figured, well, perhaps the people who can be on these juries are people who have the time to be able to sit on these juries. And this may be difficult because if we bring in people from different cultures, they may not be accustomed to speaking within a group. So I think there are some issues that we want to think about if we're going to be considering using citizen juries.

The public health perspectives in newborn screening programs may not address individual issues just as individual issues may not address the larger needs, if you will, of public health programs. So I think that maybe both need to be taken in context. So sometimes we use these bigger issues and we're talking about the individual, but it really sort of misses the mark, okay. Is that -- I hope that's clear. If you have a question about that you can ask me, but because we were talking and said sometimes that two things are going on at the same time.

Okay. There is the existing underutilized data from the time initiating a screening test for evaluating the effectiveness of how a screening test is functioning. So we can go back and take a look at that data to assess how effective it's actually, the screening test is, is, is at this point.

If a disorder for screening is not performing as anticipated, what do we do about that, how to address this? Are disorders removed from the RUSP and under what conditions should disorders be removed? So these were the types of things that were preoccupying us yesterday. And that is pretty much it. Okay.

DR. CYNTHIA POWELL: Thank you. Next we'll hear from Kellie Kelm who's Chair of The Laboratory Standards and Procedures workgroup.

DR. KELLIE KELM: Thank you very much. We had a great meeting, a lovely discussion, and we actually started off with a presentation from New York. So first this is our roster and we do also have a new member, Amy. I don't know if it's

Karger or Karger, but she wasn't able to join us this, this visit. So we look forward to meeting her at the next one.

So before we actually -- I can go through these quickly. Obviously we just have our existing projects that, the most recent one that was added within the last year was assessing impact of broad phenotypes on laboratories. And so we basically got to talk a little bit about that as well as in our discussion from New York.

So we heard about how New York is using next-gen sequencing in newborn screening and so I'll do my best to try to capture much of what Michele presented, but of course -- and I hope I don't mess up. And it looks like I don't, I don't see her here to, to help out anymore if I do. So good.

So one of the issues that New York had is that 94% of referred CF screens were false positives. And so for them a screen positive was high RT and at least 1 CF causing mutation, and I believe at the time they started, they had a

genotyping panel that included 39 CF mutations in their genotyping. But we know that not all CFTR mutations cause classic CF, and of course they had a lot of questions about how, how to, to move forward and, and what issues to think about. Let me see if I can do it.

And so here's sort of a summary of how things have changed. So they used to basically have a two-tier test. So they would have babies in the upper 5% of IRT go on to genotyping. Then they would send down babies with one or two CFTR variants or very high IRT to referral for more diagnostic testing.

But what they've done is actually added a new technology, which is a panel with NGS looking for 338 variants based on CFTR2, plus additional information from CFTR2 on variants that now have more information on being pathogenic in cases, as well as they said they looked back at their history since they've been gene typing and since 2002 on some variants, that in New York they had experience with being pathogenic as well. So they

came up with this panel of 338 variants. So that's what they're doing.

And so now -- and I can't remember what the future slide was. Let me look. And so now what they're doing is they're using this 338 variant panel by NGS and only babies with 2 CFTR variants by using that panel move on to diagnostic testing. So the babies with one variant or very, very high IRT are not moving on anymore. So you can see the numbers that they refer have reduced from 900 to 100.

And I can't walk you through all of this and what all the numbers mean, but you can see that since they've rolled out this new panel in 2018, that they are referring a vastly reduced number of babies, and in that case obviously their positive predicted value is also increasing because they are reducing the number of false positives that are moving on.

Lessons learned, referrals reduced by 83%. So you can see there's a lot of carriers in, in other infants that were negative that were not

referred, and PPV increased six-and-a-half fold and they felt that their infants with CF are being more promptly referred and diagnosed because they had a little bit more confidence in, in the ones they were referring.

And then there's some more information down below on some of the other reclassifications. The fact that they can actually look at whether or variants were in SCID and, and some other details. And then we heard briefly about some of the SCID newborn screening and where they've used next-gen sequencing as well.

So immunologists, you know, in their opinion could provide better care when SCID causing mutations are known quickly. And they also talked about the fact that I believe they said that in some cases immunologists were struggling to get sequencing covered. And so they felt that if they could include it in their labs in the state of technology it would actually help a lot.

