US DEPARTMENT OF HEALTH AND HUMAN SERVICES

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HEALTH RESOURCES AND SERVICE ADMINISTRATION

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THE ADVISORY COMMITTEE ON HERITABLE DISORDERS IN NEWBORNS AND CHILDREN

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MEETING

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FRIDAY
FEBRUARY 12, 2016

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The Committee met in Conference Room E in the Natcher Conference Center at the headquarters of the National Institutes of Health, 9000 Rockville Pike, Bethesda, Maryland, at 9:30 a.m., Joseph A. Bocchini, Jr. Chair, presiding.

PRESENT

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

PRESENT (CONT.)

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

ALSO PRESENT

DEBI SARKAR, M.P.H., Health Resources and Service Administration, Designated Federal Official
DEBBIE BADAWI, M.D., Association of Maternal and Child Health Programs
STANTON BERBERICH, Ph.D., State Hygienic Laboratory at the University of Iowa
NATASHA F. BONHOMME, Genetic Alliance
ANNE COMEAU, Ph.D., UMass Medical Center
CAROL GREENE, M.D., Society for Inherited Metabolic Disorders
JOYCE HOOKER, Mountain States Genetics Regional Collaborative
ADAM KANIS, M.D., Department of Defense
ALEX R. KEMPER, M.D., M.P.H., M.S., Duke University Health System
EDWARD R. B. McCABE, M.D., Ph.D., March of Dimes
JELILI OJODU, M.P.H., Association of Public Health Laboratories
ROBERT OSTRANDER, M.D., American Academy of Family Physicians
SUSAN M. TANKSLEY, Ph.D., Association of Public Health Laboratories
BETH TARINI, M.D., M.S., FAAP, American Academy of Pediatrics
CATE WALSH VOCKLEY, M.S., National Society of Genetic Counselors
MICHAEL S. WATSON, Ph.D., FACMG, American College

of Medical Genetics and Genomics

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

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

(9:31 a.m.)

CHAIR BOCCHINI: Thank you. Good morning everyone and welcome to day two of the February 2016 Advisory Committee on Heritable Disorders in Newborns and Children meeting. I will start the morning with a roll call. So Don Bailey?

MEMBER BAILEY: Here.

CHAIR BOCCHINI: Here. Jeff Botkin? MEMBER BOTKIN: Here.

CHAIR BOCCHINI: Carla Cuthbert?

DR. CUTHBERT: Here.

CHAIR BOCCHINI: Catherine Spong?

DR. SPONG: Here.

CHAIR BOCCHINI: Kellie Kelm?

DR. KELM: Here.

CHAIR BOCCHINI: Fred Lorey by phone. Dieter Matern?

MEMBER MATERN: Here.

CHAIR BOCCHINI: Steve McDonough by phone today.

MEMBER MCDONOUGH: Here, can you hear me?

CHAIR BOCCHINI: We can, so you must have made it to California, thank you.

MEMBER MCDONOUGH: Thank you.

CHAIR BOCCHINI: Kamila Mistry?

DR. MISTRY: Here.

CHAIR BOCCHINI: Joan Scott for Michael Lu?

MS. SCOTT: Here.

CHAIR BOCCHINI: Cathy Wicklund?

MEMBER WICKLUND: Here.

CHAIR BOCCHINI: And Debi Sarkar.

MS. SARKAR: Here.

CHAIR BOCCHINI: And then for organizational representatives, Bob Ostrander?

DR. OSTRANDER: Here.

CHAIR BOCCHINI: Beth Tarini?

DR. TARINI: Here.

CHAIR BOCCHINI: Michael Watson?

DR. WATSON: Here.

CHAIR BOCCHINI: Joseph Biggio by

phone? Debbie Badawi? Susan Tanksley?

DR. TANKSLEY: Here.

CHAIR BOCCHINI: Chris Kus, by phone. Adam Kanis, by phone?

MR. KANIS: Here.

CHAIR BOCCHINI: Natasha Bonhomme?

MS. BONHOMME: Here.

CHAIR BOCCHINI: Ed McCabe by phone?

MR. MCCABE: I'm here.

CHAIR BOCCHINI: Cate Walsh Vockley?

DR. VOCKLEY: Here.

CHAIR BOCCHINI: And Carol Greene.

DR. GREENE: Here.

CHAIR BOCCHINI: Thank you all. So this morning we're going to hear reports from the three subcommittees who did meet yesterday with the charge of evaluating the goals, determining whether modifications need to be made for each of the subcommittees, if any, and then to begin the discussion to define and potentially prioritize projects to come before the Committee for evaluation and decisions about whether they need

to be pursued and in which priority.

So we're going to start the morning with the Laboratory Procedures and Standards Subcommittee, and the presentation I guess will be from Kellie Kelm.

DR. KELM: Good morning. And Susan Tanksley from APHL in Texas is the co-chair. And so we have -- I want to present first our Subcommittee roster, and many of them were able to join us tomorrow -- yesterday.

So at this point it had been a year, I think the same as other subcommittees perhaps, it's been a year since we had last met, and really this Committee even for a period before that had been, we had been doing a lot of work on the timeliness project.

So we had not had an active project other than timeliness in our group for quite some time. And so we had, I think a year ago we had started to talk about some, a project or two, but, you know, we sort of are starting from scratch in a way. We don't have much.

We had some interesting ideas and mostly our meeting yesterday was just throwing a lot of things on the wall and seeing if they stick, and so we have some ideas here. Unfortunately we haven't yet sort of taken the next step to what are some potential deliverables.

So, you know, it's something that we can continue to work on, and obviously get the feedback of the Committee if they see anything especially here of value.

So this was when Debi -- Dr. Bocchini put up the, you know, what we had last seen in terms of the charge for a subcommittee. This was what apparently was three or four years old.

So define and implement a mechanism for the periodic review and assessment of the conditions included in the uniform panel, infrastructure services needed for effective and efficient screening of the conditions including the uniform panel and laboratory procedures utilized for effective and efficient testing of the conditions in the uniform panel.

So we did have some discussion around the charge. It was one that honestly we hadn't even used in a lot of our meetings, and there was -- and I think since none of us really remembered sort of even writing and the discussion around it, we had some interesting discussions about what each of those were and wound up having some very minor edits that we wanted to propose just for clarification.

And some of it was rearranging, so swapping the last one up to the second one, just because I think that laboratory procedures, so that to us meant the testing. The tests. So what the lab was doing when testing for screening.

And, number three, I think we broke out infrastructure and services or infrastructure and logistics needed for screening, and here's what we thought of the things that we use that are outside of the tests for screening.

So that could even be the fact that CDC has, you know, their quality assurance materials and other things that are part of the screening

process that our Laboratory Standards and Procedures group has considered, including sort of the things in timeliness.

And so one of the things that I think, we haven't greatly modified it, but, you know, whether or not the Committee thinks that this clarification may be useful and helpful, especially for us as we think about it.

So we went from there and thought about some things as part of that charge, in looking back at it, that might be useful for us, the Subcommittee, to do for the Committee basically.

So the first one was the whole define and implement a mechanism for the periodic review and assessment of the conditions included in the uniform panel. So we thought that was actually interesting and this could be especially now with NewSTEPs gathering data, you know, whether or not there could be a process that the Subcommittee could do for the Committee to periodically review data for conditions on the RUSP.

So this could be an ongoing process.

We could one or a few conditions at a time, and obviously this could lead to new projects if any issues are noted.

So I think that that's something, especially with NewSTEPs as a data resource, is something that we could go back and think about how are we doing with the tests that are already on the RUSP.

So for the second, the second part of our charge, we had a few more ideas here. And so I think there are three pages with some of our brainstorming. And so this is the Periodic Review and Assessment of Laboratory Procedures.

So, number one, should we evaluate current methods to determine if improvements are needed to enhance sensitivity and specificity and/or specificity of some of the tests that we already do.

And this is a place where we had, in part, already had done some work, so the idea of the work we had done on succinylacetone, but there was also some discussion about, for example, you

know, T4 versus TSH, and improving the sensitivity and specificity of the screening for CH.

We also heard that Piero is doing some work on, for example, assessing utility of additional data to help with the callouts and, you know, gestational age and birth weight and some changes in terms of algorithms.

And so we could tap into some of the work that's going on there and communicate that to the Committee. Second tier testing to improve specificity, we know that that, you know, is always something that a lot of labs are thinking of.

And then we had an issue and discussion about cutoffs. So percentile cutoffs, floating cutoffs, and potentially even multiple of the means that might be done. So we know labs do their own thing but we could also talk about whether or not, especially for certain cases, it makes sense to have discussion about how cutoffs are set and used.

So the second project, and this is building off of work that had already been done and published and we had shared this before, is the one

screen versus two-screens. So we know a number of states do one screen and then there are some with, for example, a targeted second screen if needed.

And then we have some states that are standard two-screen states. And so we've had -- this was a project that was started over 10 years ago, that was Harry Hannon had talked about, and then CDC, Dr. Stuart Shapira, has presented that to this Committee before.

It was published about a year ago. There's two papers where they evaluated a number of states that are one screen and two-screen, and I think they were specifically looking -- was it CH/NCH?

And what, you know, and the problem was is obviously you were comparing in some ways apples and oranges without doing a direct comparison of what would happen, for example, if a two-screen state tried to apply a one-screen algorithm.

So, you know, this is something that we could look at. I think we had some interesting discussions around that. What are the pros and

cons of each model. In this case, what do we screen for? I mean when we discuss it, a lot of states actually are testing for different things.

So, you know, from case definitions when doing this kind of work would be important -- can babies identified in the second screen with the first screen normal be identified by a single screen model with targeted resequencing.

So this is the idea about could you sort of retrospectively do that. But we were talking about whether or not you could do, what kind of studies design could we do. Could it, you know, just be retrospective which would be easier or do we need a prospective design which obviously would be harder and need time and money.

And the third thing that we mentioned that there was some growing interest in is obviously the role of next-generation sequencing and newborn screening. So screening is currently based on phenotypic data.

How do we accumulate the data to identify correlation between phenotypic and

genotypic data? Are there conditions for which screening is the only screening method? What do you actually gain or lose when you use NGS? What data do you report? What do you do with variants of unknown significance.

The discussion of carrier status did come up. And what about infrastructure needs for NGS, and I think that's obviously just going to increase as we see that moving more into clinical use.

And the last part of our charge was the infrastructure and services, and here I think we brought back the fact that we had, obviously, the major work done in timeliness. And we could go back and once, you know, the data's available from NewSTEPs, review the data related to those recommendations that were made.

And there's some other interesting projects. Recently California published their study, that they do an early specimen collection at 12 hours so what are the implications of that, because that could help with timeliness but how

does that impact the screening.

And what are some of the unforeseen consequences and costs of timeliness that we've heard some stories about things changing in order to meet it, not always for the better.

So those were our thoughts and here I've sort of tried to simplify all of those into sort of one table. And that was it in terms of the projects that we had compiled.

And I'll come back to this, but there was another interesting discussion that we had that I think we wanted to bring to the Committee.

So one of the things in terms of even assessing conditions on the panel is what happens if we want to consider moving a condition off the panel or promoting conditions from the secondary to the core panel.

And there were actually two examples that we heard from people in the Subcommittee of moving additions off the panel or moving them up, and whether or not we actually had a process to do that, how it would be done.

It really is almost another evidence review but I thought since we actually had some potential candidates that I wanted to bring that to the Committee's attention.

And then we still wanted to bring up point of care issues and how those will be addressed, especially if we ever see more tests moving to point of care, and how we want to do that. That may also be a cross-subcommittee kind of project.

So I'll put it back on this one and see if anyone has any comments, questions?

CHAIR BOCCHINI: Thank you, Kellie. Certainly a very nice presentation and very clear what directions to consider going.

I think unless there's any concern by members of the Committee, it would be very easy to accept your recommendation for minor changes in the charge of the Committee, so if that's agreed upon by everyone we'll just go ahead and do that.

DR. KELM: Okay.

CHAIR BOCCHINI: So subsequent,

let's initiate some discussion concerning these potential projects and other issues related to them. Joan?

MS. SCOTT: Thank you, Kellie. This is a very thoughtful review. I just had a question from the assessment of the folk that's on the Committee whether or not you felt any of these particular projects at this stage have higher priority over another, number one.

And then, number two, do you think you have the right folk on the Committee to be able to address them or would you need to change or add or subtract or whatever?

And I guess my third sort of corollary, keep going while there's a pause. What's the advantage to having these particular projects done under this setting as opposed to any other setting?

DR. KELM: So I think given the time that we had, unfortunately, I think we ran through it and I'm not sure whether or not I could speak to, I mean in some ways the easier ones to do would be reviewing the screening data and assessing the

timeliness, because the data will be available from NewSTEPs.

And the other ones are going to involve more, would involve more work from the subcommittee or others, identifying others. So I think we had some interesting preliminary discussions and the problem was that we hadn't necessarily finished the structure of how these would be done.

I think that the thoughts, for example, of reviewing the data, obviously the timeliness, the original one came out of our group, and of course we have, it's, a lot of it will be in part lab, or at least the, you know, the labs participating in a lot of those timeliness projects that have been going on.

So I think that our thoughts obviously were that some of the people in the group would be great to sort of assess that data and also think about it in terms of what's going on in their labs.

And the same thing I think a little bit with assessing the existing conditions was just the lab view of it as the first pass. So did you want

to add anything to that in terms of --

DR. TANKSLEY: So in regards to number two, lab procedures, there are a lot of existing questions around the current methods and improving those methods or looking for ways to improve the way we're already screening.

