U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

INTERAGENCY AUTISM COORDINATING COMMITTEE

FULL COMMITTEE MEETING

TUESDAY, JULY 8, 2014

The full Interagency Autism Coordinating Committee (IACC) convened in Rockville, Maryland, at the National Institutes of Mental Health (NIMH), 6001 Executive Boulevard, NSC, Conference Rooms C and D, at 9:02 a.m., Thomas Insel, *Chair*, presiding.

PARTICIPANTS:

THOMAS INSEL, M.D., *Chair*, IACC, National Institute
of Mental Health (NIMH)

SUSAN DANIELS, Ph.D., *Executive Secretary,* IACC,
Office of Autism Research Coordination (OARC),
(NIMH)

IDIL ABDULL, Somali American Autism Foundation

JAMES BALL, Ed.D., B.C.B.A.-D., Autism Society
(attended by phone)

ANSHU BATRA, M.D., Our Special Kids

COLEEN BOYLE, Ph.D., M.S.Hyg., U.S. Centers for
Disease Control (CDC)

SALLY BURTON-HOYLE, Ed.D., Eastern Michigan
University

MATTHEW CAREY, Ph.D., Left Brain Right Brain

WENDY CHUNG, M.D., Ph.D., Simons Foundation

PARTICIPANTS (continued):

JUDITH COOPER, Ph.D., National Institute on Deafness and Other Communication Disorders (NIDCD) (representing James Battey, M.D.)

JOSE CORDERO, M.D., M.P.H., University of Puerto Rico

JAN CRANDY, Nevada State Commission on Autism Spectrum Disorders

GERALDINE DAWSON, Ph.D., Duke University

TIFFANY FARCHIONE, M.D., U.S. Food and Drug Administration (FDA) (attended by phone)

ALICE KAU, Ph.D., Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) (representing Alan Guttmacher, M.D.)

LAURA KAVANAGH, M.P.P., Health Resources and Services Administration (HRSA)

DONNA KIMBARK, Ph.D., U.S. Department of Defense (DoD)

WALTER KOROSHETZ, M.D., National Institute of Neurological Disorders and Stroke (NINDS)

CINDY LAWLER, Ph.D., National Institute of Environmental Health Sciences (NIEHS) (representing Linda Birnbaum, Ph.D.)

DAVID MANDELL, Sc.D., University of Pennsylvania

JOHN O'BRIEN, M.A., Centers for Medicare & Medicaid Services (CMS)

LYN REDWOOD, R.N., M.S.N., Coalition for SafeMinds

CATHERINE RICE, Ph.D., U.S. Centers for Disease Control (CDC)

ROBERT RING, Ph.D., Autism Speaks

PARTICIPANTS (continued):

JOHN ELDER ROBISON, College of William & Mary

ALISON SINGER, M.B.A., Autism Science Foundation (ASF)

LARRY WEXLER, Ph.D., U.S. Department of Education (representing Michael Yudin)

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PROCEEDINGS:

Dr. Thomas Insel: Thank you, and welcome. Good morning, everybody. There's a bit of an echo in here. Let's see if we can clear that up a little bit.

Okay. Great. Thank you.

This is a full meeting of the Interagency Autism Coordinating Committee. We have some new members. We have lots of people listening and watching by webcast and phone. And we have a very good attendance here at the meeting of regular members.

So this is also probably our last meeting of the full Committee, and we'll have some time to talk about that, I hope. We have a very full agenda. Let's start by doing a quick round of introductions, and I'd also like to introduce two of our new members.

But we'll start with Walter here, just so people on the phone will know who's in attendance.

Dr. Walter Koroshetz: Hi. This is Walter Koroshetz. I'm the Deputy Director of the National Institute of Neurological Disorders and Stroke.

Dr. David Mandell: David Mandell from the

University of Pennsylvania.

Dr. Matthew Carey: I'm Matt Carey. I'm a parent.

Dr. Judith Cooper: Good morning. I'm Judith Cooper. I'm the Deputy Director of the National Institute on Deafness and Other Communication Disorders, and our Director, Jim Battey, is right behind me.

Ms. Jan Crandy: I'm Jan Crandy. I'm a member of the Nevada Autism Commission, and I'm also a parent. And I also serve as the care manager for our Autism Treatment Assistance Program.

Dr. Anshu Batra: Anshu Batra. I'm a parent of an individual with autism and a pediatrician.

Ms. Cindy Lawler: Cindy Lawler. I'm representing the National Institute of Environmental Health Sciences.

Ms. Idil Abdull: Good morning. I'm Idil Abdull. I am an autism mom.

Dr. Sally Burton-Hoyle: My name is Sally Burton-Hoyle. I'm a family member. I am a university professor and with the Autism Collaborative Center at Eastern Michigan University, run their College Supports Program.

Ms. Laura Kavanagh: Good morning. I'm Laura Kavanagh. I'm with the Maternal and Child Health Bureau at the Health Resources and Services Administration.

Ms. Lyn Redwood: Hi. I'm Lyn Redwood. I'm co-founder and vice president of Coalition for SafeMinds. I'm a parent of a young man who was diagnosed with autism and mercury poisoning. And a pleasure to be here today. Thank you.

Dr. Donna Kimbark: I'm Donna Kimbark. I'm the program manager for the Autism Research Program out of the Department of Defense.

Mr. John Robison: I'm John Robison. I'm an autistic adult, and I'm Neurodiversity Scholar in Residence at College of William and Mary.

Dr. Catherine Rice: I'm Cathy Rice, standing in for Dr. Coleen Boyle of the Centers for Disease Control and Prevention. And Dr. Boyle will be here for the afternoon session.

Ms. Alison Singer: I'm Alison Singer. I'm the cofounder and president of the Autism Science Foundation, and I'm the mother of a beautiful 17-year-old daughter with autism, and I also have an older brother diagnosed with autism.

Mr. John O'Brien: I'm John O'Brien. I'm the senior policy adviser at the Centers for Medicare and Medicaid Services.

Dr. Jose Cordero: Buenos dias. Jose Cordero, University of Puerto Rico.

Dr. Larry Wexler: Larry Wexler, U.S. Department of Education, Office of Special Education Programs.

Dr. Geraldine Dawson: Good morning. I'm Geri Dawson. I'm a clinician and scientist and professor of psychiatry at Duke University.

Dr. Alice Kau: I'm Alice Kau. I'm a program staff from the Eunice Kennedy Shriver National Institute of Child Health and Human Development. I'm sitting in for Dr. Guttmacher today.

Dr. Susan Daniels: Hi, I'm Susan Daniels. I'm Director of the Office of Autism Research Coordination at NIMH and Executive Secretary of the IACC.

Dr. Insel: And Tom Insel, your chair and Director of NIMH.

It's a real pleasure to introduce two new members -- one from Autism Speaks, Dr. Robert Ring, and one from the Simons Foundation, Dr.

Wendy Chung.

And in the spirit of our being a committee that is very outspoken, we're going to ask them to speak for themselves in terms of introduction. So, Rob, could you just take a couple minutes and tell us a bit about yourself, and then we'll move on to Wendy.

Dr. Robert Ring: Thanks, Tom. I just wanted to start off by saying what an honor and pleasure it is to actually be joining the Committee, having sat on the other end of calls and even in the room many times in the past, across various places I've worked leading up to my current role.

Just a little bit about myself. I'm currently the Chief Science Officer at Autism Speaks. This is a relatively new role that I'm walking in the footsteps of Geri to my right here, whom everybody knows very well. I've been in this role for about a year now, though I've been with the foundation for 3 years running -- I'm a neuroscientist by training. And before joining Autism Speaks, I headed the autism unit at Pfizer, which was, at the time, the first dedicated unit of its kind working on medicines development for

neurodevelopmental disorders.

And before my time at Pfizer, I spent over a decade at Wyeth, mostly working in the area of psychiatric and neurological medicines development.

My own personal area of research interest that have spanned my career has really been in neuropeptides, working mostly in the area of oxytocin and vasopressin systems of the brain. And in addition to my role as CSO at Autism Speaks, I have adjunct positions in the Department of Psychiatry at Mount Sinai School of Medicine and Departments of Pharmacology and Physiology at Drexel in Philadelphia.

Dr. Insel: Great. Thank you. And Wendy Chung from the Simons Foundation Autism Research Initiative.

Dr. Wendy Chung: Thank you. I also am very, very pleased and honored to be part of this esteemed group.

I'm by training a pediatrician and a clinical and molecular geneticist and have been at Columbia University for the past 15 years. And my practice really focuses on individuals with disabilities

and trying to understand better what caused those so that we can support them in the future.

And for the last 2 years, I've been the Director of Clinical Research at the Simons Foundation, having been with the foundation in one role or another since the inception of their autism program. And am thrilled to be with you as the foundation really tries to go more in the direction of beyond just basic discovery and doing more in terms of applications to help improvements of individuals. And so, we're really excited to be part of this.

Dr. Insel: Great. Well, it's somewhat ironic to have two new members on what may be our last meeting, but it is great to have both of you onboard. And hopefully, this will just provide the platform for the next roster of the IACC.

Before we get to actually talk a little bit about the future of the Committee, I wanted to go back and look at the minutes from last time and ask for any comments, changes, revision, suggestions, or approval of those minutes.

[Pause]

Ms. Redwood: Tom, I personally didn't get a

chance to read the minutes yet since we didn't get them until last evening, and I was traveling. Would there be a way -- I don't know if any of the other Committee members have had a problem with reading through the minutes yet. But I didn't know if we could possibly delay that until this afternoon, and I could read them during lunch.

Dr. Insel: We could delay it, but before we make that decision, is there anyone who has looked and who has comments or suggestions?

[No response]

Dr. Insel: All right. I'm fine with -- I'm not sure how much time you'll have to read them this morning, but at least maybe take a couple minutes during the lunch hour, if people would like to do that. And we'll get back to this in the period maybe after public comment.

All right. Let's move on, and we're going to shift a little bit on the agenda to hear from Susan initially about an update around IACC and OARC. So, Susan, let me have you start with the first set of slides.

Dr. Daniels: So we wanted to give an opportunity to hear a little bit about what we're

thinking about what's next for the IACC. As you know, the Combating Autism Reauthorization Act (CARA) of 2011 is going to be expiring on September 30th -- it should say 30th, not 3rd -- 2014. And without a new reauthorization, the IACC would be scheduled to sunset on September 30, 2014. And the current IACC member terms expire on September 30th.

But if there is a reauthorization before September 30th, the Committee will not sunset, i.e., cease to exist, but the current member terms will still expire, and we would be planning to reestablish the Committee under the new -- whatever the new law is, if there is a reauthorization. And it will depend a little bit on what the specific provisions are of the reauthorization.

If we do reform the Committee, we will be holding another period for open public nominations for public seats on the IACC. And so, we will be letting you know about that as soon as we know what's going to be happening.

I wanted to give you a little bit of background about the current legislation that's

under consideration in Congress. So, both the House and the Senate have an identical bill called the Autism Collaboration Accountability, Research, Education, and Support Act, or the Autism CARES Act. And this would reauthorize the IACC and some other programs through 2019.

And it would -- some of the new provisions in this law compared to the current law would be that it would establish a National Autism Spectrum Disorder Initiative within HHS that would be led by a specific official that would be charged with implementing autism activities, taking into consideration the IACC's strategic plan and ensuring that that HHS activities are not unnecessarily duplicative of other Federal department and agency activities.

The new law, if this becomes a law, would also incorporate a greater emphasis on services into various activities of the IACC, including the strategic plan, the summary of advances, and some other activities. It would also provide some further specification for membership, indicating certain members that need to be a part of the Committee.

And it would also incorporate a new, significant emphasis on adults and transitioning youth services into the report to Congress that was a part of the previous law. So those are some of the provisions in this draft legislation, but we don't yet know whether that legislation will go through.

Currently, it has passed the House, and the Senate HELP Committee has reported it out. But it has not been voted on by the full Senate yet. So we're eagerly awaiting hearing what happens with that legislation, and so we wanted to give you a little bit of background about -- about that, and that's sort of where the Committee stands.

So, as it stands, this is the last meeting of the full IACC under the current authorization. But we do have one other formal activity planned currently for September 23rd. I have a slide later. Sorry, I should have put it in after this. That we're going to be having a workshop, and we can discuss that.

So, anyway, wanted to give you a chance to comment or ask questions.

Dr. Insel: Matt?

Dr. Carey: My -- I'll say I think my read of the law is a little different. When I look at when we were appointed, the rules say that we'll serve a term for 4 years. It's not contingent on the law or on the law being reauthorized or not.

I mean, obviously, if the Committee sunsets, there's no committee, you know, we go away. But the appointments are 4 years, not the term of the law, is my understanding of it. And if you look at the, say, the congressional report that the House put with it, it specifically states that they -- and I was trying to look up the language specifically.

It specifically states that it's their intent that the IACC continues. There would not be a break in the IACC. They felt that that was disruptive in the past and would like to see that that not happen now. So --

Dr. Daniels: So, in terms of the terms, the terms, because the last authorization was only 3 years, you could only be appointed for those 3 years. We can't -- we couldn't have people appointed to serve on an IACC that wouldn't potentially exist after September 30th. So,

legally, that was the term of your appointment. So your appointment does end on September 30th.

And so, in order to continue, you would either need to be extended, or we would need to have new members in place.

Dr. Carey: Wasn't the -- I mean, wasn't the 4-year term, I mean, that's part of the original CAA of 2006, if I recall? And I don't believe it was struck in CARA. So, I mean, I'm not an attorney. I'm just pointing out that I -- my read does seem like it may be a little bit different. So --

Dr. Daniels: Well, the current appointments are set to expire on September 30th. The actual paperwork says that they do expire at that time.