And so they gave us some information on,

at first they validated two platforms for a 39 gene immunodeficiency panel. In the end what they're using right now is actually a 55 gene panel and the end of the story, because I don't have time, is they actually had 18 babies that they have done sequencing on, and out of the 18, 2 of them you can see actually had likely pathogenic variants that were found. And those babies, you know, have moved on for SCID and the other 16 I think -- I can't remember if it was all of them or most of them actually saw their track numbers resolve anyway over the time that they did some additional testing. So, and it sort of did, was consistent with the, the sequencing results.

So then we did -- after that short presentation we had a discussion of gaps, topics, etc. So over this discussion of gaps and topics, as well as even the evidence nomination review process, the one thing that kept coming up over and over again, and I think Susan said she had written down like 39 times, was clear case definitions.

So I can just tell you that number one, that's one of the top priority things is that we have to have clear case definitions and we have to use it both when we're doing our evaluation of new conditions, as well as -- and, and how can we, how can we do this because it still is a struggle to get programs, states, etc, to use clear case definitions and, of course, there is the problem of everybody else using the same one.

So there was one proposal that we discussed a lot about whether or not we should actually have predetermined performance target goals for our screening. And so that wound up leading to a lot of discussion about how difficult that would be, that there are a lot of gaps and barriers to us doing that. And some other things that we could be doing or that we actually are already doing to even be able to, to do something like that because one of the problems is, is that even how we do analyses are different state to state.

We need a harmonization of terms. We

need the harmonization of data across platforms. And so sort of even in the discussion of cut-offs in risk analysis, risk assessment, we've had this discussion about how can we make sure that we're talking the same language when we're, when we're comparing data. This is not completely novel. I remember that I believe Dr. Matern and others had already promoted the ideas of having minimal PPV and false positive rates for tests in the past.

So another gap that came up was making newborn screening conditions reportable similar to how infectious disorders are reportable to CDC, and some people feel that that would be an advantage.

Another topic that has come up many times in our discussions yesterday and in the past is more work on second-tier tests and, and this is both, you know, proteomic, protein based. This is also, you know, so MS/MS. This is also genomic to reduce diagnostic testing, you know, knowing that impact on parents for, you know, diagnostic testing can we, can we do that. And, but there

was a question about whether or not we would need to obviously weigh in the cost effectiveness of more second-tier tests.

And so that did lead to more discussion about regionalization, which has also been a theme going back years in our group and, and here. Although we had some, some of the people shared stories about how regionalization more recently had been sort of made available, but we find that not all states take, take people up on that offer. And so it's often unused, if you will.

Carla actually shared that, and I paraphrase it into adaptive learning, into a bullet that she's actually been working on a pet project for years that may be coming to fruition in the near future she hopes on sort of adaptive learning courses specifically for newborn screening topics to be determined, but she's hoping to get a lot of players to help out. She has a promising vendor that I, I'm not going to say.

And, anyway, the idea is, is that it

could be general newborn screening. And then I think she was interested in some very specific disorders and that, that could be something that people have access to CDC Train would be able to use. And so it's something that might be really helpful to the community.

So we talked -- then we, we talked about the RUSP condition nomination and evidence review process. And so I've stated here again about needing to find the terminology for the evidence review process, and of course the favorite one is case definition. You know, that setting the case definition for the condition and consideration allows states to sort of make false positive and false negative projections that really allows them to, to think about things. And, and then once they roll it out, also compare to what their projections were and what they're actually seeing in their state.

So one thing that was brought up was that obviously the external evidence review takes a lot of time and you're gathering a lot of information

that's really important, you know, to the Committee, but it would also be important to the states as they consider whether or not to start screening. And obviously that's not going to be available when the public health system impact assessment survey is created and then also shared.

And so that often can make it hard for states to give you an entire picture of what they think about in terms of screening if they don't have all that information also available. So I'm not sure how you deal with that problem, but it is something that was noted by the, the obviously state program folks in our group.

One person threw out that maybe we, the Committee should rethink the requirement for adding something to the RUSP that we have to have one case identified prospectively through newborn screening. So they wanted to bring that up as a potential topic.

Another question is that the sort of flow chart for adding something to the RUSP talks about having a, a treatment or approved treatment. I

can’t remember how it actually was phrased and I think some of the questions were does it have to be approved, what about if it’s in trial, what about something that’s standard of care, and that maybe the thought that how it was captured could be up for discussion.