So I think there is interest in that -- we would need to focus probably on one project over all of them that we were looking at. Some of them are just looking at the existing data and trying to figure out is there somewhere else to go with that.

So it may just be a presentation to the Subcommittee to see if there is something to explore. One-screen versus two-screen, we've spent years and years on that with really no conclusions or convincing evidence for one side or the other to change. And so that one would be a tough one. That would be a tough one to crack.

And then next-gen sequencing, I think we started out with this is really an exploratory thing, so is it, is the Subcommittee a place where

we could bring in people to talk about next-gen sequencing and just start formulating ideas.

There are the insight grants, and so I know a lot of that information is being explored currently, but is it also a place. Is this subcommittee a place where we could begin to think about all the issues surrounding next-gen sequencing in newborn screening and where it's appropriate.

CHAIR BOCCHINI: Cathy?

MEMBER WICKLUND: Yes, I think that was my question, you have guys have, about the next-gen sequencing piece, because there's, were you guys thinking more about the laboratory piece, or, I mean you did bring up some things about return of results and some of the issues around that too.

How did you see, so it sounds like you saw it more that we would try to get information from people currently kind of in this space and see if we can have a role there, as opposed to maybe taking the lead in developing guidelines or something about it. Is that a correct probably

reflection now?

DR. TANKSLEY: Yes, there is a lot of work being done. A lot of questions trying to be answered by others. A lot of people exploring this right now, and so I, like I said, I think we were thinking of it as a starting place to begin to assimilate the information that's already out there.

CHAIR BOCCHINI: Jeff?

MEMBER BOTKIN: I guess I wanted to pick up, too, on the next-gen sequencing line there, and maybe a little clarity about which direction you would see this going. I mean I would be concerned that, excuse me, too much attention to this would give credence to what I think is a dreadful idea in terms of whole-genome sequencing in the context of public health program classically.

Now that's different than thinking about the role of DNA-based platforms for testing which seems to me to be a productive area to think about, or potentially sequencing in the context of

affected children. And you want to better understand the genetic background of why kids respond to one treatment or another.

I think that's, you know, what's happening with some of the existing NIH grants, but I just wanted to express my caution about going down this road in a way that would suggest that folks within this environment are taking seriously the notion that every baby's going to get sequenced in the near future.

DR. KELM: Well and I think obviously it can go in a few directions, but I think that it's something that we have to figure out how we keep the Committee apprised of the, you know, of the activities.

Some of the, you know, especially some of the efforts that may be happening where targeted sequencing is appropriate and how labs are using it and how -- still everybody's having challenges with analytical and clinical validity and going forward.

I mean I think the question is how do

we sort of keep our finger on the pulse of what's going on and share that and with the Committee, because I think we sort of need to keep on top of it.

CHAIR BOCCHINI: Next I have Dieter and then --

MEMBER MATERN: Dieter Matern. So about the laboratory procedures, I think, too, for the first point what Kellie alluded to is that Piero is working with several states on congenital hypothyroidism and how to incorporate birth weight and gestational age and age at collection to help in figuring out who is affected and who is not.

And I suggest that when he is at a level where he is comfortable in sharing that, that he or someone from the group should be asked to do that.

The other, and he might actually at the next time, you might just ask him to call in, or someone from the group, to give the Subcommittee an update of what is going on.

When it comes to the one-screen and

two-screen, yes, this has been going on for many, many years. There's been a lot of work been going into and we have no conclusion what is right. So that puts the states that don't do it into the uncomfortable position where they don't know whether they provide the screening that they want to provide to the population.

And it puts the two-screen states into a position where they duplicate their effort and they cannot be totally sure whether that is really required, and it costs a lot of money I think to do this.

As these states are eventually going to add Pomp and whatever else is added to the screen, and they're going to do this in duplication as well. That makes it even more expensive.

So I think that it's really an issue that we should kind of force to come to a resolution, because I thought that this Committee also was put in place to ensure uniformity for all babies across the country.

And we do not have the uniformity when

the screening is done so differently in some states. And I think it is a significant difference between one and two screens.

And I also think that we can look retrospectively at the data and I guess I'm going to invoke PRO again.

Using R4S and putting the data in there and just freeing ourselves of the typical cutoffs and looking at the patients identified in those states and then put them through the system and seeing whether the first screen data would not have been sufficient to pick up all the cases that were picked up with the second screen and presumably not for the first, could just clarify this in a very short time.

CHAIR BOCCHINI: Thank you. I have Mike and then Carol.

DR. WATSON: So two things. I'm not as dreading of sequencing as Jeff probably. I am, I mean as the first tier test I think it would be awful right now. And I think it is worth bringing somebody in, not to drive the discussion.

But I think, you know, the inside grantees have looked carefully at the genes involved in newborn screening, and I think you can easily look at them and do an assessment of the pathogenicity of the variants that are found in those genes because nobody's -- I don't think anybody's going to be crazy enough to report out anything that's not either likely pathogenic or pathogenic and just see what are the proportion in this particular gene that you're actually going to be able to report out on newborn screening.

I think that would tell you how dreadful it's probably going to be as a first tier test.

And then the second part is, you know, we have a mix of sort of projects to learn stuff, and assessments, and the assessments, you know, things like timeliness, the assessment actually has a goal associated with it, of meeting a certain time line.

We don't have many of those and most of our, and most of the things we're assessing about conditions, I mean I presume we'd like every state

to screen for what you recommend they screen for.

But we don't really have what is, what are we looking for when we're assessing the conditions being screened in the states. And I think it would be useful to actually attach something measurable so you know where you are relative to some goal you're trying to accomplish.

CHAIR BOCCHINI: Carol?

DR. GREENE: Thank you. Carol Greene, SIMD. One screen versus two-screen, I think I'd really like to echo a lot of what Dr. Matern just said, that it's in need of resolution.

And I would also say that it allows to explore something that's been -- what needs to be explored is do you need to do everything on the first screen. If you're going to do two screens, and if you do appropriate education so that, you know, recognizing that some things are critical for timeliness, could you put, for example, Krabbe on the second screen and there would be some onus of responsibility on the family, so you wouldn't do it twice.

You would do CF on the second screen so you wouldn't scare people out of their mind with a positive first screen when the kid was too young to do a sweat test. So there's been a lot of discussion about if you start adding things to the screen and you start running out of blood spot, what belongs on a first, what belongs on a second screen, to address some of those issues of duplication and cost. What belongs on both.

So I think the one-screen versus two-screen is, the reason it's been worked on for so long is it's such an important problem and it brings in some other things, including bringing in thinking about getting people back and education to come back and later screening as well.

So I think the one-screen versus two-screen has lots of really important issues. I think the next-gen -- the sequencing in newborn screening allows for the opportunity, if done right, to bring the public health. In the end it's going to have to come back to this Committee, and if this Committee is prepared to think about the

public health issues would be welcome.

But I wanted to end by saying the assessment of data for, not just the assessment of data, but not to drop the timeliness, because we're just in the middle of making those changes and need to see what were some of the, you know, did it work and what were some of the unintended side effects.

And later on when the Timeliness Committee comes up there's some new challenges to that. There's a bill in Maryland that I think would threaten timeliness in an important way by wanting -- anyway coming back to that later.

So I think timeliness is really, a lot of work went into it, a lot of national attention, and it shouldn't be dropped. So those are the three that I think there would be a lot of room for the Subcommittee to make a lot of contribution.

CHAIR BOCCHINI: Thank you. Additional comments? Bob, and then Anne, if you'll come to the microphone.

MEMBER MCDONOUGH: This is Steve. I'd like to say something too when I have a chance.

CHAIR BOCCHINI: Sure, Steve, go ahead. We'll start with you.

MEMBER MCDONOUGH: Okay. Was there any discussion about linking the birth certificate to the newborn bloodspot, they had recommended this a number of years ago. And we were told couldn't do it because the birth certificate wasn't going to be changed until 2020.

And I'm not sure how quickly the federal agencies work. And if you want to leave this at this issue again and what timetable we need to have to begin the discussion, is a good time now, is it a year from now, is it two years from now?

Should we start something as simple as inviting someone from the Center for Biostatistics, whoever does the birth certificate, to come and discuss this with us? But this is an issue I think that we need to bring up at the appropriate time.

Oh, by the way, I can see all of you people there, and you look really good. And it's really good that you can't see me.

CHAIR BOCCHINI: All right, Kellie, any comments concerning what Steve brought up?

DR. KELM: So we talked about that in the Timeliness 2.0 Workgroup. But I do think if we want to reach out to the federal agency that deals with that, I mean I think that might be more of a Committee interest than just our Subcommittee.

But I do think Timeliness 2.0, we mentioned it as something that as we were sort of working on and were presenting on some of our suggestions of for example putting it in the toolboxes.

I mean I think that was brought up as something that we would recommend that the states seek to, for example, try to figure out how to do those linkages without necessarily, you know, pulling in the federal process at this point, whether or not that would make more sense.

But it may be worth seeing if we can talk to the agency and having them come talk to the Committee about that issue that was here before, so get an update.

CHAIR BOCCHINI: Okay, we certainly can keep it on the list for the Committee. Bob?

DR. OSTRANDER: Bob Ostrander, Family Physicians. Back to the sequencing issue, I suspect that there is at least a possible threat to things. And that this could get mandated by a state legislature outside the purview of labs and our work and anyone else's work.

And I think, and again I haven't heard any of this but I certainly know how enamored the well-educated nonscientific public is of this notion of whole genome testing. And it wouldn't surprise me at all if this found its way onto legislative agendas through other channels.

And I think it would be worth the Subcommittee keeping their finger on the pulse of that and maybe asking, you know, state lab folks to kind of let all of us know if it looks like that stuff is happening somewhere, because I think it would be worth, you know, generating a high level discussion so that that train doesn't leave the station inappropriately.

DR. MCCABE: Joe, this is Ed McCabe, if I could have a comment at some time.

CHAIR BOCCHINI: Yes, Ed, go ahead.

DR. MCCABE: I just wanted to say that the March of Dimes echoes that concern, and we're extremely concerned that this could happen as outlined. And we think it would be a huge mistake.

The correlation between genotype and phenotype is not well known for all of these disorders. It's not even known, you know, well we know that we wouldn't pick up all of the hearing loss and clinical congenital heart disease, and we wouldn't understand many of the others.

So I think it's very important that we as a community keep our eye out for this kind of thing. If you think about it, what we do is we screen for phenotypic changes, even for SCID, is still a DNA phenotype. So we just, we echo the concern. Thank you.

DR. COMEAU: Thank you. Anne Comeau from Massachusetts. This has been a very interesting discussion. I have three short

comments. One is with respect to multiple markers.

Of course that makes sense and that is something that many state laboratories are already using and such data certainly should be investigated further, but I don't think it's anything new.

Number two, with respect to standardization, I would really encourage caution from the Committee, that really what we should be standardizing is standardized quality and not so much a standardized laboratory test or a laboratory method.

With such standardization, one risks, for instance, one manufacturer running out of a particular reagent for an assay and people being stuck, and one quashes innovation. And certainly some of our best algorithms have come from the fact that state laboratories use a variety of methods and we learn from each other, and I think that that has to continue.

And, thirdly, with respect to the

next-gen sequencing, this is something that APHL's Molecular Subcommittee is putting a lot of work and thought into. And I'd remind people that next-gen sequencing, it's a platform.

And how we use it, whether we use it for sequencing or as a multiplex genotyper, is yet to be determined. And our responsibility, again, is standardized quality and to put these things forward with responsibility. Thank you.

CHAIR BOCCHINI: Thank you, Anne. So Don I'm going to give you the last question.

MEMBER BAILEY: Well it's not really a question, just a comment. So I'm on one of the four insight-funded projects related to potential implications of whole-genome sequencing or whole-exome sequencing for newborn screening.

And I think it's a technology, just like tandem mass was a number of years ago, it's a potential disrupter for newborn screening -- we do need to be prepared for it, we need to be thinking about it. We can't just ignore it.

We need to be looking at it and

exploring it and trying to understand different ramifications of it. So I would encourage us to, I think I mentioned this at a previous meeting, but to have a presentation from the Insight Group giving an update on what are the research questions.

It's a research-oriented set of activities, so what are the research questions. There's a, each project has a clinical component, a sequencing component and an ethics component. So I think we're trying to cover the wide variety of topics and issues that are being brought up. And I'm trying to understand when and under what context, if any, next-generation sequencing might be useful in newborn screening.

So I think the projects are far enough along that sometime later this year it would be appropriate to have an update from that group. And I would be glad to work with Tiina to organize that if you would like me to.

CHAIR BOCCHINI: Okay

MEMBER BOTKIN: Any chance I can do

something quick?

CHAIR BOCCHINI: Okay, real quick.

MEMBER BOTKIN: All right, my apologies, but I just want to let folks know I got a notice from a reporter yesterday asking some questions. And apparently there's a Virginia hospital that's now offering on a routine basis, or providing on a routine basis, pharmacogenomic screening or testing in newborns.

And it's about 20 different variants that are relevant to a whole host of drugs that newborns are highly unlikely to be taking. And questions being raised about whether, a lot of antidepressants for example, opioids, anti-chemotherapeutic agents, et cetera now with the informed consent of parents.

But I think it's just an example of where we may be seeing some of these sorts of technologies moving into the newborn screening domain in ways that are outside health programs but yet are promoting different test platforms that perhaps haven't been fully evaluated.