Dr. Carey: Okay. I didn't look at the -- you know, my letter --

Dr. Daniels: So those are the actual appointments you all have. Like I said that it wouldn't have made sense for HHS to make those appointments to last past when the Committee was expected to expire or be reauthorized.

Dr. Carey: In which case, I mean, one thing I would suggest, you know, if we can give advice to the Secretary, would be that to open the

nominations now so that there isn't a gap. If you look at kind of where we are in terms of a committee, our major product would be the strategic plan, which most of that work is done at the end of the year, the fall quarter, essentially.

And not only that, but I think if you look at the strategic plan that was put in place, it was really done by the previous IACC, and most of the long-term goals are really ending in 2015. I mean, the real -- you know, the time to actually do something, to redo the strategic plan is sort of next year.

And having a hiatus like we had last time, we didn't start until July. You know, I think really there's going to be a large effort next year. At least I'm hoping or expecting there to be a large effort next year on the strategic plan because, like I said, the goals are kind of written around a 2015 completion date.

So, you know, I'm concerned --

Dr. Daniels: Right. I understand your concerns. In terms of opening for nominations, we really can't do that until we know that there is a

law in place that would be renewing the IACC because it wouldn't make sense, again -- it wouldn't be legal for us to be putting people in place for a committee that's not going to be authorized.

So we need to wait for a new law to be in place. So when we have the reauthorization, of course, there will be legal consultations within the department, and they will interpret the law, and we will move forward. We will, of course, keep you informed at every step.

And if there is a time when we are going to be taking new nominations for public members, we'll definitely get you all the information. We'll make it all public, and you know we will give you all the instructions that you need for that. So we definitely plan to keep you informed of all the happenings.

It seems like there's a lot going on right now, and potentially, this legislation that's under consideration may go through. And if not, there may be other opportunities to get reauthorized before September 30th, or even after. So we'll stay tuned.

Any other comments or questions?

[Pause]

Dr. Insel: Maybe just two quick things to add. One is that we do have a new Secretary. So we'll be dealing with a different group in that sense, and it'll be important for us to get her engaged in making the appointments for the new committee quickly, if there is a new committee.

We're actually not presuming that this will be reauthorized. I think you have to wait and see how this plays out.

The second point is that there were some public members last time who asked not to be re-nominated. So if any of you feel that way, it would be good to know that fairly soon, as we start to think about what the roster might look like for the Secretary going forward.

Any other questions or comments about this process?

[No response]

Dr. Insel: And presumably, this will happen over the next few weeks if it's going to happen. As you all know, the Senate is trying to get an awful lot done. They have 12 appropriation bills

that they need to act on before they break in September for reelection and for other things that are happening.

So it's really not clear exactly where this will sit in the agenda and how -- whether this will get approved by unanimous consent or not, whether it will need to have some discussion. There's lots of unknowns here, a lot of things will play out over the next couple of weeks.

But as Susan says, we'll keep you posted as we get more information. Susan?

Dr. Daniels: Right. Well, thanks. So we'll move on to the next item. Just wanted to mention this update that there has been a resolution made by the World Health Assembly on autism, and this was a pretty significant event. And Geri Dawson mentioned that she would like to hear an update on this at this meeting.

So I wanted to give you a very brief update that this resolution was cosponsored by more than 50 countries and supported by all 194 member states of the WHO. The resolution, which is in your packets -- it's up on our Web site as well. For those who may be listening in or looking at

our Web site, it's in the materials.

It briefly describes ASD and some of the key issues for those who are on the spectrum and their families, including healthcare and human rights issues. And it also identifies key challenges and priorities for ASD policy in member states, including healthcare, service provision, infrastructure, et cetera, and protection of human rights.

There are also some requests of the WHO Director-General to engage with and support member states in strengthening their recognition and support for people on the autism spectrum, and it establishes ASD as a global health priority.

So, last year, a report on ASD was shared in the Executive Board of the World Health Assembly, and the Executive Board adopted a resolution. But this year, a revised version of the report went to the Executive Board, and now the resolution has been adopted by the whole World Health Assembly.

And the effort was led by Bangladesh, with contributions from some other nations. And as I said, it got support from all member states. And so, this represents a formal commitment from all

of those states to really make this an important health priority. So something that you all, of course, I'm sure, are aware of, but we wanted to bring it to people's attention that this significant event has occurred.

Do we have any comments from IACC members about this?

Dr. Cordero: I think it's great news that WHO is actually paying attention to autism. My question is given that the World Health Assembly already approved this resolution, have there been any contacts between IACC or NIH with PAHO, or Pan American Health Organization, with just the regional office of WHO, and the one that would be more directly with U.S. and especially member states in Latin America?

Dr. Daniels: Not in terms of coordination between the Committee and the World Health Assembly. But NIH and HHS, of course, were consulted in the process of getting the resolution through. So I think on the Federal side, we've been somewhat involved, but it would be great if there's an opportunity with the next IACC to be more in tune with this and for the IACC to help in

our country to get some of these priorities on the road.

Dr. Insel: And I might just add that 2 weeks ago or 3 weeks ago, actually in this room, we had a 3-day session with many people from around the world on global mental health issues. Shekhar Saxena, who's the head of this office at WHO, was with us the whole time, and we're now fashioning a series of collaborative efforts with WHO and NIH.

So this will clearly be part of it, and a lot of interest, mostly new interest, at WHO in autism. Geri?

Dr. Dawson: Well, I just wanted to briefly just give a little history of this because this effort really started at Autism Speaks with Andy Shih reaching out to people like Shekhar Saxena and others at the WHO and actually providing hundreds of thousands of dollars to the WHO to support their staff to begin to focus on autism and neurodevelopmental disorders and to include neurodevelopmental disorders and autism in some of their training efforts that are in many places throughout the world.

And so, and Andy, actually, when we see those

countries listed, whether it's Qatar or Bangladesh, literally, he went to every one of those places, talked to every one of those people, and got them onboard to pass this resolution. So I just want to acknowledge kind of all the effort and work that went behind this and Autism Speaks' role in that.

Dr. Insel: Yeah, if I can weigh in, Geri? As a scientist, I used to be very dismissive of this kind of stuff because it always just seemed to me like it was a resolution. So what? You had a piece of paper.

Over the last year or so, in meeting with health ministers in Asia, Africa, and parts of Latin America, it's become really clear that they take these as marching orders. So if you ask them why they're not working on X, Y, or Z, they will simply point to the MH gap report from WHO or a resolution like this and say, if we don't get it, we're not going to work on it.

We don't -- we have very limited funds, and we put our funds where we are told we need to spend our money. And so, having this kind of a resolution really does make a difference for

people who establish policy and funding for services especially in the developing world.

So it's much more important than many of us in the U.S. would understand. I think this is great, and actually, I think it's almost unprecedented to get this kind of recognition. We've had this for AIDS, but to have it for autism is really spectacular.

So kudos to Autism Speaks for getting this done. Walter?

Dr. Koroshetz: I just had a question. Geri, if you know, is there a reason why Bangladesh was especially interested? I'm just thinking are there things going on that we don't know about in some of these undeveloped countries that are important to know?

Dr. Dawson: Right. As always is the case, it's always about, you know, a special advocate in that country. And there was -- there is a woman there who is the daughter of -- do you remember the daughter of the princess or what? Anyway, one of -- just a very -- a mover and a shaker in Bangladesh. And she took this on as her own kind of personal effort, and it's a very, very poor

country. And they were able just to do phenomenal things in terms of raising the bar for services for people with autism spectrum disorder. And then they went on to then play a lead role in this effort as well.

And it's been just an amazing story to watch it all unfold.

Dr. Ring: I would just add to that. It really is a very familiar narrative in that almost always begins with a parent or someone who's been personally touched by autism at the ministry level or positioned perfectly to begin championing internally.

But like Geri said, it really takes the hard development work and activity of groups going out there at the grassroots level, finding those individuals and educating them and enabling them with information that helps bolster and support the kinds of efforts that then have to be taken in the next steps.

And I think it's a great tribute to Andy Shih and the many folks that he's worked with around the world in identifying these individuals and helping support them. But I agree with Tom. These

are viewed as marching orders, and something like this is -- the significance of this has been lost here, you know, in the States almost.

But it's still a long road ahead, and there's still a lot we have to do to help support this activity from the States. We're viewed as a leader for the kinds of information that drives this.

Dr. Insel: Anshu?

Dr. Batra: Yeah, I just wanted to applaud this resolution, and really, I have to echo what you said, Rob. I went to Bangalore, India, in December as part of a team of people to be involved in a lecture symposium to educate the medical students in the medical center there, but as well as to see patients, families of individuals with autism.

And it just made me realize and humbled me so much to see families coming from all -- hundreds and thousands of miles away, from rural, rural places in India to -- you know, to try and, you know, find some hope, some answers.

And it just -- it just made me realize it doesn't matter where in the world you are. You're a parent. You have a child who has needs, and you know, you'll do anything possible to help your

child. And again, this, I think, is a wonderful way to, you know, to start that. So --

Dr. Daniels: Well, hopefully, for the next IACC, we might be able to invite Andy to come and give us an update, and we can talk about ways that the IACC might be able to be more engaged in some of this. So, it'll be great. Thank you.

So the last item I wanted to share was just an update on the Co-Occurring Conditions Planning Group of the IACC. There is a workshop that the Planning Group has put together tentatively. It's going to be held on Tuesday, September 23, 2014, in the brand-new Porter Neuroscience Center on NIH's main campus.

The focus on this workshop is going to be on under-recognized co-occurring health conditions in kids and adults and how the IACC can support research and community/provider awareness, as well as foster development of clinical practice guidelines in areas where they may be needed.

And the Planning Group has put together a list of individuals to be invited for these four panels that will be a part of this workshop, and invitations have gone out. And we're waiting to

hear back from people, but we will certainly give you updates. And for the general public, we will put information about this workshop up on our Web site.

So stay tuned, and we look forward to working together, and hopefully, we'll make this a really helpful and productive time for the group to work together on this issue.

Are there any questions or comments about this?

Ms. Redwood: Susan, on our last call, there were a number of people who were recommended in terms of serving and presenting during that workshop. Have we received any confirmations back, or do we have any --

Dr. Daniels: We've received a few confirmations. I'll give you an update later, but they've all been invited.

Ms. Redwood: Okay, great. Thank you.

[Pause]

Dr. Daniels: So, with that, then we're ready to move on to the next section.

Dr. Insel: As we've done in other meetings, I want to just really quickly take you through new

science since April 8th, when we last met. So this is just over 3 months, and it's even still impossible to do justice to the hundreds of publications that have happened within that brief period.

I just wanted to go very quickly through some of the highlights, and again, these are in no way comprehensive or fully inclusive. As we've done in other meetings, I just try to do these by -- organized by the parts of the strategic plan. And for the sake of time, I'm going to do this very quickly today, but we can go into detail more later on any of these if you're interested and make sure you have any of these papers.

On "When should I be concerned," again most of the emphasis here is using the high-risk strategy of looking at baby sibs. We've got the paper that came out in Child Development just a couple of -- just last week, actually, showing that there is this period around 6 months when infant sibs show a delay in grasping skills picked up the Mullen and some motor issues.

Those largely resolve, or you don't see them as much at 12 months as you do at 6 months. But

there is this period around 6 months when those little ones who are destined to have autism at age 3 show the deficits, whereas, other high-risk kids who are not going to go on to develop autism, don't.

Geri here and others have been involved with trying to automate the whole way in which infants can be evaluated very early in development. So this computer vision tools, which Geri could tell us more about, is really a first foray into this idea of using an algorithm and automated techniques that allow you to identify eye tracking and other aspects of joint attention in very young children or infants in a way that would be low cost and potentially easily to -- easy to disseminate.

And finally, the brief report at the bottom in the Journal of Autism and Developmental Disorders is another part of this looking at the high-risk approach in this case at 24 months, showing these sensory processing, especially auditory processing deficits in those high-risk kids who go on to develop autism, relative to the high-risk kids who don't.

Actually, both of those groups have some differences from kids without any genetic risk. So interesting because it's a little more complicated than one might have expected.

But clearly, the story that is evolving and has over the last 3 years in terms of Question 1 is using the high-risk approach to come up with some very precise measures of subtle differences in that first year of life and sometimes in the second year of life that look like they will be predictive of who within the high-risk group is going to go on to develop a diagnosis.

"How can I understand what is happening?" A lot here. I just cut this down to three, but there were -- the staff pulled together many, many more papers than this.

Very quickly, the network inefficiencies idea is again using the high-risk strategy. These are again baby sibs from the ISIS network. And an interesting, maybe even somewhat historic project because it's showing now changes in the efficiency of connectivity, functional connectivity in those kids who, at 24 months, will have a diagnosis at 36.

And again, we've always been trying to pull out within the high-risk kids what are the predictors of the children who will show real downward trajectories? And this looks like a fairly interesting one.

It's subtle, and these network inefficiencies are not localized very much, and these are very general differences in the way that brain areas are connected functionally. But it is, in this case, predictive. So it gives us the beginning of what looks like a biomarker for predicting onset.

Simon Baron-Cohen had a paper out last month that got quite a bit of publicity. It showed up in the New York Times and many other places. It's the first study to look at amniotic fluid from -- in a large population-based study and showing differences in the level of progesterone, testosterone, a couple of other steroid hormones.

It's a little complicated. There's a huge amount of overlap between the kids who go on to develop autism and those who don't. There's like 128 kids with autism, and about 250 or so controls out of a massive population-based study. So it's very carefully selected.