There was a question about whether or not we should be doing an assessment to factors impeding labs from bringing on new conditions. And, and so we spent a lot of time talking about the public health system impact assessment. Obviously a lot of the, you know, state public health labs are in our workgroup and they feel that sometimes this assessment doesn’t really capture the, the state for, of state public health labs for adding screening.

And so one of the questions was even, you know, that we need to get even non-newborn screening program information. So how can we get information from other stakeholders because we feel like right now we’re not doing that.

So one of the questions is could we

utilize organizations that advise ACHDNC. We have obviously a bunch of people at the table over there and there are organizations that have a lot of stakeholders that are involved, especially with short-term and long-term follow-up.

Someone brought up they feel like we, we really need to get more information from insurance. You know, there's been a lot of issues once even you roll out the screening with availability of coverage of treatments that, that we are taking into account when we're making our decisions.

So we know that the survey, it's hard to change it because we need to get clearance before we roll it out. So is it possible to get some major information on public health system with, from other places, other sources? Can we use the NewSTEPs readiness tool or, or other places where they are capturing data that's outside of this whole survey process?

So anyway, so I -- that's it. We -- as you can see, we had ideas and, and thoughts from

all over the, all over the place. And so it was, it was a very lively discussion. Anyway, that's it. Any questions?

DR. CYNTHIA POWELL: So, yeah, we can open up discussion for the workgroups and thank you very much.

DR. KELLIE KELM: Thank you.

DR. CYNTHIA POWELL: Thank you all for your presentations. Operator, please open the phone lines for the Committee members and organizational reps on the phone.

DR. CYNTHIA POWELL: Bob?

DR. ROBERT OSTRANDER: Bob Ostrander, AAFP. I just want to expand a little bit on what Chris Kus said about the long-term follow up group's recommendations for the RUSP addition process. I think we were pretty firm that having some sort of vision or blueprint for long-term follow up and treatment should be a condition that needs to be met before a condition should be added to the RUSP.

I don't think it was worded quite that

firmly in Chris' report, but I think we really felt that way. And we're not talking about specifics. We, we really just felt there needed to be, again, some sort of blueprint or vision that described how these children would be, receive care, and not just initial treatment, but what their first few years of life would look like and how they would communicate with whatever data gathering.

So, you know, as you're considering an evidence review process, you know, that should be in there, and as we're giving, you know, if that is something that everybody else agrees with, you know, it needs to go, be information that's provided to those nominating conditions early on so they can start thinking about it because after all they are the experts.

The other comment that goes into this is that I think it's important, we thought it was important that the, during the evidence review process that the reviewers take into the, into account disparities among conditions. And we use

the word disparities a lot, but some conditions have a lot of resources and may bring very rich data. Some equally worthy conditions may not have those resources and I, I suspect that goes into consideration now, but it needs to be taken into consideration.

And then the other disparity is the disparity of good luck, bad luck and, and that, that revisits this notion that you have to have prospectively discovered positive case, and for rare things, you know, basically if you've got a, you know, a 200 x 200 foot screen with 1 dot on it and you grab a little circle out of that, 1 condition may be a lucky enough to have the dot in that circle and 10 other conditions not have the dot in the circle, and they're all equally worthy conditions. And so is, is, is that requirement while for more common conditions a very reasonable scientific requirement, for rare conditions is that a discriminatory requirement that should be revisited.

DR. CYNTHIA POWELL: And just to clarify,

Bob, in terms of the blueprint for what the first two years of a child's life would look like, is that something that the organization or individuals putting forth a condition for consideration should supply, or would that be something that the evidence review group should get?

DR. ROBERT OSTRANDER: No. We, we would -- our thought is, is that those nominating the condition, that should be part of what they're thinking about when they're nominating it and that they should supply, again, a, a vision. We don't think, we think it should be a very low bar, but it should be on the horizon on the radar.

DR. CYNTHIA POWELL: Anyone on the phone with any questions or comments? All right. Well, I think we've heard a number of common themes from the workgroups about brainstorming and also feedback for the evidence review project. And so we'll think about those, put them together, and then plan for further discussion in November.

But I really want to thank everybody, all

the chairs of the workgroups, co-chairs, and all the workgroup members for helping out with this and all of the feedback that they provide.

DR. CYNTHIA POWELL: So for the Committee members, does anyone have any new business at this time to bring up?