CHAIR BOCCHINI: Thank you, that's important information. It does relate specifically to this discussion. All right, thank you for this presentation.

I think what we haven't told the Committee is that at lunchtime, all of these potential projects are going to be laid out in front for you, and you're going to be able to put a marker on those that you wish to prioritize from each of the Subcommittees, and so we'll be able to begin the prioritization discussion after that happens.

So next we have the presentation of the Education and Training Subcommittee, and I guess both Cathy Wicklund and Beth Tarini are going to make this presentation.

MEMBER WICKLUND: All right, so good morning. So we are in the same circumstance, obviously, that all the Subcommittees are in, but we haven't met since, last February 2015 was when actually Don pulled up the last agenda.

And so one thing that we actually did do, the previous meeting before February, was we

actually tried to do a little bit of strategic planning. We had several questions as a committee that we were trying to think about, because, as you guys recall, we had already accomplished the three priority areas that were underneath the charge of the Education and Training Subcommittee.

And because of that, at that point in time we were actively thinking about new projects to actually take on as a subcommittee. So what we tried to do at that time was to actually go through what like the top pressing areas are and, you know, what's facing us in newborn screening.

So that was kind of how we started actually a couple meetings ago. So for this meeting what we did is we first reviewed our charge, which is incredibly broad as you guys remember.

It's really education and training of like everybody that has anything to do with newborn screening. And I think that is a challenge for our committee, because trying to focus in on what stakeholder we're thinking about trying to educate and what specific topic about newborn screening we

want to pick to educate about is really a challenge.

We actually did not refine our charge or really discuss that. We just kind of accepted our charge and all of its, you know, issues. But anyway, so that is something to maybe think and talk about as a group as to whether or not we want to focus the charge of the Committee on providers or advocacy groups or general public.

You know, where can we again, as a committee, make the biggest impact with the resources that we have. So, and I'm going to let Beth talk about some of these other things, but, so basically this is kind of like an overview of what we did for the hour and a half or hour and 45 minutes that we had.

So let me go ahead and, yes, show this broad charge.

DR. TARINI: So this is the broad charge which we discussed yesterday. I'll leave it there for their review. Okay. So we had an update from Natasha on the nomination education process, the product of which is to be an

educational guidance, these are my words, not Natasha's, to groups who might be interested in preparing a nomination packet.

It is -- we discussed at this point the update included that the Genetic Alliance/Newborn Screening Clearinghouse are collaborating with Dr. Kemper and his team and the Evidence Review Group to refine this and its content -- and the work continues and will likely be completed by December 2016.

The important point here is this is not a product of the Committee. This is a product which will come from the Clearinghouse and Genetic Alliance working with Dr. Kemper and his team and we will be available for review and to provide suggestions.

So the previous priority issues we discussed, these are broad strokes. Workforce issues, and then as I go through I'll, like much like the limitations in a paper, I'll tell you what we discussed and why we thought it was challenging perhaps. Workforce -- or are being covered by

others.

Workforce Issues, this we discussed briefly at this time, because since the discussion in February 2015, other organizations such as NSGC are taking on these issues and so we felt that they might be adequately covered by others right now. Help legislators better understand -- oh go ahead.

MEMBER WICKLUND: Sorry, let me add to that just to be clear. We also, with the Workforce Issues we recognize there are a lot of different work force -- you know, we're talking, there's genetic counseling workforce, there's MD Geneticists Workforce, there's laboratory personnel, you know, people that are working in public health departments.

And so I want to be clear that like NSGC is taking on looking at specifically a genetic counseling workforce and has employed a group to actually look at supply and demand and hopefully projected demand of genetic counselors.

But that doesn't include MD geneticists. And, again, Mike might be able to

comment later on about ACMG and what they might be doing and looking at that particular issue, but we felt maybe as a committee that this wasn't where we might make the biggest impact given that other professional organizations are looking at this issue.

DR. TARINI: And so to help legislators better understand newborn screening issues and program needs we just discussed issues of that. That actually rolls into -- some of these are going to roll into some of the projects we thought that we discussed this, we touched on this a little bit more at this meeting, especially based on education and dissemination issues, educating OB/GYNs regarding their role in newborn screening, particularly their role in discussing it with prenatal patients.

This continues to come up, obviously Dr. Botkin and his team have researched funding in projects that have targeted this. This will also come up later. And then also improving the initial communication between the clinician and the

parents regarding a positive finding. We delved into this a little bit more as well.

And we added some additional issues to the, when we first sort of took our broad stroke at what are the issues and needs, we did spend some time discussing that the Subcommittee has limited financial and manpower resources. As a result, project ideas must reflect this if they are to be feasible and effective.

So what we can do, not to be a downer but to reflect on what we do have, our existing resources, both in our human capital that sits at the table, their connections within their organizations, as well as existing resources in the Newborn Screening Clearinghouse.

And so we tried to focus our potential project ideas around this sort of powerhouse sort of we have. Additional issues we discussed -- what is the status of state educational endeavors, what is their current manpower, what are their best practices, who are the organizations active in E&T issues.

There are obviously a lot of them -- who are the target audiences most in need, and this is so that we don't duplicate efforts. So the project ideas we came up with were create an ACMG companion piece to the ACT sheets that provide PCPs with guidance and tips for discussing positive newborn screening results with parents.

This violates, I realize, all PowerPoint rules, that slide, that bullet point, but I wanted to be descriptive in it. So the goal here is, the discussion here is centered around the fact that the ACT sheets, while valuable, are clearly focused on the management from a pathophysiologic and medical perspective of the discussion with the parents, and tends not to focus or emphasize the discussion that will take place as a physician or clinician and healthcare provider might have with a parent around process, emotional, psychological, next steps, the child's health in general, and other concerns the parents may raise.

These issues we recognized and discussed have been addressed previously by the

University of Maryland, Dr. Greene working with Natasha in previous years, have touched on these issues, and so that was one thought we had. Do you want to comment?

DR. WICKLUND: No.

DR. TARINI: Okay. That was one thought we had as a potential option. This would be, in our mind, something brief that the physician or healthcare provider would have as a guide of sorts, like a crib sheet of issues that might come up, potential brief script to guide them and help them over these major points in a discussion.

This is really no different in our mind as breaking bad news guides that people might have in any other part of a healthcare interaction around that. The other -- these are not numbered, by the way. The one came up twice, but these are not ordered in any preference.

An educational outreach project in collaboration with the Newborn Screening Clearinghouse and Baby's First Test. So in this regard we talked about a few things that as I

mentioned there are a lot of entities and organizations involved in education at all levels and in all sectors.

And so we could create a visual representation of an educational web, those are my terms, I'll take responsibility for them. So that we can see who's doing, who's in the field, what are their missions, what are they doing, and who is the target, sort of a -- where's Jeremy? Is he here? This was his idea of a conceptual model as a starting point.

And then we talked about this idea of rather than sort of creating more content, which there's obviously a lot out there in all sectors and in all organizations, that we could best probably focus and leverage our existing resources on dissemination of educational resources to target audiences.

Where is Joyce? Joyce was -- I'm going to out you -- at this point of, you know, getting the information rather than a bidirectional educational focus, getting the information to

people and perhaps we would then create a list of --

MS. HOOKER: A brief back the physician or healthcare providers --

DR. TARINI: So we would -- a list of target audiences and then a list of linkages we can create and then basically create a scorecard of sorts in which we would categorize all of the linkages we could complete, those being not just connecting with people and saying yes, we would like newborn screening, but having them embed messages or content within whatever their media is.

And the linkages idea was Natasha's. Share the wealth. And the outcome therefore would be linkages achieved. One example, concrete example that came and linked with other ideas, was this idea of ACOG.

And we had our ACOG reps talking about the potential, for instance, for ACOG to endorse something for physicians and healthcare providers who are caring prenatally for women and their discussion with the women about the impending

newborn screening.

MEMBER WICKLUND: Yes, and actually they were also talking about revising their, I can't remember what ACOG calls their, you know, the bible. Yes, about newborn screening and whether or not we could play a role as a subcommittee in kind of helping thinking about how to revise, you know, some of that or be a resource to ACOG in that, you know, revision process.

So, again, if, you know, kind of like recognizing that if ACOG says something, OB/GYNs are very cognizant of that. They follow those guidelines and recommendations. So how can we get in in that way and maybe make a difference as opposed to the message coming from us specifically.

DR. TARINI: And then the final idea was to create a summary of educational initiatives among state programs so that we are aware of what states are doing and can disseminate that among the community, members of the community. And anything about that? And so we await the guidance.

CHAIR BOCCHINI: All right, go

ahead.

DR. SPONG: Thank you for that very thoughtful presentation, and I'm going to sit back here. So I think, you know, especially the second point, second bullet here could be very useful given the new requirements around research and newborn screening.

I know that we had held, NIH had held a workshop trying to figure out how are we going to be able to get to addressing those requirements, utilizing the resources that we have and recognizing that ACOG and people taking care of women during pregnancy might be one way to go at that and so this might be very helpful.

MEMBER WICKLUND: And we had talked quite a bit about, because one of our initial ideas was how do we get OB/GYNs more engaged in the newborn screening arena. And I know again Dr. Botkin has been working on that space as well, and I think that what we continue to hear back from a lot of like primary care physicians is the limited time and, you know, resources given to discuss all

of the things that you need to discuss during that point in time.

But, again, I don't think that's -- like, you know, we've talked a lot about how do we get into that space maybe a little bit more, you know, how do we partner with ACOG to get the awareness a little bit higher. And, you know, I don't know, you know, it's one of these things I think we just keep on thinking that might be a great way to raise the awareness, but I don't know how much success we will have either.

DR. TARINI: I have no delusions that having ACOG or any organization endorse something means that it will flow down to the providers and the providers will actually use it, being a health services researcher.

However, we have limited, and I'm not saying you're saying this, but like we also recognize that we have limited resources to ensure as many multimillion dollar projects have been unable to sort of get physician behavior and healthcare provider behavior to change.

However, the best we can, there are organizations in which their membership when they speak stands up a little straighter and takes a little more notice, ACOG being one of them, and so perhaps understanding we will have some trickle-down effect but not maybe massive, that might be a place to start.

DR. SPONG: Absolutely, and I think it extends even beyond ACOG although ACOG's a great place to start because, clearly, people have children through many different care providers.

And I think, you know, the workshop that we had held trying to just address how can you do this, recognizing time limitations, recognizing all of the things that these care providers are trying to impart during that prenatal visit.

But the more we can do to help provide information in a nicely packaged way so they don't have to do it themselves I think is one of those steps forward, and Tiina can probably say this even more eloquently than I ever could.

DR. URV: Oh no, you were saying it

quite eloquently. One of the things we brought together, the OG/GYNs, the nurse midwives, we brought together a first step of telling them this is what the challenge is in the newborn screening arena.

And we have representation from many of the people who are in this room, although it was kept a small meeting, and we do have intentions of going forward. They're very interested in the educational component and how education can be added into their materials and the materials they recommend.

Rather than just saying, you know, bing, we bless newborn screening, go ahead and go with that, they're looking for input from us and groups like us to help them develop materials that they can use for education, and I think our next level of meeting would start involving more people.

But that was just a first foray to those groups to let them know we have a problem and we'd like to work with them.

DR. TARINI: And then --

DR. URV: Sorry, Cathy.

DR. TARINI: And I think that what I'm hearing is that this is a potentially a ripe time for this. And, in addition, during our meeting yesterday there was discussion with ACOG about, or ACOG reps, about the idea that a shift in understanding of what we're actually asking may be helpful and is being actively pursued.

In other words, we're not asking for a consent or discussion of the level that takes place with genetic testing. We're asking for simply starting a conversation about this exists and it will happen, and if framed like that, we discussed with ACOG that that might be a much more appealing and have much more traction as a message of what our objective is.

CHAIR BOCCHINI: Thank you. Jeff and then Bob.

MEMBER BOTKIN: The -- ACOG already has a statement that says obstetricians should be addressing newborn screening issues, but it basically is phrased fairly cautiously. It says

obstetricians should make information available. It doesn't actually say the obstetrician should be doing the education.

And I think what we don't need is another brochure. I don't think we have a lot of knowledge about exactly what OBs are doing yet, but if it's simply handing a brochure, you know, we know, lots of research shows that doesn't work.

So we want to be thinking in creative terms about smartphones and videos and other ways that will take the burden off the clinician from having that knowledge. Because I don't think it's probable to get obstetricians up to speed on the details of newborn screening. So how can we use their -- the interest that the patients have in their babies in the OB context to promote innovative ways for education.

DR. OSTRANDER: I want to talk about the ACT sheet issue for just a second. I'm one of the primary care folks on the ACT sheet work group. And this is something we struggle with as we develop and refine the ACT sheets that we have, is how much

and how little to put in there to make it still useful.

And I'm a big fan of less is more, and so I've been kind of pushing not to overload the ACT sheets with things. You know, I think that, you're the one who said it, I mean delivering bad news is something that we learn how to do in training. And I don't that we, you know, primary care docs need a script for that.

Well this is, I guess this is a point for discussion, I mean I don't know that they need a script. I mean they need information, and so I think it would be, this is a worthwhile thing to talk about, but some guidance would be good so we don't make it too long.

So what we have done heretofore, essentially, is trying to give a tidbit of what the clinical considerations are. And I just pulled up the PKU one just for kicks. And it, you know, it says asymptomatic -- under the clinical considerations, it says asymptomatic in the neonate, if it's untreated, will cause

irreversible mental retardation, hyperactivity, autistic-like features and seizures.