There is a difference when you add everything together, although what it means and how well that would predict any individual's trajectory is pretty unclear. But still, Simon, as you know, has been very interested in why boys are more likely to develop autism than girls. He's had this hyper-male hypothesis, and the presence of elevated steroids in utero is interesting.

Now with respect to understanding that, this is just done in male -- males. He took the female subjects out of the study group for a variety of reasons, but worth looking at and certainly worth trying to replicate in other samples.

And finally, the bottom paper there on the race and ethnicity and nativity question, this is something we've talked about a lot here. Idil has brought this up to us many, many times about the differences in time for diagnosis, the differences in prevalence across racial and ethnic groups.

What this paper adds to other papers that have been done, this is done in L.A. County. So, Anshu, this would be in your neck of the woods. It's worth looking at because one of the things that's useful here is they separate out race and

ethnicity by whether people were born in this country or not. And there's a very striking difference between foreign born and native born in terms of overall rates.

Not so much actually in the time for diagnosis which has shown up in other studies. It doesn't show up so much in L.A. County, but the overall rates, either with or without intellectual deficits, seem to differ based on nativity, not just race and ethnicity. So first really well-done study in that regard.

Cause. We've got a large study out from the CHARGE effort, and again, people around the table have been following this closely. This one is looking specifically at agricultural pesticides, organophosphates, and others. The numbers are actually quite striking.

It's -- you know, these things are always -- when we talked about this before, the issue has always been the actual effect sizes and worrying that the effect sizes are not that great. These effect sizes are actually fairly striking, just to read it out.

Proximity to organophosphates at some point

during gestation was associated with a 60 percent increased risk for ASD. Higher for the third trimester, where the odds ratios went up to 2.0. Children of mothers residing near pyrethroid insecticide applications just prior to conception or during the third trimester were at greater risk for both ASD and developmental disability, with odds ratios ranging from 1.7 to 2.3.

So those are notable odds ratios and something that we do need to look more closely at, need to get additional data on. This is a very carefully done study using the population-based approach, which was kind of interesting, again out of California.

Familial risk of autism, again, an area that we've talked a lot about here. This is, I think, the largest such study done to date. It's again a Swedish population-based study.

Over 2 million Swedish children born between 1982 and 2006. So looking at the overall rates of autism in twin pairs. They had 37,000 twin pairs in this study. So they were able to pull out probably better than any previous study what the relative risks were and do this on a population

risk stratified basis.

The evidence is, again, as it's been for some of the other studies, a little bit equivocal. It's clearly a very much higher rate of autism amongst monozygotic versus dizygotic twins, like a 50-fold difference there. But also a higher rate between dizygotic and siblings, suggesting that — I'm sorry, not a higher rate — suggesting that there's a very big environmental component to this as well.

They end up using a lot of modeling to suggest that heritability of ASD and autistic disorder were estimated to be approximately 50 percent. So that's a bit lower than some previous studies, and it adds to this ongoing debate about whether in a disorder that's this heterogeneous we can really tease apart all the different factors when you look in a population-based survey without knowing more about the subtypes of autism.

But striking that we're able to get now some very good population-based data out of these kind of registries. I think this is a very powerful approach.

And finally, the Nature Genetics paper is just

one of several that are looking at strategies for pulling out the de novo mutations to try to understand whether there is a pattern to make sense of these at a systems level, and in this case, they're using what is called purifying selection. That is, are these mutations that are in areas of the brain that have been selected by evolution, are they highly conserved or not?

And of course, in this case, what they find and what others have reported as well, so this isn't entirely new, is that many of the areas that seem to be most affected are brain expressed and are, indeed, highly conserved. So we all have de novo mutations. The question is why do some de novo mutations seem to be associated with autism and others not?

So this one study continues this general approach to trying to make sense of the de novo mutations that seems to be associated with autism, whether they tell a story based on evolution or based on functional significance that could ultimately lead us towards targets for drug development.

Speaking of drug development, "Which

treatments and interventions will help?" This is still an area that's a bit of a challenge, I think, for the whole field, and we'll say little bit more about this later in the day, I think.

But we still don't have the tools we need to do the kinds of clinical trials we'd like. Pulled out a couple of papers here that just suggest some sort of surprising ways forward. One, the first one on corticosteroid therapy in regressive autism I note not because this treatment looks like its got particular promise, but because of the way the study was done, which was to build in biomarkers to look for very early changes, in this case in this thing called the frequency modulated auditory evoked response.

So they look at this very early on within the protocol and then use that as a kind of surrogate marker for improvement. And in fact, the claim, whether it replicates or not, is that this auditory evoked response change that occurs during treatment is predictive of outcomes much later in the course of treatment.

So I think it's -- as an approach, it's one of the things that we're hearing a lot from people

who do R&D for treatments that if we're going to make progress in this field, we've got to have some early readouts. We can't wait 6 months or 12 months to know whether the experimental intervention is helping. We need to know something at the end of 3 weeks or 6 weeks, and this actually is a strategy for doing that. Whether it will replicate or not, we need to see.

Another point to make here is that we've before, and it's in the strategic plan, about the need for RCTs to get beyond just the anecdotal reports, particularly with behavioral interventions or other kinds of interventions. And both of these from Connie Kasari are examples of RCTs.

And the one that may be most noticeable is the bottom one of using caregiver-mediated interventions. So in populations where there is not access or where there is very limited access to a team or to an intervention that you know will work, this is a way of training caregivers to do much of the work.

And it shows a fairly significant effect. Both groups improve, but there's greater improvement in

the group which receives this caregiver-mediated help.

Services. Again, this is an area that seems to be building in a lot of ways. I won't go through all of this in detail, but I have to mention David Mandell's paper because it's an attempt to, again, update us on the numbers. We've talked about the cost of autism various times here at the meeting. What David's new paper does is a kind of -- it's a review of work from both the U.S. and the U.K.

The numbers for supporting an individual with ASD and intellectual disability during his or her lifespan, $2.4 million in the U.S., 1.5 million pounds, which at the current exchange rate is about $2.4 million, $2.2 million in the U.K. An individual without intellectual disability, but with ASD is a little bit lower, $1.4 million in the U.S., and $1.4 million in the U.K. would be the equivalent.

So you start to multiply those numbers by the new prevalence numbers, and that looks like real dollars pretty quickly. So I think this is a useful and important update. As we talk about issues around cost of autism, we've got these very

carefully defined numbers from David and his team.

The last two questions, just so we don't fall too far behind on time, just mention very quickly, as we've seen in other areas, good evidence now for the business case for supported employment for adults with autism.

We've known this for a number of developmental disabilities, as well as for serious mental illness. There's really no better investment you can make than to get people back to work or get them working through supported employment. They come off of SSI, and they actually make income rather than costing income.

And this autism paper from -- at the top here from April is a good example of making the case for adults with autism and showing why this is such a good investment.

Cathy Lord and collaborators have a paper, which I think we're going to have to talk about at the September 23rd meeting, about the difficulty in assessing depression in adolescents and adults with autism spectrum disorder. It's a very thoughtful paper, struggling with how do we do this? We don't have good measures.

If we're looking at depression, the sense is this is a -- there's a very high prevalence here, which shows up with some hopelessness and helplessness. But it's very difficult to have that show up in many of the rating scales that we use for people who are not autistic, and so they call for thinking this through at a much deeper level.

And finally, just to finish on the surveillance needs, first really thorough paper on the question about reproductive stoppage shows that for families that have a child with autism, they are more likely to not have a second or third or fourth child after their autistic child is born. It's not consistent, but about 50 percent reduction in reproduction after having a child with autism, which is very substantial.

And I mentioned the last piece here in Molecular Psychiatry, which is just out online, because it's the ABIDE study, which ABIDE stands for Autism Brain Imaging Data Exchange. We've talked about the importance of data sharing and the way that's been done very successfully in genomics. What's exciting here is that the same thing is happening in a big way in neuroimaging.

We'll hear more about this in a moment from David Amaral.

But the ABIDE study is 17 different institutions sharing over 1,000 -- 1,100 brain images. And one might have thought that that was pointless because it was too difficult to put the data together from different sites and make sense of it.

But it turns out that actually it works, and not only does it work to be able to get everybody sharing data and sharing protocols, but in this case actually gives us some new insights. They went after in this paper, just as a test, a sort of proof of principle, whether they could use this very large dataset to answer questions about brain connectivity, a little bit like that first study I talked about from the ISIS network at 24 months. This is now in older kids.

But they were able to show that there's really good evidence for both hypoconnectivity and hyperconnectivity, depending on the area. And they had enough subjects here with some 570 or so kids with autism or young adults with autism that they were able to even develop subgroups.

And they're putting this out here now kind of as a foundation, asking other people now to join the effort and to create what will be a national repository for images, which could be available to many people to ask questions that haven't been asked before.

So it's a new way of doing science. It's big science that requires a bit of a change in the culture. But great to see that this is happening for the autism research community, and I think it bodes well for rapid progress as we go forward.

So that's a real quick rundown. Again, as I said, it's not comprehensive, and it's not fully satisfying. But wanted you to know that on each of our seven questions, there's lots going on and lots of progress.

Any questions or comments before we move on? John?

Mr. Robison: In your -- in the first study you cited, the clumsiness and grasping problems in at-risk infants. Just to clarify a point of definition there, we call them at-risk infants because at the time the study is published, they have not grown old enough to pass through the

diagnostic window, right?

So we cannot say with certain how much of the population would ultimately be diagnosed. Would that be correct to say?

Dr. Insel: Yeah, thanks for that question. I should have been clearer about that.

I think one thing that has changed in the last year or two is the original studies that we've talked about here of kids at risk that was a concern. They were looking at changes in vocalization, changes in sometimes sensory processing, all of that in younger sibs without knowing which of those younger sibs would be the 20 percent that go on to develop autism.

In the studies that I mentioned today, I pulled those out because those were actually only published after waiting until the children got old enough to make a diagnosis. So they could actually distinguish those amongst the high-risk kids what separated out the 20 percent who would ultimately have a diagnosis from the 80 percent who wouldn't. But everybody had an older sib with autism.

And each of those studies also had controls that had no family history. So you could -- you

had really three groups to compare.

Other questions, comments? Matt?

Dr. Carey: So, again, on the at-risk population, right, one of the next steps will be to try to generalize. I'm just wondering if you can comment on how -- is it just a factor of 20, or is it more to get really good statistics? If you want to generalize and pull in the non -- the non at-risk?

Dr. Insel: So it's a great question. We actually don't know whether the kinds of variables that are being picked up in the at-risk kids could also be predictive of the whole population. And remember, so we're talking about multiplex families, but most cases do not come from multiplex families. So this is potentially an unusual subset.

It's done this way because you can do it, and it's feasible. If you started to look in the entire population, the prevalence is still so low it would be difficult to be able -- you'd need 5 or 10 times the number of subjects. So this gives you that bump.

But it does raise a question about how well

will this generalize to singletons that don't have a brother or sister with autism. Geri?

Dr. Dawson: I was just going to mention that in Europe, there's quite a few studies now that are following infants who are very low birth weight and very pre-term in their delivery. And as another strategy to look at a risk population for autism and doing similar measures to the ones that are being done with the multiplex families here in the U.S.

So it's just another approach.

Dr. Insel: Yeah, the hope here would be that if you could come up with a package that was predictive, that was -- and noninvasive and not particularly expensive or burdensome, then you could take this to a population-based study.

And you know, frankly, based on what we're seeing, I think we're 3 years away from that. I don't think that's so far away. Maybe the data are becoming more and more compelling. Walter?

Dr. Koroshetz: And I think I'd also offer that it depends on the effect size. You know, if you're looking -- if you're finding very small changes in a defined group, when you go out to generalize,

hard to see anything. And also it's not going to be highly specific.

But if you see something that has a big effect size, then it's much easier to go out and see if it's going to hold water.

Dr. Insel: So given that we're already behind on the schedule and we have a lot more to cover, I want to curtail this interesting conversation. Just reassure you this is a very active time, and it will still be active even if we're not meeting as an IACC. There's a lot going on, in -- on the research side.

It's a pleasure to introduce our first speaker, David Amaral, who's coming to us from UC Davis. I think David has been to IACC meetings in the past, and it's been a while. So it's great to have you back.

Because David came so far, we've asked him to give two presentations, not one, and I'll only introduce you once. For those of you who don't know him, David is a world-class neuroanatomist, who before getting into autism was without question probably -- well, was the world's expert on the hippocampus and amygdala in both primate

and non-primate brains.

And about 20 years ago or a little less, began working on autism as he moved to UC Davis from the Salk Institute. And at UC Davis, he's a professor in the Department of Psychiatry and Behavioral Sciences, and he's chair of the Beneto Foundation and founding research director of the UC Davis MIND Institute.

He has championed a huge array of studies on autism over the last 15 years or so, and his work is something we've talked about a lot in this meeting. What I especially appreciate is his rigor, and like a lot of people who trained in neuroanatomy, he only believes it if he really sees it. And he only sees it if it's really there.

So it's great to have you here talking a little bit about something that we can see in terms of neuroimaging. So we've asked him to update us on two issues. One is neuroimaging, and the second is Autism BrainNet.

Dr. David Amaral: Right. Well, thanks very much, Tom.

And good morning, everybody. It's a pleasure to be here.

The first presentation will be on some of our imaging research, and it's actually going to touch on some of the topics that we already heard in terms of what Tom has been giving you an update on.

So what's clear to everybody is that autism is a credibly heterogeneous disorder not only in terms of the severity of the core features, but in the number and type of comorbid symptoms that we see in individuals with autism spectrum disorder. And I think everybody agrees that there's both environmental and genetic factors and that there are probably going to end up being a variety of different types of autism.