MS. ANNAMARIE SAARINEN: Dr. Powell?

DR. CYNTHIA POWELL: Yes.

MS. ANNAMARIE SAARINEN: Hi, it's Annamarie Saarinen.

DR. CYNTHIA POWELL: Yes, go ahead, Annamarie. We hear you.

MS. ANNAMARIE SAARINEN: Thanks so much for letting me listen in remotely today. I may have missed it, so I apologize, in the lead-in to the report. Who -- is, is it staff, Committee staff that'll be looking at collating the, the, the cross-cutting portions of these three different groups that try to follow your charge from yesterday, or is there somebody or a separate smaller sub-group that's going to work on aligning the areas that can be aligned so that we can

report back on that piece of it specifically?

DR. CYNTHIA POWELL: I think we haven't made definite plans about that. So working with the HRSA staff, we'll certainly do that. If there are members of the committee who are interested in, in helping with that, I think that would be, you know, very helpful and appreciated. So you can contact me if, if you're interested in, in working on that.

MS. ANNAMARIE SAARINEN: I, I would be interested if, if we decide to go that route. So I'll throw my hat in the ring for now.

DR. CYNTHIA POWELL: She, did she -- thank you for volunteering. Great. Thank you, Annamarie. And happy birthday to your daughter.

MS. ANNAMARIE SAARINEN: Thanks so much. I'll let her know.

DR. CYNTHIA POWELL: All right. Anything else? Yes, Kyle.

DR. KYLE BROTHERS: I just had a quick question about the topics we discussed with Dr. Kemper yesterday. What's the plan for that? It's

a similar question where Annamarie was asking like where are we headed with that or, or in terms of making yes or no decisions about different pieces of that?

DR. CYNTHIA POWELL: So I think, well, there's going to be additional presentations from Alex Kemper at the next meeting and, and then I think a final -- I can't remember. Is it finished up in November? And then, you know, we'll decide kind of what, what to do next. I mean I think that's definitely a critical question.

It seems like there's a number of areas that people feel are extremely important to address that, you know, don't seem to be information that we've been able to, to get and, you know, with the current system of evidence-based review and the metric. So I think next time we'll discuss the actual metric, and then, you know, take it from there and, you know, see what kind of changes can be made, you know, what, what should be made. So we'll -- it's a, it's an ongoing process.

DR. KYLE BROTHERS: Great. Thank you.

DR. CYNTHIA POWELL: Yes, Susan.

DR. SUSAN TANKSLEY: Hi. Susan Tanksley, Association of Public Health Laboratories. Based on the interest in the health, health informatics technology discussion today, I think it would be helpful to hear more from the states and what they're doing and perhaps see how the Committee could assist in those efforts.

DR. CYNTHIA POWELL: Yeah. I think we also hope to, to do that to get more information from individual states. So that, that is planned and is important. And, Melissa Parisi, do you have?

DR. MELISSA PARISI: Melissa Parisi, NIH. In follow up to what Susan just said, I mean I wonder if there might be consideration in the future of a workgroup that would be addressing some of those issues related to interoperability and, and IT since it seems to be such a significant challenge and one where there's also a lot of opportunity too.

I had one other comment which was triggered, I think, by the concerns about availability of treatments and for some of the conditions that are currently on the RUSP, and I'm thinking specifically about SMA which was just officially added to the RUSP about a year ago, correct?

I'm just wondering if in one of the upcoming meetings it might be a good opportunity to sort of see what the current status is with regard to SMA screening (cleared throat) -- excuse me -- screening and access to treatments.

MS. JOAN SCOTT: Just as a reminder, there was a request when that got approved by the Secretary to get a report back. And so that is part of also what Alex's group is compiling information about implementation. So, so he'll be presenting on, on that. I'm not, I don't remember what the time -- February 2020. Ask and you shall receive.

DR. CYNTHIA POWELL: Anything else? All right. Well, I'd like to thank Catharine Riley,

Debi Sarkar, Joan Scott, Alaina Harris, and all the others behind the scenes for helping put this meeting together. It's very much appreciated. And before adjourning I just want to wish everyone a happy Newborn Screening Awareness Month in September since the Committee won't convene again until November. And that being said, I'd like to officially adjourn this meeting. Thank you all.

(Whereupon, at 1:45 p.m., the meeting of the ACHDNC was concluded.)