Treatment will usually prevent these symptoms. And that's, you know, that gives you a handful of things to tell the parents when you're discussing it with them as you're making the immediate referral to the specialty center. And if you -- if folks think that there needs to be more than that for the average primary care doctor to have that discussion, I think, you know, we in the work group would be real open to the notion of what other people think.

As I said, there's a, you know, a very small primary care, well I guess it's a pretty small work group, a fairly small primary care representation there, and, you know, my perspective may not be the perspective.

DR. TARINI: Do you want me to respond or do you want Carol? So having my career development award based around communication on newborn screening issues between parents and providers, most of the time, when we've been doing

the interviews there seems to be -- this is my gross summary of it.

In a 2x2 table in which doctor knowledge is one, is a negative positive on one axis and attention to parental questions and issues outside of the medical consequence and treatment is a negative positive on the other.

Everyone would love the doctor who both discusses the medical issues of the consequences and what are the -- what is the disorder as well as it tends to parent issues. Went in excruciating detail as the level of which the highest specialist and the best-trained doctor could do.

When you start to trade off one for the other, parents tend to appreciate more of a discussion on what are the issues -- and attention to what is PKU and what are the issues ,but tend to appreciate more the physician who then attends to the issues of, for instance, some quotes where, you know, I don't know this area.

This is what I understand about PKU. But I will access the specialists who do more and

then have more deeper discussions about what are your concerns, what are your thoughts. You know, what are your biggest worries going forward? And so -- so that's number one.

Number two is I think that there are scripts and simple word choices that we may or may not use or we may think we're using and we're actually not using, as primary care providers. We often think that we're doing better jobs at things than we are when we're talking with parents, myself included.

And, third, I think that we don't need a large area. It doesn't need to be long. It simply needs to be attentive. This, I sort of say, in reference to things happening in cancer when we give people a cancer diagnosis. This is an area in which people studied long and hard about what to do and we weren't doing it well at some point in time. We probably still have areas to improve.

So I believe that in newborn screening, in an issue in which we, as primary care physicians don't deliver bad news as many times as the

oncologist do, that we probably have less practice.

MEMBER WICKLUND: And I just want to add something from a genetic counseling perspective. And I think that, again, like reading, it's not so much the information. It's how you communicate the information but then also the impact of the information on the individual and the family.

And I think that's what we're trying to get at with these companion sheets. And it would be just one. Like I view this as -- because it doesn't matter what you're talking about. The psychosocial impact issues are very similar in each case that you're kind of talking about.

So that's, I think, what we're talking about, not so much the nitty-gritty, what is PKU. That's important to know, but it's also like how does it impact this individual to get a positive result. How can you help them emotionally cope with that information and what's the impact on them and their family?

That's, I think, what we're getting at. So if -- and, again, some people are going to do

it really well, without anything else. And some people are going to think, you know what, it might be helpful for me to have some --

DR. TARINI: Guidance.

MEMBER WICKLUND: -- extra information.

DR. TARINI: Yes.

CHAIR BOCCHINI: Okay, I've got Don and then Carol.

DR. GREENE: I feel like I'm piling on, sorry. Carol Greene, SIMD. I am probably one of the few people in the room who actually gets the second contact after the primary care provider.

And I talk to the primary care providers. And what they universally want to hear most from me is not the details about the disease. That's -- they've got the ACT sheet, that's great.

They want to know, from me and the State Health Department, how likely is this. Is this more likely to be a false positive or a real positive. And then they want to know, what do I tell my family? And what we do -- because I've done, not as much

study as some, but what the families say is nobody told me that I needed a referral.

Nobody told me I had to go somewhere. Nobody told me how long it would take. Nobody told me it would be a blood test. Nobody told me that, you know, I couldn't park the car in the 15-minute slot because we had to get a urine test.

So it's that kind of stuff that the pediatricians want and the family practice doctors want me to tell them not just about the disease but, you know, what do I do while we're waiting and what do I tell the family and where do I send them.

And that -- we actually, Natasha and I did a multi-step process with some grant support -- actually grant support from Genetic Alliance -- and met with families. And we heard from the families what they wanted their pediatrician or their family practice doc to know what to say.

And it's distilled down into, I don't know, 20 lines which could be reworked and attached. And it's precisely that. It's not getting into the detail. It's just what questions

do I need to anticipate and how do I address them.

DR. TARINI: And to add to Carol's point about the logistics which is very pragmatic, I can imagine this just from anecdotally. Because when you're in an area, you've just found something that's, I have no control over, you then want to know, what do I do.

And so having -- adding any more uncertainty is problematic. Knowing what you can do and doing it, taking those concrete steps in making it easy is important. And it's -- now that you say that, we've created a guide like this for cystic fibrosis in our state that we're going to give to the providers.

And it has a section, just as you talk about, about logistics. We don't call it that, but it does have a few bullets about, for the primary care physician, about what needs to be done next, who do you call and what do you do.

Now some of it is in the letter they get, but it's in concrete text. This is very bullet-form but it does have, exactly as you say,

separate out the logistics as well as these questions.

DR. GREENE: Just, really simple, is just to tell a pediatrician, and I'll read here, "As you prepare to wait for the results, have the parents consider how they cope with stressful situations, including do they want to talk to somebody else or search for more information or would they rather wait. Cover the basics. Is there anything they should be watching for."

I mean, just really basic, basic stuff.

DR. TARINI: We think we do that but I -- but we also think, I would say, out and -- but if you go and look at Mike Farrell's work where he actually audiotapes people and scripts with them -- we say things. You might say to a physician, did you talk to them about their emotions and their angst?

And they say, yeah, we told them not to -- don't worry. And, actually, that's a fundamental -- I'm not a communications expert, but that's a fundamental misstep. And I do it

reflexively -- don't worry. It's like, tell my mother -- how I was raised. It's like, don't worry.

But it's not -- me telling you not to worry is not actually helping you process your worry.

CHAIR BOCCHINI: All right, Don, you get the last word again.

MEMBER BAILEY: No, somebody -- well, just in support of some of the things that Beth was just saying, so there's a long and well-established literature on family-centered practices more broadly.

And that cuts across many different settings and not just newborn screening but pediatric care and nursing and that kind of -- I mean it's -- and that literature is pretty clear on three things.

One is there's a pretty clear, now, understanding of what are the specific components of family-centered practices. We know what those components are, and we can define them. We can operationalize them. We can measure them.

Secondly, it's pretty clear that people think they do family-centered practices. And not everyone who thinks they're doing it actually does it. And sometimes, like you said, it's unconscious. And so assessment of that, you know is very helpful in most situations.

And then, third, the literature is very clear that for -- whether it's in pediatrics or in nursing or wherever, if you follow family-centered principles and practices, that you get better outcomes in terms of families adapting to their child's condition, to the information that they get and then their follow-up on specific recommendations if it's done in that kind of way.

So I think this is an ongoing kind of thing for all us is. And it's not like a one ACT sheet is going to fix it. It's more -- and it's a much broader training thing. But I do think it's a -- it falls under the auspice of this Committee, to be thinking about how can we continue to enhance family-centered practices in the context of do more screening and not just in the informing of families

about this but throughout the longer process.

CHAIR BOCCHINI: All right. Thank you very much. It was good discussion. Thanks.

I think we framed the issues very well. Thank you for the presentation. I think we got what we need to consider prioritizing some of these projects and then which we need to continue to work on to develop. So thank you both very much.

Okay, the third subcommittee presentation is from the Follow-up and Treatment Subcommittee. And, Steve, are you going to do that by phone or have you --

MEMBER MCDONOUGH: I'll try. Can you hear me?

CHAIR BOCCHINI: Yes. We're going to see if we can put the slides up.

MEMBER MCDONOUGH: Is it coming through too loud or crackled?

CHAIR BOCCHINI: No, you're fine.

MEMBER MCDONOUGH: Okay. Well, thank you. I want to thank Kamila. Can't thank her enough. She, on short notice, agreed to run the

Committee after I had go to the airport. And she took really good notes, and she actually helped prepare slides. So thank you so much.

And I, there was part of the Committee I did not get to hear. And I would sort of like to hear what went on here after I took off.

We spent approximately about first half an hour of the subcommittee discussing the excellent presentations yesterday, the long-term follow-up and sequence symposium. And there were some comments on what people got out of that and which had carried over into the priorities that were -- we've discussed.

That over 20 people are participating, I did circulate an attendance list and then promptly forgot it -- because I went to the airport. So, but -- and we had about five or six people on the phone who also participated. And that was very much appreciated.

Some of those who some of those priorities here. And there were some common themes that came up as everyone articulated what

they felt we should be doing for the next year, year and a half.

The first one I have here is access to long-term follow-up and treatment. From my own perspective, it's so frustrating to hear in 2016, after all the changes that have been made in healthcare, that parents are still, many of them, having the burden of expensive treatment being denied through health insurance.

And this is an issue that is -- the Committee has attempted to address before. And I -- there was a strong interest in revisiting this and adjusting it again, not just including medical foods which are really important, but that conditions in the RUSP, they're identified and have treatments, that these treatments should be covered by insurance.

Access also involves access to healthcare specialists, specialty clinics. And then, in rural areas of the country, that's a problem, and what can the Committee do in that regard. So access to treatment, long-term

follow-up came up multiple times and is -- I think it would be a priority of the subcommittee.

Another area that multiple contributors or subcommittee members brought up was the need for standardized clinical quality measures, not for all conditions in the RUSP, but that we need to start growing out in this area and will be great benefit to clinicians.

There were subject areas such as congenital heart disease brought up. We've heard from California that if ALD gets included in the RUSP, that this, there will be challenges in bringing in different healthcare providers, neurologists, endocrinologists. And what should be the best approach for quality care and how do you determine if you're doing a good job?

So this is, I think, an area that multiple subcommittee members felt was important. And I just want to let you know I'm a little bit sleep-deprived, and sometimes I get a little disinhibited when I'm sleep-deprived and say things that maybe I shouldn't.

But I know Dr. Kemper has done such brilliant work in the condition-review process. I don't know if we have people that could be tapped into to bring in specialists to have either evidence-based quality measures or, you know, in the absence of that, consensus of experts in the field, short of evidence-based, things that could be discussed.

But I think it would be very exciting. I really enjoyed participating in this process and just seeing all the really good ideas that people were bringing up. I think there was a fair amount of excitement, things that we can move forward in the next year. And this clinical quality measure's one that I think would be definitely worthwhile.

There is discussion on what are quality measures for the public health versus clinicians. Separating that out, maybe we'll go on to the next slide. And there's about a 15 -- I don't know, about a 10, 15-second delay here between the audio and the visual, just to let you know.

There was discussion on long-term follow-up being lifelong rather than childhood. And I'm not sure about this, but apparently the Committee itself, that it's been in the past, respective to the childhood age and there's obviously a need to go beyond that to make it lifelong.

And if we can't do it somebody else should, but I don't see why we can't do that. But that's something that this Committee could possibly wrestle with and discuss.

We also had discussion about the state infrastructure for long-term follow-up -- whose job is it to achieve or assure or assess long-term follow-up and what's the different -- how are states doing this?

I'm particularly interested in whether or not we could discuss state's efforts and long-term follow-up because that's been done recently. I've personally been very impressed with the outstanding work that APHL has done in our -- looking at adding conditions to their RUSP.

And their surveys of readiness of health departments. We've gotten great information from that and barriers that states have in implementing new conditions. And I think there would be interest in learning more about barriers that states have in improving their long-term follow-up.

I think Dr. Botkin, in previous meetings, had suggested that states increase their fees a dollar or two per bloodspot to help fund long-term follow-up. And I think, you know, things like this, could be really a lot of fun to do in the next year, year and a half and would maybe be very productive.

Other issues that were discussed were documenting best practices, prioritizing what we can do with existing data. There's interest in publishing a framework paper from the group and also to prioritize what we need in regard to increasing data collection.

There were several comments that the data for long-term follow-up is very expensive and

that their existing systems out there, such as was presented by -- yesterday that we could perhaps help this along as well.

So I'd like to thank all the contributors at the subcommittee. I was quite nervous in the beginning because I've not done this in quite a while. But I thoroughly enjoyed the experience. And I know we'll have some, probably issues that'll come up in the future, differences of opinion.

But I want to thank everyone on the subcommittee for being so nice to me yesterday. But I guess I should be quiet and let others comment now, and particularly Kamila, about what happened after I left.

CHAIR BOCCHINI: Thank you, Steve, very much. That was a very nice presentation. Thank you.

Let's go ahead and open this for discussion. Any comments for Steve and the Committee? Dieter?

MEMBER MATERN: Yes, thanks, Steve,

and to comment you for that work. I understand that it's not only about the collecting data but also using it. But I think we really need to find a mechanism to collect it and to fund it.

And in talking to Dr. Berry yesterday, I understand that the way her project works, that, actually the physicians who submit data are being paid whenever they submit something. So they get a specific amount.

And I just wondered, and I'm not an expert in billing and coding and so on, but is there a mechanism that one could actually make it a billable service when you submit, to a central database, information?

CHAIR BOCCHINI: I'm not aware, but maybe others, yeah. All right. That's a question that we could pursue but I doubt there's a mechanism to do that.

MEMBER MATERN: For laboratory tests, I mean, CPT codes, basically there's a mechanism to go through AMA. And I just don't know whether the clinical services are different or, so.