And one of the messages that I will try and get across this morning is that looking at the brains of individuals with autism may provide some evidence to define different types of ASD.

So unlike the ABIDE study, many of the previous studies that had used MRI to look at autism were plagued by a number of problems. One was that oftentimes the sample size was very small, dozens instead of hundreds. Oftentimes, the sample was very heterogeneous. Males and females

in an age range that would go from 3 to 30.

Most of the studies previously were cross-sectional, and the vast majority of studies previously focused on older and higher-functioning individuals.

There really is a scarcity of large-scale longitudinal neuroimaging studies of infants at all severity levels of autism spectrum disorder. So that if you do a PubMed search and you just put in the terms "autism" and "MRI," you get 1,433 studies, a bewildering array of studies.

But if you put in "autism" and "infant" and "longitudinal" and "MRI," now you're down to 18. And even those 18 are not truly longitudinal studies on infants at all levels of severity.

So the premise for my presentation this morning and for much of our work is that when you study the brains of young children with ASD using MRI, particularly if you do it longitudinally and you study the trajectory, you'll see different neurophenotypes. And what I mean by different neurophenotypes is that there's different patterns of brain development that will be idiosyncratic for different types of autism spectrum disorder.

So how do we go about this? Well, my colleagues and I at the MIND Institute many, many years ago realized that heterogeneity was really the major problem in understanding autism and in designing clinical trials and everything else. So we developed a program called the Autism Phenome Project.

This started in 2006. It was designed as a large-scale multidisciplinary project that recruited families and children just shortly after they were diagnosed. So children entered this program between 2 and 3 1/2 years of age.

The study was designed to actually try and parse autism spectrum disorder into more homogeneous subtypes. So there were very, very few exclusion characteristics, things like the child may have had some metal implants that wouldn't allow them to go into MRI. But beyond that, there was very, very few exclusionary features.

This study actually has boys and girls included, and we have a smaller group of age-matched typically developing children that serve as controls.

From the start, the study was designed as a

longitudinal study, and so the children have come in now three times annually after the first visit to the MIND Institute. And we take blood samples from the subjects, from their siblings, and from their parents.

This is a very extensive study. The first year, the families actually come to the MIND Institute five times. We have a diagnostic confirmation. We do additional cognitive and behavioral testing. As a medical exam, we do a 3D dysmorphology image. We then do an MRI, which I'm going to talk to you about, and we also gather EEG and ERP data on these children.

So the families really make a commitment to this. But what we find is that the families actually find it enjoyable to have this much interaction with the clinicians and scientists at the MIND Institute.

So just a few facts about the Autism Phenome Project. We've stopped recruiting at the moment, although we hope to begin again. We have 366 families that were involved in the project. We've recruited at the prevalence rate for autism, boys to girls. So more boys, nearly 300 boys and about

70 girls in the study to date.

They're well matched in terms of males and females and in terms of the age of the ASD kids and the TD controls, all about average age of 3 at onset of the study.

We have tried to make this as representative as possible. We're in California so we can have a relatively balanced both race and ethnicity, and we make every effort to recruit broadly.

The kids in the study, this is the autism severity score -- 4 being the cutoff for getting a diagnosis, 10 being the most severe individuals. What you can see is that these kids who are recruited early tend to be more severely affected with autism.

And this is an early measure of their IQ, and while there's a very broad diversity of IQ in this population, the average is in the 60 range. So in the range of intellectual disability.

So the question was if we wanted to actually look at the brains of these very young kids, how were we going to do it? And we initially got permission to -- at least for the kids with autism to do anesthesia. But we did focus groups of the

families and said, you know, how would you feel about having your child anesthetized to have an MRI? And they said, well, we'll do it once, but that's it.

And of course, we had in mind that we would be bringing these families back annually, and so we had to come up with a different method and the method we came up with is doing MRIs at night when the children go through natural sleep.

So the process -- and you know, when we sort of talked to our colleagues in 2006, they said, you can try natural sleep, but we don't think it's going to work. And maybe you'll get 50 percent of kids with autism. The thought was that particularly kids who had severe autism don't sleep at night. We wouldn't be able to keep them asleep in the magnet. But we went ahead anyway.

So what we do is a training procedure where we have a mock scanner. The kids come in. They get habituated to the scanner, and then we send the families home with an MRI practice kit. The scanner is noisy. So we have to provide them with ear protection.

Many of the kids have a sensory tactile

sensitivity. So it takes weeks for the families to actually work to get the earplugs in. But every night what we do is have the families, when the child goes to sleep, put the earplugs in and the earphones on, and then we have a CD of the MRI gradient sounds, and we tell them to play it as loud as you can possibly play it.

And this goes on for 2 weeks, and then they come to the scan. And fortunately -- oh, here's one of our practicing subjects now. And they come to the scan, and what we do is this is our scanner before. It looked sort of scary, but we turned it into a child-friendly environment, cover everything with child-friendly fabrics.

We actually turned the gantry into a queen-sized bed. And if the child comes awake, the mom or dad or both can go onto the standard gantry, read the child a book or show them a video, whatever it takes to get them to go to sleep.

Sometimes if we're lucky, it takes 20 minutes. Sometimes when we're not so lucky, it takes 3 hours. But we've become very, very patient. And eventually, the child will go to sleep.

We then put the child into the head coil,

insert them into the magnet. We have two junior specialists who are with the child for the entire time. The parent can be there as well if they like. And if the child stirs, we immediately take them out. We don't want them to be panicked by the situation.

But we have had enormous success with this procedure because it really is a collaboration between the researchers and the parents. And I want to acknowledge Christine Nordahl here in front and this team of bleary-eyed researchers that, really, they have made it happen. And they're dedicated. And again, like I say, some nights it takes an hour. Some nights it takes 4 hours, but we've been very patient.

And the success has been amazing. So Time 1, we've had 279 children go through the MRI, and 88 percent success rate. And you can see at Time 2 and Time 3, its equivalent success rate. So nearly 90 percent success rates in getting high-quality MRIs from these very young children.

So, of course, this has generated a huge amount of data. I'm just going to -- I'm not going to go into much data because I'm actually more

interested today in telling you about the feasibility of getting data on individuals on the full spectrum of autism spectrum disorder. So I'm just going to use as an example a couple of findings. One is the total brain enlargement finding.

And so, what is the sort of dogma is that individuals with autism have big brains. And so, we've looked at that early on, and it turns out on the left, what you see is this is all the kids with autism in red. The kids that are typically developing in blue. And sure enough, the boys with autism have a larger brain, by about 6 percent if you take all boys with autism together.

Interestingly, in this paper that we published in PNAS a year and a half ago, we didn't see any difference in girls. Now this is a smaller sample, but it actually speaks to an issue that we see happening over and over again, and that is that the neural systems in brains of girls with autism may be -- or the alterations may be different than the neural alterations in the brains of boys with autism.

So, fortunately, Christine Nordahl is going to

be able to recruit a much larger population of girls, and we'll be looking at this more intensively. So we know we need to replicate this with a larger number, but fortunately, she's going to be able to do that now.

But the thing that we noticed early on, these dots are actually the brain sizes of all of the children -- all of the boys now with autism, the red dots, and then boys who have typical development in blue. And what you can see is that there's a huge diversity of brain size.

In fact, there are some boys with autism that seem to have a really large brain, but the vast majority of boys with autism, the brains overlap with those that are typically developing, and you can even have some boys with autism that have a much smaller brain. So we've started to investigate the correlation between brain size and various kinds of things.

The first thing that we looked at is onset status. Do the kids that have the big brains, are they more likely to have early onset, or are they the kids who have a regressive onset?

And we -- we thought when we were starting

this study, we thought, well, it's going to be the kids who have early onset that have the big brains. It turns out we were wrong.

This is a plot again of the boys with autism here. Here is the typically developing boys, and it turns out that the boys that have the early onset form of autism, their brain size actually wasn't different from the typically developing controls. It's the kids who have the regressive form of autism that have the big brains. That was a little surprising to us.

But because this project has all the medical records as well, we were able to actually go back in time and determine when were the brains of these boys who had the regressive form of autism, when did they start deviating from normality? And this is based on head circumference. Of course, we started doing the MRIs when the kids were 24 to 36 months, but we had the head circumference from birth.

And these are the three plots. The blue is the typically developing kids. The dashed lines are the kids with early onset autism, and here's the line of the kids who had the regressive form of

autism. And it turns out that they started having a significant deviation from the controls at 4 to 6 months of life.

So even though their behavioral regression wasn't happening until 18 to 24 months of life, we started seeing biological features that were altered very, very early on, suggesting that there was a process ongoing that only manifested itself in behavioral differences much, much later on.

So the point is that when you look at many, many brains of individuals with autism, there's actually very little difference between autism and typically development, at least in terms of this gross representation of total brain size. But there is a population, 88 percent of kids, actually, who have a regressive onset have brains that are much larger, and you can see that this brain, for example, is 200 cc's larger, nearly 20 percent larger than these two brains that are exactly the same age.

So we also -- at the time we were doing this, we also got interested in the issue of, well, are these kids that have big brains because they're just bigger kids? There is some evidence in the

literature that kids with autism tend to be taller and bigger.

And the short story is that there are some kids in our population of kids with autism that are very -- much larger, much taller, larger than the typically developing kids, again in blue. But it turns out that they're -- on average, there's no difference between ASD kids and typically developing kids in terms of their height.

Moreover, I've color-coded the kids here. The kids who had the really big brains are now shown in green. This is all autism now. The red is the kids who have a typical size brain. And the gray are actually the kids who have a smaller brain than normal.

It's not the kids who have the big brains who are tall. It's actually the kids who have the smaller brains who are tall. So it doesn't seem to be the case that these kids have big brains simply because they're much larger and bigger.

So we think one of these neurophenotypes that I was talking about earlier on, we call it disproportionate megalencephaly, or ASD-DM. This would be a type of autism based on brain size. And

we now formalize it to say ASD-DM is when a child has the brain ratio to height is 1.5 standard deviations above a control mean. So that's our operational definition of this form of neurophenotype.

And when you do that, it turns out that this phenotype accounts for 15 percent of kids with -- of boys with ASD, okay? So the first message is that, yes, some kids have big brains. But it tends to be the boys. It's actually only 15 percent of the boys in this population that we see.

So then we can start asking questions, well, what causes the brain to be bigger? Is it that the cortex is actually thicker, or is there just more of the cortex? And we use a program called Freesurfer to do that.

And the answer is actually very straightforward, that this is a plot of the average cortical thickness. This is all ASD compared to all TD. No difference in cortical thickness, but the surface area, that is how much cortex there is, is much larger.

And even when we break it out so that now we look at ASD-DM separate from all ASD, no cortical

thickness difference. And again, showing that it's surface area really rather than cortical thickness.

This is a really busy slide, but it really answers the question. Is it that the entire brain expands, it's sort of proportionately grown larger, or is there certain regions that are disproportionately larger? And the answer is that it's different regions, certain regions that are disproportionately larger.

And I won't go into the detail of which regions, but at least some of them make sense, regions that we think are associated with social behavior and language and other things like that.

So then, at the same time that we do the structural images -- oh, the video isn't going. Okay. This was actually a nice video that showed pathways and things like that. Imaging it rotating and all kinds of that. Translation problem.

We've looked at the pathways in a different technique of MRI that we do at the same time called DTI tractography, and I won't go into how we do this. Simply to say that it actually is a technique that allows us to define many of the

well-known pathways into the brain and to see whether they are organized similarly in kids with autism versus typically developing controls.

And again, one of the things that we found, work that was done by Ryan Johnson, who's a postdoc in the laboratory, is that the development of these pathways is actually different in boys and girls. And I'd recommend, if you're interested in that, taking a look at this paper because it shows that the trajectory of these fiber pathways in their development is actually quite different.

So if you combine boys and girls together in a study, it's going to complicate things. So we've actually been looking at boys and girls separately, girls with autism versus typically developing girls and boys with autism compared to typically developing boys. And again, the short story is that even in the kids who have a normal-sized brain, some of these pathways are actually altered in their development.

So all of these pathways here, and I'm not going to go into detail what these pathways do, but show irregularities in their organization in boys that have autism. And so, the question is, is

it the same for the kids who have the big brains? And it is. All of these pathways that just regulated into the kids who have autism in the big brains.

But what we find is that there are other pathways that are also affected in the kids or that are additionally affected in the kids with the big brains. So it looks like there is a more extensive disorganization of connectivity in the big brained form of autism than in the form of autism that has normal brain size.

And so, what we're doing at the moment is trying to look at the distribution of the irregularities of these pathways and try to map them on to the clinical features of these children and to determine whether some of these pathway irregularities will lead to other neurophenotypes. That work is in progress.

So just to say we're looking at other brain regions at the same time, and in fact, the strategy for our program is not to look at a single brain region at once, but actually to look at large numbers of brain regions and look at the distribution of changes across many, many brain

regions.

But we had earlier done work on the amygdala. The amygdala is interesting. It's this structure here in red. It's interesting because it's been associated with emotional regulation and in autism with anxiety disorders. And the short story about the amygdala is that we find three neurophenotypes.

Forty percent of boys with ASD have an abnormally rapid growth of the amygdala. In the age range between 3 and 4, it's growing twice as fast as in typically developing kids. We have 20 percent of our population with ASD who have an abnormally slow amygdala growth. It's growing about half as fast during this period. And then, again, 40 percent of boys with autism have amygdalas that are growing at the typical rate.

So the question is does this mean anything? Is this going to turn out that the boys, the 40 percent of boys who have the rapidly growing amygdala are the ones who ultimately end up with a larger amygdala and are more prone to things like anxiety disorders, perhaps seizure disorder?