CHAIR BOCCHINI: It would still go through AMA and it would still be that same coding. There would be a coding caucus that would be responsible for that sort of thing. So we could look into that. Jeff?

MEMBER BOTKIN: Yeah, this is just a quick idea. Picking up on yesterday's conversation, there was some talk about whether data could be collected from the families directly as opposed to just from the clinicians, which really seems like a wonderful idea.

The Precision Medicine Initiative is getting started. And one of the characteristics of that, really, is to be fully engaged with the participants on an ongoing longitudinal basis. So I'm guessing that, I mean, I think that's going to be pretty well funded.

And there may well be valuable tools developed that will help engage families in a longitudinal fashion to collect various sorts of data. So, assuming some resources are put into that element, that may be something that could be

transported into this domain as a way of helping families be participants in the long-term follow-up.

CHAIR BOCCHINI: Additional questions? Comments? All right, if not, we've heard from each of the three subcommittees. And we've had some really good comments from the Committee and from the organizational representatives and others.

And so I think -- and we are ahead of schedule. So I think what we'll do is, instead of having the prioritization process done after lunch, we'll do it now. So I think what we'll do is we'll take a 15-minute break.

And then, during that break, we'll, the different recommended projects from the different committees will be laid out. Each committee member will be given, when we come back, an opportunity to indicate which of the projects in each of the subcommittees, they feel, should be prioritized. And then we'll see where we are after all the counts are taken.

So at this point, let's go ahead and

take a 15-minute break. Is that enough time for Alaina? Okay. So we'll come back promptly at ten after 11:00 to begin the prioritization process. Thank you.

(Whereupon, the above-entitled matter went off the record at 10:55:35 a.m. and resumed at 11:28:40 a.m.)

CHAIR BOCCHINI: Okay. So the committee members have voted. I think Dr. McDonough is still in process of sending in his votes electronically. But first I want to thank the subcommittees for not lobbying at the poll booth and everybody following appropriate recommendations for not campaigning. So that's good.

So the first, for the Follow-up and Treatment Subcommittee, the two projects that both received, actually, equal number of votes, and clearly the majority of the votes were -- one was Project Number 2, promoting the role of clinical quality measures to promote long-term follow-up, not just data collection.

And then the second was to examine -- State Project Number 4, examine state infrastructure for long-term follow-up. And so I think those are clearly, I think, these interests, certainly, partially predicated on the great discussion that we had yesterday that brought up a number of issues that, clearly, would potentially benefit by searching further and getting more information for the Committee. So --

Okay, so what we'll do is, we are going to have additional presentations on long-term follow-up from the State perspective and other things that are in process. So we'll have that at May. So I guess for the subcommittee, then, we'll have Project Number 2, promoting the role of clinical quality measures, as the primary and have this as the second priority.

MS. SARKAR: And once we finalize all the priorities, I will be sure to send it out to all the subcommittee chairs, co-chairs and then the HRSA staff.

CHAIR BOCCHINI: And the other thing

doesn't mean that the other committee projects fall by the wayside. We'll still keep them in the hopper and potentially they will rise for work.

But I think, as far as the Committee is concerned, any additional comments to make related to those two? Clearly, this is the voice of the Committee that has selected these two. Any other issues related to that? Okay.

All right, next, for Education and Training Subcommittee, Potential Idea 1, create the ACGME companion piece to the ACT sheets. That provides PCPs with guidance and tips for discussing positive newborn screening results with parents.

And, number two, Potential Idea Number 2, the Educational Outreach Project in collaboration with the Newborn Screening Clearinghouse, Baby's First Test. So those were both highly selected by the Committee.

And then, third -- third, the Laboratory Standards and Procedures Subcommittee, Task Number 2, to define and implement a mechanism for periodic review and assessment of lab

procedures utilized for effective and efficient testing of conditions included in the Uniform Panel. And that was, explore the role of next-generation sequencing in newborn screening.

And then the second was Potential Project 5, Task 3, Infrastructure and Services. And this was, define and implement a mechanism for periodic review and assessment of infrastructure and services needed for effective and efficient screening of conditions. And this is a portion of the Timeliness Initiatives fit here.

And so this is, review data related to testing. What are the implications of earlier specimen collection? And that is less than 24 hours. And what are the unforeseen consequences of and cost of timeliness?

So those are the two that the Committee selected for priority for that committee. And I think, although we're still getting Steve McDonough's vote, these, by far -- he's not going to change the outcome. But we do want you to vote, Steve.

MS. SARKAR: And Fred. And Fred.

CHAIR BOCCHINI: And -- oh, Fred's on? Okay, great. So then Fred as well. All right, so I think we've got the priorities set for the subcommittees going forward. And I appreciate all the work that everybody's done to get the subcommittees back and focusing on how we can go forward to best serve the Advisory Committee.

And so I think the next step is certainly to review the membership of each of the subcommittees and be sure that we have all the people that we need representing the areas necessary to make the subcommittees function effectively. And then we can go forward with any additions or changes to membership to make things work better.

Okay, so with that, is there any additional discussion related to going forward for the subcommittee work? All right, hearing none, we are back on schedule. So we will go take a lunch break now. We'll be back promptly at 12:30.

And so we'll begin the Timeliness --

well, we'll begin the Workgroup discussions a half hour early. All right. Timeliness will be on there. Thank you. Timeliness on return. All right, thank you all very much. We'll be back at 12:30.

(Whereupon, the above-entitled matter went off the record at 11:35:33 a.m. and resumed at 12:34:56 p.m.)

CHAIR BOCCHINI: Let's go ahead and start the afternoon session. We need to start with a roll call. Don Bailey?

MEMBER BAILEY: I'm here.

CHAIR BOCCHINI: I'm here. Jeff Botkin?

MEMBER BOTKIN: Here.

CHAIR BOCCHINI: Carla Cuthbert?

DR. CUTHBERT: Here.

CHAIR BOCCHINI: And Tiina Urv is back in the --

DR. URV: Here.

CHAIR BOCCHINI: Okay. Kellie Kelm?

DR. KELM: Here.

CHAIR BOCCHINI: Oh, Fred Lorey by phone.

(No audible response.)

CHAIR BOCCHINI: Dieter Matern, were you able to get online from the airport?

(No audible response.)

CHAIR BOCCHINI: Steve McDonough?

MEMBER MCDONOUGH: I'm here.

CHAIR BOCCHINI: All right. Kamila Mistry?

DR. MISTRY: Here.

CHAIR BOCCHINI: And Joan Scott for Michael Lu?

MS. SCOTT: Here.

CHAIR BOCCHINI: And Cathy Wicklund had to leave. And then Debi Sarkar.

MS. SARKAR: Here.

CHAIR BOCCHINI: All right, so for the organizational representatives, Bob Ostrander?

(No audible response.)

CHAIR BOCCHINI: Beth Tarini?

(No audible response.)

CHAIR BOCCHINI: Mike Watson?

DR. WATSON: Here.

CHAIR BOCCHINI: Joseph Biggio?

(No audible response.)

CHAIR BOCCHINI: Debbie Badawi?

(No audible response.)

CHAIR BOCCHINI: Susan Tanksley?

DR. TANKSLEY: Here.

CHAIR BOCCHINI: Chris Kus?

(No audible response.)

CHAIR BOCCHINI: Adam Kanis?

MR. KANIS: Here.

CHAIR BOCCHINI: Natasha Bonhomme?

MS. BONHOMME: Here.

CHAIR BOCCHINI: And Cate Walsh Vockley?

DR. VOCKLEY: Here.

CHAIR BOCCHINI: And Carol Greene?

(No audible response.)

CHAIR BOCCHINI: All right, so we're

going through --

MR. MCCABE: Joe, this is Ed. You may have said my name and I missed it. Sorry, but I'm here.

CHAIR BOCCHINI: Okay. Thank you. So in this session we're going to hear from the three workgroups who are going to provide us updates. And I know I got everybody started wrong yesterday by saying that they met the day before, but now everything is settled. They met yesterday.

Okay, so the first workgroup is the Timeliness Workgroup. This is Timeliness 2.0. And Kellie will make this presentation.

DR. KELM: Cathy left me, so it's just me. I know. So Timeliness 2.0, gosh, I think we've been, it's maybe been about six months or so.

And we've spent a lot of the last six months both in the meetings here as well as on calls, just trying to, number one, get a grasp about some of the activities that are already happening in Timeliness as well as finding out, you know,

where we can make a contribution.

And so, obviously, this is sort of looking, bringing Cathy in from the Education and Training piece and thinking a little bit beyond the lab to some other places where we can think that we can make a contribution to Timeliness, sort of before the lab and after the lab.

So we spent the hour and a half yesterday having a really interesting -- we sort of built off our last phone call that we had in January in trying to get perspectives from our workgroup members on where we could play a role and what kind of project that we could have.

And so, first, I want to thank our membership, who has really been helping us in bringing a lot of their perspectives to it. And so, and Cathy is the co-chair. And so we have a lot of people from Education and Training piece. We've involved some people from Nurses Association, you know, follow-up people and some others.

And so it's really a great mix. And so

I want to thank everybody for all their help. So the charge that our group had from the Committee was, we had these three bullets.

So the first one is to optimize successful strategies to address newborn screening specimen collection and transport.

Number 2, collect and disseminate timeliness-specific practices from state newborn screening programs, including programs that have implemented efficiencies in collection, transport, screening, and follow-up.

And the last one was investigate strategies for improved standardization of communication of newborn screening results to providers and families.

So we had a discussion around all three of these. And I can tell you a little bit where we wound up in our DF for our current project and then things down the road.

So here I've sort of combined the first and second charge together. I think right now we're still in the collect and disseminating

practices stage. Because I think we need to gather those strategies in order to see if we can optimize them and make them more successful.

You know, obviously, this timeliness -- I mean, improvement of timeliness has really been the last, about, two years since the Milwaukee Sentinel Journal article came out. I think it was two years. And so, you know, what we've been doing already, and I think what we want to continue doing, is to gather success stories from states, their programs as well as some of the other things that hospitals themselves are doing.

And to put those together, because a lot of the programs and hospitals, I mean, what we've heard is each of them can operate very differently. And so if we put these strategies, the toolbox strategies together, in one place, and provide that as a report or toolbox, if you will, from the subcommittee and the Committee, then the --

You know, as people are thinking about what they themselves can do to improve timeliness, they can look at these papers and see what fits,

what they could use in their program. So, as I said, we already heard from Iowa and Michigan. And I think that we already heard from some other programs that are excited to share with us some of their success stories as well.

And so I think that's one place to go for us to collate those. So the other thing that we had heard, there is some work being done with some stakeholder groups. We heard about some meeting coming up between, with A-1, you know, nurses, Baby's First Test and NewSTEPs 360 to sort of work with some, you know, some small groups with nurses and do some work there.

So I think some of those efforts are already there. But, you know, how can we raise awareness and what groups can we touch that may not have been there, you know, part of the story, yet.

So we thought that what we could do is work and try to partner with other stakeholder groups. And we thought of, for example, the American Hospital Association -- you know, hospital administrators and the risk coordinators

and, as well, as the -- a nurse's association to raise awareness by disseminating some of our success stories and these strategies within their group.

And what we thought would be great, and of course the question is whether or not this could happen, but, you know, we, obviously, have had, you know, APHL, you know, our groups that have webinars -- I've already had a number of webinars or groups on timeliness.

But can we see if we can get in the webinars or information sharing of AHA and ANA to, number one, you know, talk a little bit about newborn screening, the history, why it's important to convey that message again and then share some of our success stories, whether that be us or even finding some of these people that have the success stories and having them participate as well.

So, and then if we had our white paper available as well as, you know, other information then the idea would, obviously, be that that could hopefully disseminate within those groups. And

that would be sort of a start. And maybe, within those partnerships, we can find about some other ways that we can work with them to talk more about timeliness and how we can work with those groups.

So we haven't dropped the ball about Joint Commission. Unfortunately, our recent call was canceled. But do know that's still interest for us to talk to them about whether or not there is a possibility of partnering with them on timeliness, and making that some feature for Joint Commission to work with hospitals on.

I wish I had more there but, unfortunately, that's not moving very fast. The other thing our group wants to do is to keep hearing about the efforts in Timeliness, these groups that are already, that are moving forward. So NewSTEPs 360 has a lot of, not just data collection but they're doing a lot of work with different groups.

As I said, there's the one with the nurses. And there's some other pieces. And think we're going to have to -- We would love to hear about what they're doing. And we're going to need to do

that to make sure we're not duplicating efforts. And March of Dimes is, obviously, also in that space.

And the other thing is, you know, as NewSTEPs starts putting out some of the data they're collecting, we'll also get a better view of what the data is, to know what parts of the process may need more attention because, I think that, still, we need to drive us because we don't have that piece yet. You know, we, obviously, only have the survey that we did a year or two ago.

And I think that, in terms of the standardization of communication, we do have some interest in this space about working on this communication piece. But I think that we still felt that we would need to see the Timeliness data that's coming out of NewSTEPs first because we honestly don't even know. You know, we did not have any bits to the survey that we did as part of Timeliness 1.0, did not include it in this communication piece. So it was up through, sort of the lab finishing their testing.

And the new measurements through NewSTEPs is actually going to include metrics, for example, for collection through 12 months of age including the result to the PCPs and the time to confirmatory diagnosis. So we're going to need some of that data to really find out where we are and see whether or not there's going to be -- you know, and, in that case, what can we do?

So I, as I said, I think I sort of left that there's several possible projects in this space. But I think that they're going to depend on the data and the areas of need which, right now, we just don't know.

So that's it. So any comments, questions?

CHAIR BOCCHINI: Let's open this for questions. Carol?

DR. GREENE: Should probably see if there's any questions. I mean, that was terrific. Probably see if there's any questions from the Committee because my comment is about a threat to Timeliness that I'm hoping that the Committee might

be interested in saying something about, a new threat.

CHAIR BOCCHINI: All right. I see no questions from the Committee.

DR. GREENE: So thank you, Debi, forwarding to the members of the Committee and the liaison something that I brought from Maryland which is, I think, a significant -- I think it's probably -- I haven't spoken with the people who proposed this bill. I'm sure that there are excellent reasons for interest in this bill. But it is a very definite threat to timeliness.

And I have heard that there are some things happening like this in other states. And what this is is a bill that would change the Maryland newborn screening so that -- and I will read the relevant language.

So currently Maryland newborn screens to the State Health Department. It's a two-screen state. There's charges involved. The charges support the follow-up. There's systems in place for careers to get samples to the laboratory.

It' an excellent laboratory. They have a follow-up system. They're connected back to physicians and specialties of different kinds and all -- connected to the primary care physicians all over the state of Maryland electronically. It's a working public health system.

And, of course, it doesn't do every newborn screening test known to be possible. And some other labs do additional tests.

So the new language would be that, instead of requiring that it goes to the laboratory is that at the request of the parent or guardian of a newborn infant, perform the initial tests on specimens collected to screen for hereditary and congenital disorders including the tests that the Department of Public Health Laboratory would also perform -- would otherwise perform that they can be sent to a laboratory of the parents' choice, which means -- now historically I'm familiar with the concept of supplemental screening, that you do what your state does and you also could be required to inform people that there's other screening

available, but you do the state screen, and you can do additional.

This would be instead of the state screen. This would mean that it could go to any one of a number of excellent laboratories that do fabulous testing and that do their due diligence to try to get the results back in a timely fashion, but they don't have the connections and the regular connections -- it's not public health.

It's not connected to every pediatrician electronically by the way the pediatrician knows to sign in. There aren't couriers to this laboratory. So it is a threat to timeliness, both of the test -- the sample getting to the laboratory and the results getting back.

And I think that that is a very serious threat to timeliness, and it's happening in multiple states. And I'm hoping that the Committee might be interested in saying something in a very rapid turnaround because this is, the question is whether this bill will go to hearing. And I've heard other states are going through the

same things.

CHAIR BOCCHINI: Very important to bring that to our attention. Joan?

MS. SCOTT: Do you have any knowledge of when or where this might be happening if there are additional tests that are being offered on top of the -- what would generally be part of a newborn screening and the evidence behind those tests that -- other tests that might be done?

DR. GREENE: This bill is just to say that a parent or guardian could ask for the sample to go to some other laboratory, and that other laboratory might be one that does lysosomal storage or it might be one that does SCID or it might be one that does any number of other things.

So, no, I don't believe -- I don't believe that that would be the reason -- anyway, this is just that the parent could direct. This is not directing any hospital to send to any other laboratory. It's that the parent could choose to bypass state.

CHAIR BOCCHINI: So has this been

proposed by a single member of the legislature? And does it go before Health and Education or Health and Welfare committee?

DR. GREENE: Delegate O'Donnell introduced and read first time February 8th, 2016. Assigned to Health and Government Operations.

DR. BADAWI: And, Carol, if I could chime in, this is Debbie Badawi from AMCHP. We, we're actually in the process of responding to this bill. As far as we know, yes, it was proposed by one legislator, and it's now scheduled for hearing on February 23rd.

And we believe the intent of this intent of this legislation was to allow parents to have their infants' newborn screens sent to a lab that may be doing a broader initial screening panel, particularly including lysosomal storage disorders.

So, while we understand a parent may desire to have that broader panel, we wholeheartedly agree with Carol and are opposing this bill because it is not in addition to our

public health laboratory newborn screen; it is in lieu of, which obviously puts, creates multiple barriers with regard to timeliness and accurate reporting of results.

CHAIR BOCCHINI: Yes, it would certainly appear to me that the best approach would be to bring experts to bear at the committee meeting to make people understand the negative implications or negative results of going ahead with that kind of a bill and, hopefully, stop is at that point.

I'm sure you'll be involved with that, Carol.

DR. BADAWI: Thank you. Yes, we are -- Carol is one of our experts.

DR. GREENE: I'm one of the, in -- yes, there are other people who are more the lead. And I'm sure that everyone is aware that when passion and family is involved, that, you know, with the laudable goal of making sure that people get to have the opportunity to have their children tested for everything possible, sometimes strategies are

selected that have some unexpected adverse events.

And the reason that I raise it here is that, you know, Maryland is not the only state -- as I understand it, Maryland is not the only state facing this. And, certainly, Maryland, were able to fairly expeditiously marshal experts, that doesn't mean that it will get stopped or modified.

And other states, you know, if it were thought to be reasonable that this committee were to make some sort of a statement, that would be useful to other states as well facing this.

CHAIR BOCCHINI: Well, I think that, I guess, you know, this is probably more of a local issue. But I think it does have national implications. But I do think that -- has anybody had a chance to talk with the legislator who has put this forward? Okay.

DR. BADAWI: We had -- this bill came out after our deputy secretary -- I'm sorry, this is Debbie Badawi. It came out after our deputy secretary had a conversation about another newborn screening-related bill. And we have not yet had

the opportunity to have a conversation.

But the process is such that once we put in our position, there will be discussions, I believe, between our legislative office and Delegate O'Donnell.

CHAIR BOCCHINI: Natasha?

MS. BONHOMME: Natasha Bonhomme with Genetic Alliance. I think it's really important that this issue is being brought up. I also just encourage that when you're talking about, particularly when speaking to legislators and bringing experts, in terms of bringing families who are expert in going through the experience of newborn screening.

And they would know all the benefit of going through the public health channel. Because I can very easily see someone, a group, latching onto this and saying, why are you opposing giving parents options when, in fact, what we are trying to do is provide all the options to parents that happen to be within the public health system.

And so whether in Maryland which, you

know, obviously I'm very close to since I'm born and raised there, but also in all, any other states that are facing this, to really think about bringing the parent and family perspective because I think we've seen how, in other situations, experts have been -- discredited is not the right word, but seen as being on only one side of the issue.

And I think bringing in a coalition, and I use that word lightly, but really bring all the different perspectives, including the perspective of those who would directly be affected by this, would be very valuable, particularly on this topic.

CHAIR BOCCHINI: I think that's a very good point to bring families or parents. And then, I would imagine the Maryland chapter of the American Academy of Pediatrics would be very interested in being a partner as well.

DR. TARINI: I'm sure they would. And March of Dimes, if they haven't already heard about it, knows about it now.

And, I mean, I would just offer from me

personally, a very simple fix is to change the language so that families are required, as in some other states, to be educated about the option of supplemental screening so that people would be -- I mean, that would actually reach out to people who didn't already know as opposed to just restricting it to people who come in knowing and asking for it.

And there are plenty of states that have a requirement for educating people about the availability of a supplemental screen. And it goes in parallel. And, for me, that would be a simple and acceptable fix. But --

MR. MCCABE: Joe, this is Ed. May I say something, please?

CHAIR BOCCHINI: Yes, go ahead.

MR. MCCABE: So, Carol, please, if you can send me a summary in an email, that would be fantastic.

CHAIR BOCCHINI: I think that's going to happen.

DR. GREENE: Actually, Ed, you probably already got the bill from Debi Sarkar who sent it

to all the liaisons.

MR. MCCABE: Oh, okay. So it's not there in my email.

DR. GREENE: Okay.

MR. MCCABE: All right. Did Debi send that to us now?

MS. SARKAR: I did.

MR. MCCABE: Okay. Sorry, I just -- it's not on my screen. I'm sure it's there.

CHAIR BOCCHINI: Did --

MR. MCCABE: I'm just not in it right now, not caught up. Thank you.

CHAIR BOCCHINI: Thank you. Cate and then Jelili.

DR. VOCKLEY: Carol, I'm just wondering, is this really about supplemental newborn screening or is this coming from the folks who don't want the government to have my baby's DNA?

DR. GREENE: I don't believe that we know the answer to that question. And to the extent that the answer is known at all, it would -- Debbie Badawi might know but I don't think she's had an

opportunity yet to get more information.

DR. VOCKLEY: It just doesn't seem like something a legislator would instigate without some serious support from behind.

DR. BADAWI: Well, and -- this is Debbie Badawi. We don't know. We don't have information on what prompted this to be introduced. But I do know we had a discussion at an Advisory Council meeting about educating families about the possibility of requesting supplemental testing.

And so our, you know, it's possible that this grew out of that discussion, although Carol and I are certainly on the same page in that our recommendation is that families be offered supplemental testing but not in lieu of sending the baby's first specimen to our state public health lab.

DR. VOCKLEY: Just an additional question, is it possible to share that document with others? Because I've already had a couple of emails from people from Save Babies and elsewhere asking to see what they can do?

DR. GREENE: It's a public document.

DR. VOCKLEY: Okay.

DR. GREENE: It's posted on the Maryland Legislature --

DR. VOCKLEY: Okay.

DR. GREEN: -- web site, is my understanding.

DR. VOCKLEY: Great, thanks.

MR. OJODU: Jelili, APHL. Thank you for sharing that information. We were aware of this a couple of days ago from the folks from the newborn screening program.

Just a couple of points. I think this an issue, an ongoing issue that we continue to help states address. It not only affects timeliness but just fracturing a newborn screening systems as a whole, especially follow-up.

We do have a policy statement, we've had a policy statement on the role of state public health programs in newborn screening that addresses this particular issue. And so we certainly -- I agree with Natasha that we need to

build a coalition of folks, not just experts, to be able to help them understand what's going on here.

I want to distinguish what we're talking about here. We're not talking about supplemental -- I think it's definitely more than supplemental screening. I think, at least from what I've heard, that there may be a thought that, by doing this, folks from the state or parents can get conditions screened that's not on their current newborn screening panel.

And who's going to pay for that will be key as well, so we are certainly going to work with everyone to address this with you all.

CHAIR BOCCHINI: So, Carol, Debi and I will search to see what potential role the Committee could play. Obviously, because this is a state legislature issue and potentially lobbying would be in the state, is an issue we need to clarify.

But certainly the policies of the Committee are, you know, we certainly support

what's been said. And the need for the primary series of testing being done through the state system and not moving in that direction.

DR. GREENE: Yes, and thank you very much, if there is anything the Committee can say that would, you know, clearly not be directed at a single bill and a single state, but to, you know, affirm the importance would be most welcome. Thanks to APHL and March of Dimes and everybody else. Thank you.

CHAIR BOCCHINI: So, Kellie, thank you. This is a very clear and thorough presentation. And we appreciate the work of this, the ongoing work of the Timeliness Workgroup.

So let's turn to the Cost Analysis Workgroup. Alex Kemper will present where we are with the Cost Analysis Workgroup. And actually this and the Pilot Study Workgroup, these are being done in tandem to help define going forward how the Committee can adjust its work so that we can meet the 9-month deadline from acceptance of a condition to get through the process of the evidence review

and then evaluation and approval or rejection by the Committee.

DR. KEMPER: Thank you very much, Dr. Bocchini. So in the next five hours I'll go over where were are.

(Laughter.)

You know, I have to say, it's kind of surprising to only have 15 minutes on the schedule, which I'm sure delights everybody in this room as well, although I will notice that they put me in the afternoon, right when everyone's blood sugars are just about to go off the end.

So what I want to do is briefly present where we are with the cost analysis. And I'm very lucky to work with this really wonderful Cost Analysis Workgroup which we lovingly refer to as the CAWG. And I'd like to, again, publicly thank KK for all of her hard work in doing this.

We've had a number of very interesting phone calls, and then we had a chance to meet as a group virtually yesterday afternoon as well.

So just to remind you why we're doing

this, the charge to our group is to consider methods to assess the cost of newborn screening expansion as required by newly re-authorized legislation. So, again, not just a good idea, but it's a law. And that's, we're really required to do this.

The deliverable for this product I'm talking about it to come back with recommendations to the Advisory Committee about how to incorporate cost assessment into the decision-making process. And I think we've gone a long way towards thinking about how to do this and what our methods will be and the kind of metrics that we're going to suggest.

And then, as part of that, we plan to do some pilot testing, I guess, you would call it, do some, do some actual cases to see how it plays out.

So just to recap, and I know that we discussed this before, but our general objective is going to be looking at, specifically, the budget impact on states. I know this is only one component of the cost, but given the constraints that we have, it's what we can really more reliably

go after.

So our methods are going to include various interviews with those who either have or are planning to adopt the screening test for whatever the condition is under consideration, surveys with programs that are doing screening, surveys and discussions with vendors and, of course, looking at other places where data might reside.

So in terms of data, the primary, most important thing that we're looking at is going to be the costs incurred to states to add newborn screening for whatever the particular condition is. And that's going to include looking at screening and laboratory costs through short-term follow-up.

And we had an interesting conversation about, you know, at what point the short-term follow-up end and then when does it go into long-term follow-up.

What I proposed, and what I think what we agreed on, is at the time that you're actually

confirmed to have, for example, if it's a condition that's diagnosed by having low enzyme activity levels, you actually, you know, are certain that the child has low enzyme activity levels and maybe support a genotype. Again, it's going to vary a little bit by the condition under consideration.