And we don't know yet because these kids are

still relatively young. But at this point, we'd like to be able to bring them back to do another MRI and to evaluate whether there is an emergence of a distinct pattern of both autistic symptoms as well as comorbid symptoms.

So here are the questions that at this point we're very interested in. Do these early neurophenotypes persist into middle childhood? Do we see that these lead to perturbed brain organization that's going to persist throughout life? Do the early neurophenotypes predict different patterns of autism severity or cognitive function and comorbid syndromes?

And one that I'm actually very interested in and got particularly interested in the last couple of years. Is there a pattern of early brain organization in autism that is associated with optimal outcome? That is the kids who actually ultimately lose the diagnosis or at least have a much reduced severity.

The way that you would answer these questions is to bring the kids back again and reevaluate them. And I think that there's many of the sort of dogmas in the field of autism that are probably,

that probably need reinvestigation through these kinds of longitudinal studies.

So let me just talk again about the total brain size. The field of the view now about total brain size is, I think, best been articulated by Eric Courchesne, and this is from a review paper that Elizabeth Redcay and Eric Courchesne published some years ago. And what it shows is that if this is the normal size of the brain here, these are different studies, each one of these circles here that had populations of people in the study at different ages.

And what the illustration showed was that in the studies that had very young kids, the brain was larger. But then if you looked over time, that the size of the brain relative to normal actually decreased such that if you looked in adults, there was no difference any longer.

And the problem with this is that it seems sort of neurobiologically implausible. What's going to take place to allow a brain that's 10 percent larger here to be normal sized down here? And I think actually this picture of the trajectory of brain size may be an artifact of the

way that these studies are done.

So that, for example, many, many of the kids who are seen in these studies of younger kids have low IQ and more severe autism. Whereas, the vast majority of the people that are involved in these studies have higher IQ because they're compliant. They're the ones who can actually get into the scanner.

So what is needed is for us to be able to image individuals at all severity levels longitudinally to see if a kid has a big brain at 4 years of age, is he going to have a big brain at 10 years of age, or is it going to be smaller?

Our initial data, here is the data from our three time points. Here is the ASD-DM, shows that there is no indication whatsoever that the brain is getting smaller. These kids, if anything, have larger brains compared to typicals than they did at the earliest time point.

So the question is does something happen that they come down to normality, or do they keep having the big brains? So the IACC actually proposed the kind of study I want to do, in 2009, a longitudinal biobehavioral study that would take

the same population of kids and looked throughout life.

But here's where aspiration and pragmatics bumps into each other. We've proposed to do this, and the reviewers came back and said, well, this would be terrific if you could do this kind of study, but you can't do it. You can't get a kid who's 10 years old, whose IQ is 40 who has severe autism in the magnet. You know, unless you anesthetize them, and we've already said we're not going to do that.

And so, my response to the reviewers, which I think are perfectly reasonable, is to say, well, we have to put up or shut up. You know, we either have to be able to show that we could do it or we shouldn't be writing this application.

So we did that. Over the last 6 months, we actually did a pilot study where we brought in 12 of our Autism Phenome Project kids. They're about 9 to 10 years of age.

We brought in six who have an IQ in the normal range, very compliant, verbal. We brought in six who are nonverbal, IQs in the range of 40 to 50. And we tried to set up a procedure to do imaging

with those kids, not asleep any longer because we're not going to be able to get these kids to go to sleep at night, but in an awake scan where they're watching a video.

And I'm just going to give you a couple of examples. This is one of our subjects, a 9-year-old boy has an IQ of 41, fairly severe autism. This is the current testing. We actually had a video of him going through his current behavioral testing, but because of how public this is and because it's actually very difficult to watch this video, I decided not to show it.

He's nonverbal. He engages in self-injurious behavior and aggression to his mom and to the researcher.

What we decided to do was to get behavior analysts to try and study intensively these children, figure out what makes them tick, what are the reinforcements, and use those reinforcements to shape them to their ability to come into the scanner environment, to lay down on the scanner, and ultimately to hold still.

And you know, I guess we were all a little suspicious whether this was going to happen or

this was going to work. But the bottom line is we had two incredible behavior analysts, Audrey Nightlock and Melissa Mello, who spent a huge amount of time interrogating the families. You know, what do these kids love?

For subject NB, his primary motivation was Russian cartoons and pistachios. So using Russian cartoons and pistachios, they were able to train him both -- two times, actually, it took two times in the mock scanner to get him comfortable. But ultimately, on the third try, he came back to the scanning environment, and we were able to get him in.

And it turned out that once he was actually in the tube and watching these Russian cartoons, he loved it. Nobody was bothering him. Nobody was asking him to do anything. All he had to do was stay still and watch the cartoons.

And it turns out here is the MRIs from NB just done actually a few weeks ago. Beautiful MRIs. It took us four tries to get the MRIs, but it's actually doable.

Here's another child, ACL, another boy, IQ around 50. This shows that we have MRIs for this

child when he was 3, 4, 5, and 9. And it turns out, amazingly to ourselves, that all six of the low-functioning kids were able to get into the scanner, and we got high-quality scans from each one of them, six of six.

I don't think we're going to keep up with that record, but it is entirely feasible. So this gives me confidence that we are actually going to be able to do a longitudinal study of individuals at all severity levels of autism, and now these kids are 9 to 11. We'd like to bring the entire APP cohort back to see what's actually happening. Do the kids with the big brains continue to have big brains?

But my aspiration is that for Christine Nordahl to watch these kids. She actually has expertise in aging as well. So she will be able to follow this cohort as they become adolescents and into adulthood, and finally, we'll be able to know what's going on with the brains of individuals with autism through the lifespan.

So I'm just going to acknowledge a few people. First of all, I really want to acknowledge the families that have participated in the Autism

Phenome Project. They're incredible.

You would think they wouldn't come back after everything we put them through, and they love coming back. They actually ask us at the end of a session, you know, what's next? So it's been terrific working with them.

A large number of colleagues at the MIND Institute, particularly Sally Rogers, but a number of others have participated in the Autism Phenome since 2006, and we appreciate. The project is so old that actually some of the junior specialists who started with the imaging are now residents at different hospitals. So they've been around.

Also the financial support. This was bootstrap by the MIND Institute. We got substantial funding from the NIH and NIMH, and many donors have contributed to the Autism Phenome Project, including initial founding grant from the family of Peter Bell.

So, with that, I think I have 33 seconds or, no, I'm 33 seconds over. But I was close. So I'll stop with that presentation.

Thank you.

[Applause]

Dr. Insel: Thank you, David.

Since we're a little bit over time, if it's okay with the Committee, maybe we can go on to the second presentation, and then we'll have time for a full discussion of both of them.

Dr. Amaral: Sure.

Dr. Insel: The next one, which is highly related to the one you've just done, is about Autism BrainNet, and that's with Alison Singer as well. So why don't we launch into that, and then we'll have some time for group discussion.

Dr. Amaral: Okay. Okay, well, thanks, Tom.

And I'm going to -- I'm going to just say a few words, and then we'll have Alison come up and give the bulk of the presentation.

So I want to tell you about a new collaboration called Autism BrainNet. This is a collaboration between the Simons Foundation, Autism Speaks, and the Autism Science Foundation, and it speaks to the issue that we need to go deeper than MRI in order to understand the neurobiology of autism.

So I've just spent a half an hour telling you that MRI is valuable, and I think it is valuable.

It actually gives you the big picture. It's the 30,000-foot view of the brain, and I think what it will tell us is what parts of the brain are particularly important to look at in more detail.

But ultimately, each voxel of the MRI has 50,000 neurons in it and hundreds of millions of synapses. So if we're ultimately interested in looking at -- and the MRI has, you know, limitations. So if you could have a person or something in the imager for 30 hours, you might actually be able to increase the resolution substantially.

But given that we're already working with children who are squirming and stuff like that, we're not going to be able to do better with the MRI. So the issue is that we really do need to develop a substrate of postmortem brain donations to look at the cellular architecture of the brain.

And I'm sure you're all aware that this period of time between birth and the first few years of life is a period of time when the brain goes through these incredible maturational processes.

Neurons mature, synapses are formed, connections are formed, and we think, ultimately,

that there's going to be something in this process or many things in this process that leads to the disturbances that are associated with autism. But frankly, there just aren't enough brains available to do the kinds of sophisticated science that is -- that can be done.

This is a bottleneck. And in order to understand the neuropathology, but even the genetics -- as Tom was saying, some of the best genetics now is coming from tissue samples of brain tissue -- and well as the neurochemistry of autism that might actually lead to pharmaceutical therapeutics, we're going to need to have postmortem brain material.

So from what I've already said about MRI, some of the features that we need if we're going to get adequate postmortem brain material is would be not just a couple of brains, but a large number of clinically and genetically well-characterized brains for analysis. We're also going to need appropriate control brains for comparison and well-organized cohorts to optimize research replication and complementarity. I'll say more about this in a moment.

In consultation with many, many people, many people in this room, we decided that the best way to approach this was to develop a regional approach where centers around the country and, hopefully, eventually around the world could reach out to their local communities, make them aware of the need for donated brains. And then actually enhance the quality of the donated brain by decreasing the amount of time between when somebody decides to make a donation and when the brain is acquired.

Maybe some of you don't know that the quality of brain tissue for science depends on what's called the postmortem interval, the time between death and when the brain can actually be prepared. If that is short, the tissue is actually optimal for doing research. If it's long, the possibilities for doing research start decreasing.

So what we've established, again with funding through the Simons Foundation and Autism Speaks, is a network. This is really the founding network. It was established this year. We have four sites in Sacramento, Dallas, Boston, and New York.

We have four directors, all who are familiar

with autism research or who have substantial expertise in neuropathology. So Cyndi Schumann, a colleague of mine who is the director of the BEARS, Brain Endowment for Autism Research Science, at the MIND Institute. Carol Tamminga is at UT Southwestern. Matt Anderson is at Beth Israel Hospital, and Patrick Hof is at the Icahn Medical Center.

We actually have just included our first international site in the Oxford Brain Bank, which is one of four brain banks in the U.K., run now by Olaf Ansorge has agreed to join Autism BrainNet. One of the advantages of this brain bank is that it's the brain bank designated in the U.K. to acquire control brains for the entire country.

And so, we hope that Olaf will help us not only in collecting autism brains, but in control brains as well.

So where this stands at the moment is that these four nodes, five nodes now are established. We've created a Web site at AutismBrainNet.org, and it has a lot of detail about the organization. It actually talks a little bit about how this is governed, and I won't go into that now.

I should say, though, the one point that we've been absolutely consistent from the very beginning is that this has to be absolutely transparent. So nobody will have preferential access to these brains. In fact, the node directors don't have preferential access to these brains.

They will have to make an application to Autism BrainNet, which undergoes review by a scientific review committee completely independent from the node directors, who will judge the scientific quality of the application. And only once that's done will tissue that rates highly -- or applications that rate highly get access through the network.

And I want to say something about the development of cohorts. Because this is actually a new strategy for autism research, although the Stanley Foundation has used this for schizophrenia and other psychiatric disorders in the past, and that is at the moment, there are -- let's assume that there is this pool of brains. Well, what's been happening is if scientist A or scientist B apply for some brains, scientist A might get bits and pieces of these brains, where scientist B will

get these brains.

And the problem with a disorder so heterogeneous as autism is they may not come to the same conclusions. But it may be that both of their science is good. It's just that there's different things in different brains.

So what we would like to do is approach this in a cohort strategy where we will establish through Autism BrainNet cases and controls, and that tissue will go from this cohort to all investigators. So you might imagine, for example, that an investigator wants DNA. Well, we will, within the Autism BrainNet, produce the DNA and then distribute it to the tens or twenties or thirties of investigators that want DNA. They'll all be starting with the same resource.

We'll be doing the same thing, actually, with tissue sections as well. So the hope is that this will yield much higher level of replication and also complementarity because all of the data will have to come back to Autism BrainNet, and we're committed also to sending all of the data to NDAR as well.

So what would these cohorts look like? Well,

we're still actually taking input on -- you know, the problem is when you create a cohort, it's going to take a little time to create the cohort. And so, investigators want tissue right now, and so they're sort of incompatible processes.

But we're thinking of things like ASD versus age-matched controls, or ASD versus epilepsy versus age-matched controls, or perhaps genetically defined forms of autism like ASD with 16p11.2 deletion and controls. Again, no decisions have been made at this point in time. We want to get more input about that.

So we're not starting from scratch. There aren't very many brains available at this point in time, to be honest. But it's not zero.

And because of the autism tissue program that's been functioning over the last 15 years, there is actually a set of brains. It's a little hard to see this. But this is the age -- these are just hemispheres that are available currently from individuals at these different ages that either are formalin fixed for histology or are frozen for -- for genetic or molecular strategies.

And so, there are brains available that we've

inherited from the Autism Tissue Program, and I should say that Autism Tissue Program has sort of evolved into the Autism BrainNet, is a fully enfranchised partner of Autism BrainNet. Hasn't gone away. It's just reemerged as Autism BrainNet.

And what we're hoping by having the other nodes participate is that almost immediately we'll be having other brains. So this is the number of brains that are available from the MIND Institute. So, again, another eight brains. Still a small number. But we actually haven't yet got this underway in appeal to the community.

The final note that I want to make is that this is a really, really hard topic. This is probably the most difficult topic I've ever had to deal with, when you approach families and say, you know, would you consider making a donation of your child's brain or your relative's brain?