We plan to look at a two-year time horizon, so annualized over those two years. We are looking at other outcomes so, you know, treatment and longer term outcomes. And so to the degree that we're able to, under all the other constraints that we have, we'll certainly look at that.

But, you know, I like to be optimistic and think that we can find something there. But I certainly, given the various constraints, don't think it's necessarily going to happen.

So we've been doing a lot of pre-testing. We're thinking about pre-testing, developing our draft approach to doing this. And, again, we want to assess the feasibility and the effectiveness, how good we're actually doing it,

getting the costs that we're interested in.

And we've really thought about three key conditions for this pilot testing -- Pompe Disease and MPS I which are, you know, both in the same group of lysosomal storage diseases, as well as X-linked adrenoleukodystrophy.

You can see in there when the recommendation came forth from the advisory committee to add them on. And we recently pulled from NewSTEPs what states were involved in screening for those particular conditions. Again, it might have expanded beyond this list. And we would revisit that when we move forward.

So we've had a lot of conversation about whether or not to target MPS I or Pompe Disease. And, you know, as you're going to see in a second, I think it actually makes sense to go after both because you can certainly, you know, test for each one individually or you can multiplex and go get both at the same time.

With both of those conditions there's dual platforms that are available -- tandem mass

spectrometry as well as digital microfluidics. There's this tension between laboratory-developed tests and commercially available tests.

And one of the advantages from us, for at least doing MPS I, is that we can go back and look and see how that compared to cost estimates based on the MPS I review when we did that.

So, of course, the question came up around which one to look at. Both the MPS I and Pompe Disease illustrate a lot of the complexities that would come forth as we start doing this. So why choose one? Let's do the whole enchilada.

It's funny, on one of the conference calls I said, this is the whole enchilada without really, like, explaining what my thinking was. And there was like this long silence. And so KK actually found this picture of me. And I am dramatically more gray since that picture, but it's all in the service of newborn screening.

So I think we really have landed on looking at both MPS I and Pompe Disease, thinking about, you know, doing a single test versus, you

know, a multiplex test. Because I think, in reality, if someone's going to have one lysosomal storage disorder, they're going to add, you know, multiple ones.

And I think that, really, by pushing things and by testing things we're going to find out, you know, what works and what doesn't work as we go forth. So let's think a little bit about costs.

There are so many variables that impact the cost of screening for a particular condition that can sort of make your head spin, right? So there's issues of birth rate. There are geographic issues. There's existing laboratory facilities and personnel.

There's what's going with a particular state's laboratory information system, whether or not a state uses an outside lab, the degree to which there are shared resources with other states, the availability of having contracts with specialty centers, service contracts related to the equipment and so forth, how newborn screening is

funded.

I mean, I can go on talking about all the complexities in here. But it's really, you know, at the end of the day, and I'm sort of jumping ahead of where my slides are -- but, you know, I think what we can reasonably do is provide ranges of costs so that the advisory committee at least understands, you know, in general, what it is.

So, again, we've come up with a whole litany of assumptions, being clear that you have to start somewhere. And as we bring forth these data we're going to have to be clear about what all of these assumptions were.

So, to simplify things, you know, assuming a hypothetical state with 100,000 births, presuming that it's a single specimen instead of a two-specimen screening state, looking at the purchase of equipment and supplies, modeling this as an in-house laboratory screening test, and then we talked about two-year cost projections.

And there's this, you know, term that's being used now, the conceptual confidence ranges.

There's other terms that people are using. I think that we have to think about the assumptions that we make and kind of give a range.

And, again, too, there's different estimates that we can provide to the group. Again, I'm jumping ahead of where my slides are, but it makes sense to talk about it now. There's the cost to, you know, the fixed costs to begin screening. There's the -- one could figure out the cost per child screened.

We could report out the estimated cost per case confirmed up to the point of long-term follow-up. There are lots of different metrics that we can provide once we begin to gather these data.

We have gone ahead and grouped things into buckets to be able to get to these costs, the cost of equipment, the cost of disposable supplies, reagents, that kind of thing, installation and maintenance of the equipment which, depending on the state and how they report it, may actually be bundled with the cost of the equipment. There's

the staffing for both the screening and the initial management. There's the cost of modifying the laboratory information management system to be able to track the results.

Again, there's issues in training and education and all the outreach and that sort of thing for confirmatory testing and short-term follow-up.

So what I hope to impress on you -- and I don't think we need to, this afternoon, drill down, but we have lots of buckets and they're in the process of developing spreadsheets to allow us to capture those data.

John Thompson yesterday, who's, as a matter of fact, he's at the great state of Washington, shared with us a spreadsheet that he uses when he tries to calculate these numbers. So I think that, you know, we're moving in the right direction.

There are these secondary cost categories which I just want you all to know that we're thinking about but I'm not entirely

optimistic that we can get related to long-term follow-up and treatment both from the public health perspective, the healthcare system perspective, from the family perspective.

I mean, of course, all these things would be wonderful to estimate but I don't think that these follow-on costs we're going to necessarily be able to get.

So issues that we're facing now include how best to get the cost estimates from the states who already have screening mandates, who have already begun to screen without causing them too much pain. We developed spreadsheets and so forth to begin to capture this.

And we also, again, want to gather costs from states and vendors to try to supplement this. And somebody on the phone call yesterday said that, for example, she was very interested in helping us look at the costs that Hawaii might face for adopting one of these screening tests that they haven't begun to think about. One is lysosomal storage disorders.

So as we get those, the numbers, in it would be interesting to include another state just to kind of see how things would look to them because, you know, I suspect that the estimated costs at the end of the day are going to be a lot different from those states that have really been thinking about planning about it to other states that it may not be on the radar yet and may have other barriers to implementation.

So here's my overly aggressive timeline which I don't think we're going to get to. But it includes where we are right now which is finalizing how we're going to go about doing things. And then, in the month of March, gathering information from newborn screening programs and then in April synthesizing that.

And then in April/May develop a report that we can give to the advisory committee so that we can come at the next meeting and show you how this played out. And I know, from talking to a lot of the folks that have been working with the project, they think that this whole thing is crazy,

and it likely is.

But what I can promise you is that when we come back we can at least have some numbers and show you what the -- you know, what surprising lessons we've learned so far. I think that some of the things that we want to do are going to turn out to be harder than we think. And being the optimist, I think that some of this stuff is going to turn out to be easier.

But, you know, it's the first time we've done this sort of thing. So it's going to be interesting. So our next steps, again, immediately, are to scope out the costs from MPS I and Pompe to identify states that are either screening or preparing to screen, gathering the cost templates and then working to fill this together.

And, like I said, I'll be back in May with some actual data. There are a lot of big questions that are looming. And these are things that we'll have to discuss with the other workgroups as well as the advisory committee as a

whole in terms of the minimum requirements for us to be able to get these costs as part of the evidence review.

And then, thinking about, you know, I wrote how useful, but really what are the useful components for the advisory committee and how will they be used in the decision-making process. And, again, you know, how they're used and fit into the matrix is not within our purview but within the advisory committee's purview. But I want to make sure that whatever information you need is something that we're actually gathering so that it's useful at the end of the day.

So this is my little valentine picture. That was my dog, who's curled up and her black dots were separated on her body, but when she did that it actually made a heart. I feel like I should copyright it because every time I put it out there, they're like, woo. And it's funny because, since I took that picture, she's never sat in that way again, so.

Anyway, I'd like to -- do you like how

I have like painful mundane things with cost, and I show this cute picture so that you get side-tracked and don't ask me things I can't answer? I just gave away my secret.

CHAIR BOCCHINI: Thank you, Alex, very much. Sounds like there's been a lot of effort and thought put into this workgroup. And I want to thank you all for doing so. Any questions or comments where we are now?

DR. KEMPER: I going to run back to my seat now before anyone comes up with --

CHAIR BOCCHINI: All right, well thank you. Okay. Thank you.

DR. KEMPER: Thank you.

CHAIR BOCCHINI: All right. Next Dr. Botkin is going to give us an update on the Pilot Study Workgroup.

MEMBER BOTKIN: Thank you. Now let me make sure I know the technology here. Is this advance over here? Great, thank you.

All right. Here's an excellent group that we've had together for about the past, well,

maybe a little bit over a year or so. And our original plan was actually to submit our report today but I have effectively renegotiated a delay in our timeline, so I think the next meeting is when we're hoping to have a report ready for this group.

And so I wanted to run through both a little bit of background information about how this report is shaping up at this point and then where we are in the process of specific recommendations that will be coming forward from this group to the Committee.

So here was our charge, recognize and support current efforts regarding pilot studies, identify other resources that could support pilot studies and then identify the information required by the Committee to move and nominate a condition into the evidence review process.

And so I think what we see here is sort of two broad agenda items. One is what are the threshold issues that will help the review process in making sure applications are ready for evidence review. And I'm going to talk for a second about

how that is a challenging issue for the Committee to be addressing at this point.

Then the other issue is how do we design a system, how do we support a system that will facilitate the conduct of pilot studies. And I think we talked many times here, you have to have the data for an evidence review process. How do we support a system within our country that will try to promote and facilitate the conduct of pilot studies so that we have an evidence, robust evidence review process for putting conditions on the RUSP or perhaps taking them off.

So here's our focus. Question is what data are the minimum necessary to move a nominated condition to the evidence review process? Again, mentioning this as sort of one aspect of our charge, not what evidence is necessary to approve a condition for the RUSP.

And I would say that this is just an ongoing challenge to try to keep our heads focused on that first threshold, to get it into the review process as opposed to saying, you know, what's

going to be necessary to actually get it on the RUSP. And this will be a continuing challenge for us.

And I think the debate we may want to have, and particularly once our report comes forward, is how high to we want to set this threshold. If we set it very high then we're going to have a lot of, then we know the evidence review process itself will have a lot of good data to review.

On the other hand, it may so high that it will turn people away from our process and they'll decide, you know, it's going to be a whole lot easier just to strong-arm my legislator into getting my condition on the state panel.

So striking that balance, I think, is a critical challenge. And we obviously don't want the bar so low that we have a lot of half-baked proposals coming into the review process that aren't going to be ultimately successful.

So our nomination form has three core requirements at this point, validation of

laboratory tests. Secondly, widely available confirmatory testing with a sensitive and specific diagnostic test. And then, thirdly, a prospective population-based pilot study.

So to some extent, we're going to unpack a little bit of these. And part of the question, again, for our group is to what extent do we have current problems with sort of this general list, to what extent do we need more specification within this list for the pilot studies.

So, quickly, I'm going to review just what our current outline is for the report. And charge to the workgroup, little bit of information about our review process, review of the types of data necessary to support an evidence review.

And then we do want to talk about recent changes in federal policy, specifically, the Newborn Screening Reauthorization Act. And I think most folks recognize that that is in place now as federal law. The common rule and the NPRM, Notice of Proposed Rule-Making, has finished with its comment period, over 2,000 comments coming in.

So there's vigorous input on that. And that, once that is finalized, which we think is going to happen sometime this fall, those requirements will eventually supersede the Newborn Screening Reauthorization Act.

Now that may -- the new common rule elements that relate to biospecimens may well have a three-year run-in period. And so we could well be dealing with the Newborn Screening Reauthorization Act for a couple of years.

That will create challenges, I think, for our community in sort of deciding how do you design a pilot study that's going to grapple with a short-term regulatory requirement. Nevertheless, this is a big issue for at least the next few years in designing pilot studies.

So we want to talk a little bit about the definition of pilot studies. We've gone back and forth and, I think, have decided, at least on a temporary basis, that we have a good definition or a couple definitions that are close out there in terms of population-based screening with real

babies, identifiable babies as sort of being the pilot study.

But we're also talking in this enterprise about other sorts of what I've labeled here as preliminary studies. You know, laboratory studies, the test validation stuff, is probably not what we would phrase as a pilot study. Nevertheless, it's part of our set of responsibilities to think about what should have been completed in that domain prior to moving on to an evidence review.

I want to talk a little bit about some of the models of parental decision-making that are out there, all this, very brief, and a little bit about the Committee's experience with pilot studies, both in terms of conditions that were not entered into a review process because folks said there's not been a pilot study. We want to reflect the fact that that's been a requirement for the Committee in the past. And, perhaps, talk, again very briefly, about what's the nature of those pilot studies for conditions that have made it to

an evidence review, whether or not they have succeeded in getting onto the RUSP -- what's been, how robust have those pilot studies been in the history of the Committee.

So then we want to move on to recommendations. Identify the information required by the Committee, et cetera. And we really have two aspects of this. One is what I've labeled here as sort of feasibility study.

Recommendations regarding the minimum criteria for an adequate evaluation of test modalities for analytic validity and clinical validity. And I'm going to get into that in a little bit more detail here in a second.

And then there's the second-level issues. How about net benefit to the kids and families? Recommendations regarding prospective population-based screening of identifiable newborns.

The second recommendation is going to be about recognizing and supporting current efforts regarding pilot studies. There's a

variety of federal agencies, of course, in addition to the states that are working on different domains of this.

The CDC, HRSA, FDA, NIH, of course, all active in various aspects of pilot studies that we want to both recognize and seek opportunities to see how we, as a committee, can suggest to the Secretary perhaps better support, different kinds of support for this enterprise.