And I just want to say that we've had several experiences at the MIND Institute where the families come back to us after the donation process and they say, you know, this was the most positive aspect of this whole terrible situation. We've had on our Web site, on BEARS, there's a

woman named Valerie Hund whose son was 16, died of a seizure.

She called us and said, "I would like to make a donation." She has been one of our most vocal advocates because she feels that it helped her in her grieving process, that this made actually some sense out of a terrible tragedy.

So what I think we need to do is sort of communicate this message better to the community, and I think that the Autism BrainNet will only be successful if the community is fully engaged. And the thing that I think will be different is that it's going to require a nationwide and maybe a worldwide outreach effort that communicates the message that it takes brains to solve autism.

And I couldn't be more delighted than to have Alison Singer being the one who's shepherding this outreach campaign. So I'm going to have her tell you about what she's done thus far.

Alison?

Ms. Singer: So, as David said, in order to make progress in autism research in terms of diagnostics and treatment, we need to have access to the affected organ. That's how progress is

made. And unfortunately, as he described, there are very few brains that are available for study.

So I think as part of the Autism BrainNet, I really want to thank the Simons Foundation particularly for recognizing that reaching out to families to encourage them to donate tissue was a critically important piece of this project. You know, it's great to have this organized network of nodes that will disseminate brain tissue, but if there isn't any brain tissue, there's not going to be much value to the network. So this is really a critical part.

So when we started thinking about what are the best ways to reach families to encourage them to donate tissue, we started by really surveying the materials that were out there to date. So there were brain networks. There was the ATP. There were other networks, and we looked at their materials.

And most of those materials were focused on the process of research, that we need brain tissue in order to conduct research. And the materials included pictures that a lot of families found a little scary and, to be quite frank, just yucky.

And when we showed them to families, they

physically recoiled from some of these photos of actual brains that were stained blue, videos of the brains being sliced, and it was, again, very much focused on the process of research rather than on what families respond to, which is the outcome of research.

And so, when we looked for something that would be parallel, we thought about organ donation. So organ donation has now become widely accepted. It's a very similar activity in that it starts off from a tragic event where, in the case of child organ donation, a child dies tragically.

But the families have already thought about the idea that if something tragic happens, they would want, as David said, something positive to come out of this tragic situation. And so, we wanted to use that as a parallel when we made our outreach materials for this campaign.

And again, we wanted to focus on the outcome in that we wanted not to show the brains themselves, but we wanted to talk about the value of the research in terms of improving the real lives of individuals with autism.

So this Committee, the IACC, has understood

the need to increase awareness about the need for donation. Since 2009, the very first strategic plan, we've included the objective of having a targeted outreach campaign that spoke specifically to the value of donating tissue for research.

And a few projects have been underway against this objective, but this, I think, is really the first large-scale project. And again, when we began this process, we had done a little bit of focus group research back in 2007 at Autism Speaks for the Autism Tissue Program, and so we started to hear from families that what they wanted to focus on was really the outcome of research.

So we started this project by launching focus groups. I'm not going to get too much into the focus groups, but we did four different groups. We divided the families by age of their child, and then we did one group that's focused specifically on individuals with autism because we're also, in addition to having parents' consent to donate tissue from their children, it's also very important for adults with autism to consent to donate their own tissue. And we realize that their needs and desires might be different.

So we showed -- we started to talk to these families about the outcome of research and what types of materials would they respond to? And after talking about materials that were a little bit gentler and really spoke specifically to the needs of the families, we got some very good response.

What you want to see after focus groups when you're showing families, when you're showing materials is that people will take additional action. That's really the sweet spot. You want to show families the materials, and you want them to do something.

And so, what we saw is that each of these focus groups contained four participants, and we had good response in all of the groups in that most participants said after seeing the materials they would think about the issue. They would go to the Web site. They would Google brain tissue donation.

And we also learned that really our target is in this group the parents of kids who are 11 to 17. What we found in the earlier group was that those parents don't really want to think about

brain tissue donation because they're busy getting their children into school, and this group was a little more focused on their children who were transitioning into the adult world, and so this was really our sweet spot in here.

And here, we had one adult who came to this focus group and basically said there is no circumstance under which I would ever donate tissue. I don't even want to talk about it, who didn't really participate. So this three is really showing that all of the adults did respond well to the idea of tissue donation.

The second piece of research that we started -- that we did before we got underway is we worked with Harris Interactive to do an online survey just to gauge the general sense of what was the baseline level of awareness? So we -- using Harris Interactive as basically an online survey where people sign up, they fill out a long questionnaire about whether they own a cat, what kind of car they drive, do you have a child with autism?

So when people participate in an actual survey, they don't know whether they're going to be getting questions about coffee creamer or their

experience with children with autism. So we had 412 people participate over the course of about a month. These were all parents and individuals -- parents who had children with autism or individuals who identified themselves as themselves having autism.

And what we saw is that about a third of people were aware. So, you know, only one third of people, even given the amount of attention that's been paid to tissue donation, were currently aware that they could donate brain tissue. Only 29 percent realized that they could donate their -- that family members who did not have autism could donate tissue, and fewer knew that they could register to be a tissue donor before their child had an accident or they -- or they died.

And this is really important because, again, when we think about the parallel to organ donation, the reason organ donation works so well and so seamlessly is because people have thought about the idea of donating organs before their child is in the PICU. So this was really the crux of this is that we want people to be thinking about the need for tissue donation, the idea of

donating tissue if something tragic were to happen before they're in that mindset of their child has just had this tragic accident.

Again, in the Harris survey, when we looked at questions of whether people would be willing to consider registering to donate tissue now before their child had an accident, we got some good response. So we had 51 percent of families who said, yes, they would think about the issue and consider registering before their child -- before they reached a time of need.

Thirty-eight percent said that they would consider donating their own tissue or tissue of their child with autism. This was their own tissue or their child with autism, and this was other children. I thought that was kind of interesting. I think what this speaks to is that families realize the value of donating tissue of the affected child, but we also have to talk about affected siblings.

One thing I wanted to point out that I think was quite interesting is we asked some of the participants whether they would consider registering to donate tissue for a consortium

where we talked about the branding of the organizations behind this project. And we said specifically would you consider donating tissue for a group that was overseen by a consortium of the Simons Foundation, the MIND Institute, Autism Speaks, and the Autism Science Foundation, and several major U.S. universities? And the willingness to donate tissue went up.

So I think there are two interesting ideas there. One is that there's the power of branding that people feel confident knowing that the tissue would be used wisely. And secondly, I think another possibility is that this community has been so fractious on so many issues that I think when families saw that all of these organizations agreed on the need for tissue, that that lent them some additional comfort that this was necessary and that the tissue would be used wisely.

So this was the key question from my point of view. We asked people who participated why they would or wouldn't be willing to register to donate tissue. And here, 55 percent of the people we asked said, yes, they would be willing to donate tissue. And their primary reason was to help other

children.

Okay, and the second reason was to support research. But this is really, again, parents are not focused on research, per se, but on the outcome of research and on its potential to really make a difference in changing people's lives. And so, that's where we needed to target the message of the outreach campaign.

Of those who said they were undecided about whether they would donate tissue, this is also good news. A third of them said it was because they just were completely unaware that you could. So, again, that is a group that with good outreach materials, we could potentially convince to donate tissue.

And about a quarter of those respondents said they just haven't had time to think about it. They would need more information. So, again, the top two categories are, I think, groups that with good outreach materials we can try to convince.

There was about 18 to 30 percent who said they're just completely unwilling. They don't really want to think about it. Twenty-eight percent of them said it's just highly unethical to

even consider donating tissue. They would not donate organs. They would not donate tissue. Now I think this is a group that we will not convince.

And then we had about 22 percent of the respondents who said I don't want to think about this. I don't want to think about my child dying, and I really need to think about getting him into EI. So, you know, again, I think the parents of the youngest children are so overwhelmed by the process that they're not really receptive to the idea of donating tissue, and this is the group that says just, yuck, get away from me.

So that's not really very easy to see. So taking all of this data, we created a campaign that really tried to approach the concept of a very difficult, often morbid topic with humor and really tried to take advantage of what we had learned from the data we had collected.

And we came up with this "It takes brains to solve autism," which is a nice double entendre. It takes smarts to solve autism, and it takes physical brains to solve autism. And the idea behind this concept is that families who are raising children with autism are heroic in their

everyday activities and in their continued quest to do everything possible to help their children.

But that families who take the extra step and register to donate tissue are superheroes. And so, we're positioning this family that you see in the ad. This is the Matthews family, Christine Matthews is our spokes-model. This is her adorable son Casey, who is 16 and is diagnosed with autism. He is the sweetest, loveliest young man you would ever meet.

And they are our superhero family, and they have all registered to donate tissue. And we hope that other families will listen to what the Matthews family has to say. They speak a lot about why they want to donate tissue on the Web site and a video that you can go to, TakesBrains.org, and watch and listen to why they felt it was important for them to donate tissue.

Why if something tragic ever happened to one of their children, they would want other families to benefit. And not just one family, the way organ donation would benefit one child -- one kidney, one child -- but that research has the potential to benefit thousands of families.

And so, in addition to the print ad, which you will start to see. We just released this in May. So you'll start to see it in Autism Spectrum News and in some of the university quarterly journals. We also launched this Web site, TakesBrains.org.

Again, we tried to be very -- it's not a deep Web site. We have a lot of great information, but we really tried to just stick to the three key buckets, answering families' questions and individuals with autism's questions about the nuts and bolts of registering, and what happens to my tissue?

What happens to my child's body? Things like that. What are the religious questions? So these are the questions. And as families go on the Web site and look at the questions, the answers come up underneath.

The second bucket was really to try to focus on the outcome of research. Again, families spoke very specifically about their need to understand what is the valued outcome of the research that uses tissue. So, in this area, we'll focus on the valued outcome, how families have been helped by this research. And then here we have our sign-up

page.

And again, the important thing to remember for families is that when you register to donate tissue, you're not making a commitment at that time. Okay. You're not -- I'm a registrant. I'm not committed now to donate my daughter's tissue.

If my daughter were to tragically have some accident, I would need to give consent at that time. So the registration really means I've thought about this, and I'm making a commitment that this is an important thing to think about and to move forward with if a tragedy should occur.

So we've already been out and about at many of the Autism Speaks walks, talking to families, registering them. I think we've registered over 300 families already at just two walks to donate tissue.

When you talk to families about this and you talk about the need for tissue in terms of moving the research forward and that lack of tissue is one of the greatest -- great limiting factors in autism research, they really do respond. But it does take having that conversation and approaching it in a family-friendly -- family-friendly way and

an understanding of what the family's goals are.

So I hope everyone who is watching at home and everyone who is here will take a moment to go to TakesBrains.org and to register to donate tissue. It literally takes 5 minutes. There are only five fields because, again, you're not actually consenting to donate tissue. What you're doing is reaffirming that this is something you've thought about and this is something that you want to make a priority in terms of your family's commitment to research.

So, again, I want to thank the Simons Foundation. They are one of the partners in Autism BrainNet, but they specifically sponsored the outreach component. It's been wonderful to work with them, particularly Jerry Fischbach at the Simons Foundation.

So I will leave it at that, and if there are questions, I hope David will join me up here to answer questions about Autism BrainNet and TakesBrains.org.

[Applause]

Dr. Insel: Thanks to both of you.

We're a little bit over time, but let's take a

few minutes for questions or comments. John?

Mr. Robison: I'd like to thank both of you for your efforts, and I actually have a comment that relates to both your presentations, David.

One of the things you spoke about was brain imaging studies of optimal outcomes, and what wasn't really made clear, but I think is true, is that optimal outcomes are really observed in adults who go out and make their way successfully in life and turn autism to either be an advantage or they minimize its disability, depending on what aspect we consider. That would be, I think, the universally agreed optimal outcome.

And that says that you need to be doing MRI studies of adults to find that, but you've made clear that MRI has its resolution limits. And therefore, that same optimal outcome research has to be done on adults.

And one of the things that is not really coming through in this initiative in what I've heard so far is the -- first of all, the recognition that most of the autism community consists of adult people. And when we talk about families and donations, most of the donors

potentially should be people like me, not people like a 6-year-old son, if I still had a 6-year-old. And I think that we really need to make a stronger effort to get those adult brains.

I think that we need to make an effort to get a spread of brains across the autism spectrum. One of the things that concerns me is that when we look, for example, at how we defined autism 10 years ago, and we look at the samples of brain tissue that would have been donated at that time based on that understanding of autism, we would end up with a set of tissue samples that were disproportionately skewed toward the much more severely impaired end of the spectrum.

And you already spoke at some length about how we are clearly defining several autisms of which that is only one. So I think that we need to really deliver the message that we need tissue samples all across the spectrum, and we really need to be -- to be looking at those optimal outcomes from those tissue samples because I absolutely agree with you. I think that that's -- that's a real question. We don't know why some people score so beautifully on tests, and they

cannot get employed, maintain a family, you know, be independent adults.

I agree. We don't know that. We need to know, and I think that this is a key step, and I think we need to expand the initiative to address it.

Ms. Singer: So, in terms of the outreach, when we started doing the research, we recognized that we needed brains from both children and from adults, but that the message to families who are thinking of donating their child's brain is very different than the message to an individual with autism who is an adult and self-consenting.

The next step of this project, now that we've done the ad and the video for the family, is to do a separate ad specifically for individuals with autism, themselves with autism, featuring an adult with autism, talking about -- we haven't cast it yet -- but the reasons why he or she has registered to donate his or her own brain. And what we heard from the individuals with autism in the focus group was very different than the parents of children 11 to 18.

They were willing to donate and interested in donating their brains because they wanted

scientists to think that they were unique and different, and they wanted people to learn about why they were different and what made them unique. So that will be the focus of that new ad. It won't be the superheroes. It will be you should think about donating your brain because scientists think they're really unique and cool.

So that is the next step. We absolutely recognize that that is a key constituency, and we're moving there.

Mr. Robison: Yeah, I just think that we need to speak for our own community as autistic people, just as when I look at -- when I look at other diseases, for example, that affect certain ethnic groups, and the people who speak on behalf of that research are members of the affected group, and I think it's great.

Ms. Singer: Absolutely. The Matthews are a real family, and we looked at many real families. And for the ad for adults, it will be an adult who is diagnosed with autism talking about why he or she thinks it's important to register to donate.

Mr. Robison: And you've raised a good point, too, you know, that we have -- yeah, we want to

show the world maybe why we're special, but we also -- I think we need to be realistic and recognize that we have specific medical problems associated with autism. We have challenges in daily life, and I think we want to be seen as special. We wanted to be respected and accepted, but we want help solving those problems.

And this is a pathway to achieve that goal, and I feel very strongly that our community needs younger adults, older adults. We need to speak for ourselves in this matter. I think it's very, very important. And I absolutely support what you're doing. I just would add to that that we need to be our primary speakers.

Dr. Insel: Thanks, John.

Lyn, you had your hand up?

Dr. Amaral: Can I, Tom, just make one comment to what John said? Sorry. Because I agree with you that what we need to be doing is recruiting and then looking at the brains at all ages, at all severity levels.

I think that there's actually different scientific questions that are most germane to different populations. So at least in my own view

as a neuroscientist, looking at the youngest brains, either with imaging or postmortem, is probably going to get you closer to understanding what is the etiology, what's the neuropathology that might lead to autism spectrum disorder.

Whereas, looking at older brains and individuals who have optimal outcome, now you're actually starting to deal with issues like what is the compensation? What's the reorganization? What's the plasticity that leads, as you say, to individuals going on to having a high-quality life?

I think that they're slightly different questions, both extremely interesting. In fact, I'm getting much more interested in the issue of plasticity and compensation.

So I do think that this initiative needs to reach out to all portions of the community -- parents of individuals who are low-functioning, but also people on the spectrum. And you know, we're a new effort, and we really welcome -- I think Alison and I both really welcome input from the community about how we can get this message.

The message is not going to be scientists

talking to scientists. We've already agreed on that. It's going to be family members. It's going to be self-advocates bringing the message. And we see this as, you know, the community being the ambassadors about the need.

You know, in the State of California, we've estimated that every year there's 50 individuals on the autism spectrum that pass away. Yet the number of those brains that are coming into research are minimal, right? And I think the reason for that is because people simply don't know of the dire need, the real bottleneck.

You know, we're stymied in doing research. And this is why I'm so delighted that Alison has developed this campaign, and you know, we'll continue working together for the next many years to refine the message, to broaden the message, and to hopefully make people feel comfortable with the possibility of making a donation if circumstances require.

Dr. Insel: So we're way beyond time, and there are lots of hands up. I also want to point out that Tiffany Farchione and Jim Ball are both on the phone. We couldn't get their audio before, but

we can now. So they may have questions as well.

Let's quickly go around, and we'll just try to make these much briefer. Lyn?

Ms. Redwood: Real quick. I have a comment for Alison and a question for David.

Alison, I worked a few years ago at the Autism Research Institute and the Maryland Brain and Tissue Bank to try and increase donation. And one of the avenues that we took was to reach out to medical examiners. And you know, you're saying that of the 50 that die, you may get one. The medical examiners are in a perfect position, so increasing awareness with that group.

Many of the children who die accidental, they're going to have autopsies already. They're in a perfect position to be able to ask the families about donating brain tissue, and many of them were not aware.

The other obstacle we ran into is they did not have freezers. So the Autism Research Institute actually was purchasing freezers into go into these areas so the ones that had agreed to obtain tissue, the only thing they needed to do was alter their intake questionnaires to ask the question

whether or not the child had been diagnosed with an autism spectrum disorder.

Along those same lines, we found that you need to be very careful with the control brains in that autism is a spectrum of disability. In some of the studies, the control brains were actually children that had ADD, ADHD, developmental language delays. In one study, there was a control brain from a 13-year-old that had committed suicide. So we need to be very careful with what we specify as a control brain.

So I just wanted to offer those caveats to don't forget the medical examiners. The Autism Research Institute has wonderful posters, very colorful, that we mailed out to the medical examiners, but there needs to be follow-up.

I actually went in person and met with the medical examiner in the State of Georgia, and he was very receptive. Having a family person go to talk to them about this need also was something that really motivated them.

David, a quick question regarding the brain overgrowth you're seeing at 4 to 6 months. I was following some of Martha Herbert's work, and she

was finding those exact same findings in the 4- to 6-month-old and that those abnormalities in the growth seemed to be driven by the white matter increase in the brains. And she saw that exact same pattern in children with developmental language delays.

So I was wondering if you could expand a little bit more in terms of what might be driving that overgrowth at 4 to 6 months and what your thoughts are on that?

Dr. Amaral: Yes, so we don't actually do the MRIs at the 4 to 6 months. That's just based on head circumference. We have a little bit of data, although it's only on 55 kids in an infant sibling study and where we also saw brain overgrowth. And that study, which again is more limited, it's not -- the increase was not limited to white matter. It was actually gray matter and white matter.

What causes that, I think we have absolutely no idea. And I think this is actually one of the huge unanswered questions. For those kids who have big brains, what is it?

And again, I don't think MRI is going to answer that question. We actually have to get down

to looking at tissue samples. And that just hasn't been possible without the tissue.

So I think it's a replicated finding. I think we can come up with some subtle differences in terms of I know Martha is focused on white matter. We see it in both gray matter and white matter, as has other groups.

But what's the underlying cause of that, and is it more neurons? Is it more glial cells? Is it inflammation? Is it edema? You know, I think we just don't know at this point.

Dr. Insel: David, before we go on, just a clarification about Lyn's question. You said that the group with the large brains who also were more likely to have the large heads at 4 to 6 months were regressive?

Dr. Amaral: Yes. Yes.

Dr. Insel: So even though you're calling them regressive, there is some abnormality that's being picked up at 6 months of age?

Dr. Amaral: Yeah. So, I mean, and that was the surprise to us. That, you know, at 12 months of age, typically you wouldn't see any behavioral manifestation.

Maybe with some of these newer, more sensitive behavioral assays, but you don't actually see any behavioral alteration until the kids are much older. Yet they're -- and I think head circumference for these very young kids is actually a decent proxy for brain size.

We also have some other additional data that there are some kids that have increased extra-axial fluid, the fluid between the brain and the head. So it's not a perfect proxy, but it's close.

But you're absolutely right. I mean, 88 percent of the kids that had a -- 88 percent of the kids with the big brains had a regressive onset. So it's much more associated with regression than with early onset.

Dr. Insel: Anshu?

Dr. Batra: Question for both of you. So, Alison, another -- again, you're talking about a very charged, sensitive, emotional sort of issue, which again, you know, you cannot bring up at the time of death.

But again, another avenue to discuss this, I think, would be in the pediatrician's office where, again, just like you know our 'well child

check' that we do, just our guidance that we do for, you know, head injuries and, you know, skin care. I think for targeting the families that, you know, have children with special needs, especially, you know, ASD, I think that would be a dialogue to have at that point and introduce the concept, you know, with the flyers and this and that.

So that, you know, if, unfortunately, that event happens, then at least it's not a new concept, and it's not going to be something that's, you know, just negatively sort of taken.

And I think that it would be something, again, you know, it's an easy enough thing to do, and again, so vitally important. And people just don't think about it because it's just not -- you know, it's just not -- it's so emotionally charged.

David, I had a question about, again, the head circumference. Again, I'm always excited when I hear about some very simple biomarker that I can do in the office that, you know, can help me, you know, determine treatment plans and just, you know, the next steps as well as just looking at risk factors and potentially offsetting some

downstream effects.

So, again, with head circumference, I think that's a very, you know, nice, quick easy way to sort of assess, you know, alterations in development. But, you know, again, I wonder about, you know, just benign macrocephaly, you know? Kids with big heads have parents with big heads and uncles with big heads and grandpas with big heads, and how your findings might correlate with just, you know, that population.

Or the children who have developmental coordination disorders that may also, you know, very often have larger size heads, and you know -- and how, you know, the findings specifically that you're seeing for the ASD population and how that might, you know, correlate with other groups of children with large size heads that may not be ASD in nature.

Dr. Amaral: So I think, unfortunately, it isn't going to be, you know, a biomarker that defines autism. Again, we find the big brains and big heads in 15 percent of boys. I want to try and get that point across that it's actually a minority of boys in our sample that have the big

brains.

We have found that those kids, when we image them at 6 months -- this was a paper that we published in Brain last July -- may also have increased extra-axial fluid, the cerebral spinal fluid between the brain and the dura, and that that actually may be a danger sign as well.

So I think, you know, the practical take-home message is that if you have the child who is infant sibling of a child with autism in your office, and there's rapid head growth, I would monitor that child very, very closely. And we would advocate that it actually might make sense to do an MRI and actually look for this extra-axial fluid.

Although, conversely, we don't actually have anything to offer at this point in time, even if there was extra-axial fluid, other than perhaps getting that child into early intensive behavior therapy as soon as possible. But, you know, I think it can be an adjunct to your clinical judgment, but it's not a biomarker.

Dr. Insel: Last comment. Idil?

Ms. Abdull: Thank you both very much.

I have -- first, I have just a comment for David. I'm glad. I always see everything from a racial point of view as a black person, and so I'm glad that out of your 366 children, that 18 percent I think you said were Hispanic and a little less were African American. And so, I'm glad that researchers and scientists are including children of color, as America is a nation of immigrants and a nation of multi-ethnicity.

And I'm also happy that you've included nonverbal children and older nonverbal children because often that's a population that is missed or put aside because they're not cooperative and they're not compliant. Not because they are low functioning, but maybe because there is a lot of things going on.

So I'm glad that you said either put up or shut up. I like that.

On the head size, I remember my son. I felt like you were talking about me. Because the head was smaller at the beginning, and then around 6 months, it got bigger. And I remember my pediatrician telling me don't worry, he'll grow into it. And I remember he told me -- this might

have been maybe when Jamie Foxx was a coming up star.

And he said Jamie Foxx did an interview where he said he had a big head, and he'd grow into it. And so, your son is going to be an Academy Award winner. And I was like, oh, it's not autism. He's going to be an actor.

So that might be something for pediatricians, I think, like Anshu to watch and see if that's happening so then we can get those children into early intensive therapy.

And for Alison, I was just wondering for -- and thank you as well for your presentation. I was wondering if there is a way to make your Web site more culturally and linguistically appropriate, and if there is a way to outreach in communities of color, particularly African Americans and Hispanic Americans, if there is a way that you can do that?

Ms. Singer: Thank you. Do you want to --

So this is a brand-new project, and there is a lot that we know we need to do and want to do. So specifically to Anshu's point and Lyn's point, we absolutely want to reach out to the medical

examiners. We want to get into the pediatricians' offices. We want to create more materials that target under-represented populations, particularly in tissue donation.

So that's all ahead. It's just, you know, we're 6 weeks in. So those are all on our list of to dos.

Dr. Amaral: I just want to comment to your point about working with nonverbal, sort of lower-functioning individuals. And this has been really a wake-up call for me. Because I think the basic scientist or even the clinical scientist who's looking for basic mechanisms will say, you know, there are certain things you just can't do with a subset of the population, right? In fact, that's what the reviewers said. They said this would be great if you could do it, but you can't do it.

And having the behavior analysts work with the families and actually come up with what makes each one of these kids tick, and it was different for every kid. So it's time intensive, labor intensive. And you know, for one girl, we actually had to have her come back four times for the training, and then we had her come back twice for

the imaging.

The imaging, we tried seven tries, and she just wasn't being stable and whatever. We finally -- and the behavior analyst said we're not being productive here. Let's have her come out. Let's have her do her thing.

Her thing was actually rotating around in a chair like this, just going around. That was her reinforcement. She did that for a while. She went back into the scanner, and we got beautiful scans with 20 minutes of her holding still.

So what it says to me is I think it's sort of a -- it's not a cop-out, but it's sort of the kneejerk response that you're just not going to be able to get. NB that I was mentioning, you know, if you watch the behavior assessment when he's frustrated and he's banging his head on the table and he's self-injurious, you say no way are you going to get this child into a scanner, right?

But behavior therapists were -- again, Russian cartoons and pistachios was his thing, and they were able to sort of walk him in. And an experience that wasn't actually traumatic for him. He actually, in the end, enjoyed it.

So I think, number one, to me, you know, we're going to keep pushing the envelope and trying to get the entire spectrum in the scanners and through all the other things we do at the MIND Institute. And number two, it makes me wonder in terms of all of you who are involved in therapeutics, if we could devote as much time and effort as we devoted to these six kids to get them into the scanner for everyday life, you know, what would be the potential there, right?

We're just not tapping that because we don't have the time or the effort or the resources. So that was my other take-home message.

Dr. Insel: Well, this is a great discussion. I let it go on a little longer than we had planned, but I think it's really worth having a chance to talk about some of these issues which, as you said at the beginning, are difficult to really dig into, but absolutely critical.

It's part of our strategic plan. It's something we haven't done well. In addition, some of these suggestions about pediatricians and medical examiners and, in fact, researchers themselves, why aren't we, after collecting all

this other data on all of the subjects that are part of this big strategic plan, why aren't we reaching out to also enlist and get some kind of donor agreement at the same time that we're collecting images and collecting genetics and everything else.