And then thirdly, recommendations regarding identification of other resources that could support pilot studies and evaluation. And here we're not going to talk too much about that today. But I see this as sort of the big-ticket issue -- what sort of system do we want to promote this type of work in our country to make sure this testing is done in the most appropriate way?

So here's where we are with some of the graph recommendations at this point. I'm going to try to go through these quickly but, obviously, any feedback that the Committee and others want to provide to us at this point would be quite welcome.

So these are recommendations regarding the minimum requirement for the tests. And we are aware that this is both the initial Stage 1 screening as well as the confirmatory testing. Both of these will have to have been evaluated to some extent prior to being eligible for an evidence review.

So what do we want to say about that? And here I'm not sure I've got quite the right language, but there are established criteria. And I'm going to look very much to Carla for her help and Dieter, for others to help us get the right language here in terms of exactly what, how we want to articulate this.

Clear requirements, FDA verifications, et cetera are going to be necessary for the test platform to go forward. We also want to make sure, and this is an element that these other aspects don't pay attention to in our context, is the scalability to high throughput platform -- how do we know that this is a test that can be conducted on 100,000 babies a year. For example, what sort

of evidence do they have that this is a scalable technology.

This is the clinical validity aspect. How do we know, what evidence do we have about the clinical validity of the test. And so there's two aspects to that, of course -- the sensitivity and specificity. So with sensitivity we want to speak to the evaluation of the tests through analysis of newborn screening bloodspots.

And I think we're going to say here real bloodspots from real babies as opposed to spiked bloodspots with target analytes, from known true positives, carriers and from clinically relevant variant of that condition.

So this is where those bloodspots are going to be such a wealth of value for, that have been retained for kids who have known conditions.

Specificity, we're a little bit less targeted here -- evaluation of tests with the analysis of known true negatives, how many of those, obviously, show up to be false positives.

Here's the set of issues that we have

targeted at this point in terms of prospective population-based screening of identifiable newborns. Again, part of the general expectation now. We have had some active discussion about whether, in fact, the population-based screening pilot is necessary or not.

I think we're moving in the direction to say, yes, we think it is because it's an evaluation of the newborn screening system. You can evaluate the test, you can evaluate the treatment. But without actually having a population-based analysis how do you know that the different treatment or different system elements work together in an effective way to get kids into treatment?

Sufficient newborns screened to identify a case, lots of discussion here. How many babies do you have to have screened in your pilot in order for it to be considered an adequate pilot?

SCID folks may remember, a few years ago we recommended a pilot. And those pilot went forward, and once they identified one case we said,

good, right, it works. One effective baby.

Is that sufficient for our purposes here? Do we want to be -- and we had lots of discussion of this. It might well be to say we can identify the characteristics of the system without ever identifying a baby.

And if you know the treatment works through other sorts of studies, not population-based studies, maybe we can connect the dots and say here's a screening modality that's highly likely to work in a population-based model.

I don't think right now the group is moving in that direction. Again, we would like some input. So what this bullet, then, says is sufficient newborns screened to identify a case. So if the known frequency for effective newborns is 1 in 10,000, you probably ought to have a pilot study that screened at least 10,000 kids.

You know, maybe -- did you identify an effective baby in that first 10,000 or not? I think this is sort of where we're sitting with this debate or discussion right now within the group.

Studies showing efficacy of early intervention necessary, but such studies can be separate from the population-based study. So you might, of course you might set up a population-based screening study to do longer-term follow-up of the identified kids and say how do they do compared to kids who are identified clinically and try to demonstrate efficacy of the early identification.

Or you could have alternative approaches. Second kids in families where the second child is identified at birth as opposed to symptomatically. And, again, SCID is an example here where we had a high level of confidence that bone marrow transplant worked for these kids. And we didn't have to show in the population-based pilot that transplant was efficacious in the outcome for the kids who were identified.

So again, we're piecing together different types of studies to try to say when it's adequate to go to that review phase.

And then, lastly, we said

population-based studies should be conducted in a newborn screening system that's similar to the United States. So these are system issues. So if you've got a study that's coming out of Paraguay and they screen babies at five days' of age or some such thing, that's probably not a good pilot for the purposes of our review process.

Now we had some discussion but I think we're probably not going in a -- different populations may well have different manifestations, different phenotypic expressions of a particular condition. Does that matter? I think it will ultimately matter at the evidence review stage. Wasn't clear to us that it mattered at this initial threshold stage to get it into evidence review. But, again, welcome any thoughts or comment about that.

So here are the recommendations we haven't made a lot of progress on quite as yet. Recommendations to recognize and support current efforts regarding pilot studies and evaluation. I think this will flow pretty easily. Lot of good

work going on out there that we can articulate and encourage continued support, if not additional resources of one sort or another for this enterprise.

And then, lastly, recommendations. We've got identification of other resources to support pilot studies and evaluation. Again, this is the system sort of notion. What do we want to see in terms of a broader system to support this?

You know, from my perspective, I would love something that is, has some analogy to the Children's Oncology Group from years ago where you had rare conditions. You had lots of clinicians who were doing their best treating these kids, but everybody was treating them in a different way.

We developed a system where kids were enrolled consistently into research protocols. And it's had an enormous effect on morbidity and mortality from childhood cancer. So we can -- can we set up a pre-established system that, when conditions come along, we have willing states, willing IRBs, knowledgeable investigators that can

take up these pilot studies in an efficient way.

Now I think part of the challenge is we wait for the investigators to submit a proposal to some extent. I think that's already changing at the NIH level. But it's perhaps a little bit more reactive system than what we might want to have longer-term in developing a pre-existing infrastructure for the conduct of this type of research on rare conditions.

All right, I'm going to stop there and turn it over to Joe.

CHAIR BOCCHINI: Jeff, thank you very much. That was a very nice presentation. Thank. All right, this is open for any comments, any feedback to Dr. Botkin or his workgroup. Don?

MEMBER BAILEY: I'm on the group and it's -- thanks, Jeff, for putting all the discussion together yesterday. I mean, clearly, we have a bit of a -- well, we have a lot of challenges.

But one of our challenges is we want to make sure that when we send a condition to the

evidence review group we've done enough review of it so we're not wasting the evidence review group's time, but yet the threshold is not so high or the review process is not so complicated that we're asking the nomination review committee to actually do an evidence review before we send it on.

So I think we've got to be, you know, we need to be thoughtful about that. And I think this group's task is primarily with regard to the pilot studies component of it, but obviously there are other pieces too.

So there are good reasons why we haven't come up with recommendations yet because these are complicated issues. But I'm optimistic that in the next couple months we'll be able to work through some of them.

CHAIR BOCCHINI: Very pleased with the process. I think you're going in the right direction. I agree. Tiina?

DR. URV: So I also agree that the bar should not be so high that it would be like replicating it. But I also believe strongly,

coming from the NIH perspective, that the science that is there needs to be rigorous and that we can't bend down and forget about the rigor of the science in order to keep the bar low enough to let everyone in and then not have them go to the states. We have to have standards.

CHAIR BOCCHINI: Agreed. Carla?

DR. CUTHBERT: Yes, I'd like to reiterate what Tiina said. It's really critical that, again, we not, we be mindful of the volunteers' time who get together on the Prioritization and the Nomination Committee.

They do a lot of good work, and we want to make sure that there's enough good, sound data that's available. And certainly that CDC's been at least aware and involved and has started doing and putting together quality materials, especially -- particularly if it's a dry bloodspot test.

We need to have been informed a long time prior so that we can actually have good lead time to make good quality materials and that we can start developing an in-house method as well.

CHAIR BOCCHINI: Again, that's a very important component that we cannot forget about. I think that was part of what we wanted to have in place as well.

MEMBER BOTKIN: And I would say, too, that I think we have an opportunity to work with Alex and his group in terms of the thinking about the nomination process and to the extent that if these elements become acceptable, might -- how would the nomination process look so that we can facilitate decisions about what data exists on particular conditions.

DR. KEMPER: So there are a lot of pieces to the puzzle but -- oh, Alex Kemper. So there are a lot of pieces to the puzzle. There's the nomination process. There's the evidence review, and there's the decision-making process.

And I think right now, based on the experience of the Advisory Committee as well as the work that we've done to support the Advisory Committee, it's time to take a step back and really think about how all those pieces are working and

work together.

So certainly KK and I have been working with Natasha to think about how to structure the nomination form in a way that somebody's not steeped in the arcane world of evidence review can put it together.

I think that we need to think about the stuff that we're doing in evidence review so that instead of, you know, just going through and doing every little piece, working with the Advisory Committee or the liaisons to our process, if it's clear that there's a critical gap in evidence, being able to stop at that point and communicate that to the Advisory Committee.

Because it's my sense that if there is one of these critical gaps, that's actually an important thing for the nominator to know because then they can work with the NIH or other potential funders to resolve what that gap is and, you know, put forth what we hope, you know, will eventually improve child health outcomes.

And then, of course, we're going to be

developing all these new pieces for the Advisory Committee and thinking about how that plays into the decision-making process. So, you know, it's sort of an exciting time, I think, to reflect back on how all of this fits together and, you know, keeping the level of rigor and keeping the level of transparency and, you know, just helping moving, you know, everything along in the way that we think is best for the population we care about.

CHAIR BOCCHINI: Yes, we certainly want to know what issues on the cost side need to be in the nomination packet. So that is an important component. So as the two groups kind of come to, you know, their decisions, working together for revising the nomination packet itself as well as the information that's required in there is really important. So that would bring it all together.

All right.

DR. LOREY: Joe, this is Fred Lorey. Can you hear me okay?

CHAIR BOCCHINI: Yes, we can. Go right ahead.

DR. LOREY: Hi, there's a little bit of a time delay between the video and the phone, so I'm a little bit behind the times. But I just want to make a comment with your overview.

Is this going to include things such as -- I know I sound like a broken record, but harm that can come from requiring informed consent? And this goes back to the California Mass Spec pilot, so it's within the pilot period.

When informed consents are required, there are two big places of human error. One is the hospital, many of them, like half of them, just refuse to participate. They say they're understaffed and they're not going to take the time to present an informed consent.

And then the second is the Rheibold case which most of you have heard about where this family would have requested the supplemental testing. And this was a child which, one that was not caught because they were not offered testing and is, you know, permanently impaired.

So inherent with those sort of general

guidelines, is there going to be anything in there about the harms of informed consent in pilots?

MEMBER BOTKIN: I think we're clearly going to talk about the barriers that the informed consent process offers. And I do express it as a barrier because that's sort of how I see it, my own personal bottom line here.

But, of course, there's also substantial advantages too with the trust element that that bring to the whole process. So there's some pros and cons. But I think my sense is that we will describe those a what's required now as part of the process and thus, a given in terms of how new pilot studies are going to be designed.

They will just simply have to take that into account and, because of the Re-authorization law. Now whether the Committee wants to get into anything further than what it already said about the NPRM in terms of whether that sort of requirement is wise or not, you know, that's not really part of our charge.

So I think our group will probably

simply describe the experience to date and how different consent models have either made pilot studies more or less feasible based on that element.

DR. LOREY: Okay, that sounds good. And I wasn't really referring to the common law issue because, in this case, we followed their procedures, and that's what led to this poor child who is permanently incapacitated from GA1 because he wasn't screened. And then his parents sued because they said they would have accepted the supplemental screening.

And this was called a pilot. So that' the approach. As long as it's included in there somewhere, I see the pros and cons, too, of course. But in this case, that's a pretty hard con. So I just want to make sure it's at least mentioned. So thanks.

MEMBER BOTKIN: Okay. Yes, I'd like to learn more about that particular case and what the -- because the terminology here is important. And so how people use the term, "pilot study", is quite

variable. So, Fred, if you have some information you could send me on that case, I'd be interested in hearing more.

DR. LOREY: Sure, I'll do that.

CHAIR BOCCHINI: Microphone?

MR. BERBERICH: Yes, I'm Stan Berberich State Hygienic Laboratory at the University of Iowa. And I just had a comment that, the concern about not setting the bar too high implies some things too, and that is that there will be some rejection rate associated with it.

So I was thinking, it's much like the dilemma we have in the laboratory, false positives and what happens with that. But just the consequences, allowing these nominations to go forward into the evidence review, knowing that we've set the bar at a height where some will effectively be rejected and not be added to the RUSP, just a consequence of that, what additional pressures that may create and was wondering if part of the nomination process, if the bar is lower, if it's understood that there will be some guidance

and so forth that's given to those so it's not, ends there, but that, how they would move forward then with that condition, based on the evidence review.

CHAIR BOCCHINI: In fact, the Committee has done so both at the nomination prioritization level, and the Committee has chosen not to proceed to evidence review. And then the following evidence review, the Committee has given feedback for those conditions that have not been accepted. And that certainly will continue. That's important. So important comment, thank you.

All right, any other questions? Thank you. So is there any new business to be brought forward to the Committee? Hearing none, I want to thank everybody for an excellent meeting.

This is sort of a real transition meeting. We've re-established the subcommittees and their work. We've given them priority projects to begin to consider. And we moved ahead very well with our three workgroups and actually, one is definitely coming to a close in May.

And so I think we're making real

progress. I want to thank everybody on the Committee for your contributions, the organizational representatives, the members of the subcommittees and all of you who participated in the meeting today and yesterday. So thank you all very much. I'll conclude the meeting. Also, thank Debi for all the work that she's done to get this organized and run in the fashion, the successful fashion it has been. So thank you all very much.

MS. SARKAR: Thank you.

(Whereupon, the above-entitled matter went off the record at 1:48 p.m.)

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