It seems like it's a no-brainer in a sense. We need to start going in that direction. Thanks to both of you—excellent presentations.

We'll take a 10-minute break now and get started again right at 11:30 a.m.

(Whereupon, the Committee members took a brief break starting at 11:20 a.m. and reconvening at 11:31 a.m.)

Dr. Insel: All right. Moving on with the theme of brain donation that seems to be the topic of the morning. I wanted you to hear very briefly about an NIH effort on the same topic, and Michelle Freund from NIMH will take us through that in record time.

Dr. Michelle Freund: Record time, absolutely.

So I first want to thank David and Alison for their great presentations. They have told you why brain donation is important and all of the -- all

of the complicating factors we have to consider when pursuing this endeavor.

I wanted to talk to you today very briefly about an effort that's led by the NIH, and in no way is it conflicting with the effort that they presented today. We like to hope that we'll be working together towards this common goal. And the project that I wanted to tell you about today is called the NIH NeuroBioBank, a platform for postmortem brain research.

Currently, this effort is funded by three ICs at the NIH -- the National Institute of Mental Health, National Institute of Neurological Disorders and Stroke, and the National Institute for Child Health and Development. We had taken a group together to study our efforts at brain banking here at the NIH a couple of years ago, and we realized that by funding independent brain banks through grant mechanisms we perhaps were not utilizing our resources as best as we could.

So through a long effort of seeking information from the community and talking to other folks that are involved in this process, we decided to pursue brain banking through contract

mechanisms. So we put out a request for proposals a year and a half ago, and just starting in September of 2013, we made awards to five individual sites that were previously doing brain banking through grant mechanisms, but now they're funded through a contract.

This allows us to have more control and more involvement with these sites in determining what donors they were seeking and increasing the amount of tissues that they are soliciting. So instead of focusing on one particular brain area like autism or schizophrenia, we're encouraging these sites to solicit donors from a wide range of disorders that are all relevant to the institutes that are putting money into this.

So the NeuroBioBank is a federated brain and tissue repository network that's integrated by a common IT infrastructure, and the Web site is shown here, https://NeuroBioBank.nih.gov. I encourage you all to go take a look. You can browse through and see what we are doing.

These sites are funded, as I said, by NIMH, NINDS, and NICHD. And we have a focus on quality management, sharing, and outreach. So what we are

doing now that these five banks are working together, the PIs or directors of these sites are working very closely together to make sure that they are following common standard operating procedures and methods of tissue collection, as well as characterizing the tissues that they -- that they gather.

So they are very carefully characterizing all of the medical information and phenotypic information they can get from these donors and making that available through the common Web site, where people will then be able to -- researchers will be able to make requests for tissue.

Just a screen shot of the Web page, and there's a link here. I won't bother going into it now. But you can go there, and the first iteration of this Web site we just had up for the public so the public could learn more about why brain donation, ask a lot of the common questions that the directors get. And now we're in the process of actually uploading the information from the independent sites about the tissues that are available.

This is a work in progress. People can now go

and make tissue requests, but they can't actually scan the inventory yet, as that's not fully complete but should be within the next month or so.

Why are we doing this? We're doing this to increase the availability of tissue for really important research, to standardize the quality metrics, and importantly, to return data derived from the banked tissues to a public database. So once a researcher makes a request for tissue, they will also be expected to put their data back into the NeuroBioBank or into another data repository, such as NDAR.

Just briefly outlined here, the NeuroBioBank and the different -- different areas that we're interested in. I have some repetitive slides here. I think it's the same one.

But basically, the brain and tissue repositories communicate with the research community, as well as providing outreach to the community for why brain donation is important. The NeuroBioBank is a site where all of these different folks can come together and get this important information.

Just put here a slide of the governance. So the way it's organized right now, there is an NIH NeuroBioBank team. I've been helped with a great number of colleagues here at NIH, primarily Roger Little, Anna Taylor, and Cathy Ng, in the most recent months of this project.

We've established an ethics and science panel that is advisory to the NeuroBioBank directors. They will be working directly with the directors, rather than with NIH, to make sure that they are all using the state of the art for brain banking and addressing issues, you know, issues about what are the best methodologies, et cetera. And then they will keep us in the loop. We're invited to those meetings, but we're not -- we're not running those meetings.

And then there's a tissue access panel, and that is really comprised of the folks on the NeuroBioBank program team, and we solicit advice from the NeuroBioBank directors. As the Autism BrainNet, the folks who are funded to collect brains still have to apply to get access to the tissues. We keep very close records of what donors they bring in every month.

Every quarter, we have a quarterly progress report. So they're not allowed to just get donors with the money they've been funded through the contract and do research themselves. They have to make a request.

They're also allowed to continue with their own steering committee, advisory to their independent sites. And we really are not involved in that terribly much.

Here is a list of the folks that have been recruited for the inaugural ESP. I think here we have one that was supposed to be -- I didn't update the slide, but we now have a person who Mary has nominated from NAMI. And we've had our first meeting with this group, and another one is planned in the next couple of months.

So, as I said, the researcher site -- this is also not correct because the researcher site is now available. We don't have the complex inventory available yet, but you can go in and make a request for any specific type of tissue that you want, and the five directors of the banks will come back to us and tell us what tissues they have available, and decisions can be made.

The five sites that have been funded to date are the University of Miami, Harvard University, Mount Sinai, UCLA managed through Sepulveda Research Corporation, and the University of Pittsburgh. And we're also in the process of negotiating a sixth award from the second round of funding.

So the PIs of these banks all meet to centralize, standardize their methodology. We will be offering toxicology services so they can all have the brain tissues assessed for different chemicals. And that will be paid for through us rather than through the contracts. And the last proposal was reviewed in April, and we're about to make an award.

So, again, the NeuroBioBank will focus on quality management. All of the tissues that are collected that are paid for under the contract have to have a certain set of characteristics that come with it -- pH, PMI, postmortem interval, RNA integrity numbers. And the reason for doing this is to increase the amount of tissue available to the research community.

Another part of it in the -- each of the

contract sites have a significant amount of their work focused on outreach to these advocacy groups and to the community as a whole. And these currently are geographically distributed.

Many of the banks that are funded have outreach programs. They have connections with medical examiners across the country. So even though the site is located in Miami, Dr. Mash has a wide network where she is able to collect donors from across the country.

And we mentioned in the previous presentation about the importance of the medical examiners. We have a member from NAME on our ESP, and we actually are in the process of writing a white paper to -- a position paper for the medical examiners to bring more of them onboard for this important project.

So these are just a list of a few of the deliverables that are required from the PIs or the brain bank directors. They participate in regularly scheduled PI teleconferences. We have quarterly progress reports where they have to tell us what brains they've collected in that period, as well as any problems they've encountered.

They've had to provide us with a transition plan in case of their funding ending. So they've provided how they will get those brains to the NIH or to another site that would oversee them afterwards, and then boring details like IT security.

But what I wanted to highlight was during these quarterly progress reports, so they've been funded since September, and we received our third quarterly progress report last month. And each of the sites is funded to collect approximately 100 brains per quarter -- per year, and they've all come very close to meeting this milestone already.

So if we were to have more money available, we might be able to increase the numbers of brains collected.

And that's it. This is just a sample of a brochure that we put together. There are a few of them on the back table if you're interested in looking at them. Happy to answer any questions.

Dr. Insel: Okay. Thank you, Michelle. Questions or comments? Again, this is not autism specific. This is across brain donation for Parkinson's, schizophrenia, bipolar, the whole

range.

Sally?

Dr. Burton-Hoyle: I've a question. Are you going to include -- and I guess this is to any of the previous speakers, too, include hospital organizations? So that hospitals know about this process as well.

My brother died 5 years ago from a cardiac event. And I had a brochure in my car -- because I'd been director of the Autism Society of Michigan -- for an autism tissue project. And I remember calling it, and nobody called me back.

And then I, of course, was wild with grief. And the hospital didn't know anything about it. And so, consequently, we just did organ donation and didn't do.

Dr. Freund: So the most important thing from our perspective is the preregistration process. So, of course, having the discussion with your family and being able to have that information readily available in the case of a sudden death. The people at the hospital do not know.

So if that happens, you've already registered with the site, a number of different sites. You

contact them, and they can make the connection with the hospital.

Yes, David?

Dr. Insel: David, can you come to a microphone? Maybe over here.

Dr. Amaral: We have a 24/7 telephone number that you will get a call back if you call in. And we are starting to do communication to hospitals. In fact, when I give presentations in California, the physicians in the audience will say, well, you should come to the trauma unit, or you should come to this unit.

And I think this is one of the things over the next couple of years that we've been talking about. It's all communication. It's getting the word out.

The other point is that it's not getting it out once. I mean, you go to a medical examiner, and you say -- and they'll say, sure, we'd love to help you. But you have to go back, you know, 3 months later and say, remember me? Oh, yeah, we'll help you.

And it's a constant sort of communication process. So I think all of these are really good

ideas, but it's a whole program. I think it's actually acquiring the brains once as a donation is actually the easy part of this. Communicating the need and getting the word out is really going to be the difficult part.

Dr. Koroshetz: David, before you go to the microphone, I wanted to ask a question. So, in trying to get the answers, one could make an argument that what you need to do is to image the autopsied brains before they get dissected out, and so -- because in autopsy condition, I mean, you can get amazing details using the highest field magnet scanning over 12 hours at a time.

So it gives you this amazing ability to look at the brain on the macro scale before you go down to the micro scale. The question is people thinking about this and what --

Dr. Amaral: I can just -- so this is an ongoing debate about whenever you get brain tissue, there's a series of compromises that come in. If you image the brain, you can image the brain for 12 hours and get very nice resolution.

Of course, you know, if the brain is fixed, that's terrific. If it's not fixed, then there's

deterioration of the tissue. So, yeah, it's got to be fixed. And so, this is actually one of the things that we're considering to do sort of in-house.

There's many things that with Autism BrainNet --

Dr. Koroshetz: Don't you fix half?

Dr. Amaral: I'm sorry?

Dr. Koroshetz: You guys are fixing half of the brain?

Dr. Amaral: Yes.

Dr. Koroshetz: So you have half the brain fixed?

Dr. Freund: Yes.

Dr. Amaral: And we're really excited about NeuroBioBank, I should say, because one of the hardest parts of this whole effort -- I think we'll do a good job with getting donations from the autism community. But equally necessary is getting control brains, and I see this is one of many places that we'll be able to collaborate with NeuroBioBank.

Dr. Insel: Lyn?

Ms. Redwood: Speaking of control brains, I had

a question about how are you actually controlling to make sure that the control brains are not -- do not have other underlying medical conditions that would really maybe not make them the best control brains?

Dr. Freund: So each of the sites have very specific protocols for the amount of information. So, you know, when you get a brain that you're not expecting, there's very little information with it. Then they go back and they do their due diligence by going to get as many medical records as possible.

Once they -- you know, I said in the quarterly reports, we have close to 100 brains for most of these sites. We don't have any of those available yet because they're still doing all of the work-up on those tissue.

So getting the medical records, verifying the diagnosis, having the pathology come in. So all of those things are done before that brain is made available for research. And --

Ms. Redwood: And then is that information also made available to the researchers themselves?

Dr. Freund: Absolutely. Absolutely.

Ms. Redwood: Okay, great.

Dr. Freund: They will not be given a brain unless they have all of that information.

Dr. Insel: Okay. Thanks, Michelle.

We wanted you to hear about this. So this is the NIH approach to the same question. It's not yet autism specific, but we think over the next year or so, there will be more of a focus on collecting pediatric, as well as adult autism brains.

We're going to move on to a very different topic, and this is the briefing on the "state of the States" effort, and I'm going to turn this over to John O'Brien to introduce the topic. We're so far behind schedule I'm going to ask you to just forgo lunch a little bit because I think this is so important for you to hear about.

But we can -- we built some buffer into the schedule later. So I think we're okay. John?

Mr. O'Brien: All right. I'm going to just do a brief background on a couple of our efforts as it relates to some of the reports that we've been working on at the direction of the Committee.

One we released almost 4 years ago, which was

the environmental scan of the evidence for ASD services. The other one is this report which was a state of the State review, which was really an inventory of what States were doing as it relates to both service coverage and other types of activities as it relates to both policy and financing of ASD services.

It was not necessarily Medicaid specific. We actually had a much broader review of what States were doing in this particular area.

I'm going to turn this over to Sonya Bowen, who is the project officer for this particular report. She, I think, took the baton from Ellen Blackwell, who did a terrific job in the beginning of this project, which was probably about 3 years ago, Sonya, if my memory serves correctly, in terms of the design and the implementation of the report.

Sonya is with our Division of Long-Term Services and Supports and happy she's here.

Ms. Sonya Bowen: Thank you. I will try to stick to the meat and potatoes of this presentation because of the time.

I'm not going to be talking so much about the

methodology behind the study. That information is available elsewhere, and I'll mention that a little bit later. This is more talking what the report is, what's in it, and how folks could potentially use it.

So this report was finally released in early January of this year.

[Pause]

Ms. Bowen: If I could get some help with -- oh, here we go.

So the study, it was -- first of all, it was funded by NIH, which CMS thanks NIH for the opportunity to do this kind of project. And we contracted in 2009 initially with L&M Policy Research to do the study and basically talk to the 50 States and the District of Columbia, talk to folks at the State level who are involved in the delivery of services.

So that might be your Department of Developmental Disabilities, Education, Vocational Rehab, State Medicaid director, those sorts of agencies that are providing those direct services and supports for individuals with autism spectrum disorder and their families.

And in addition to the funding from NIH, the study was meant to support the 2010-2011 IACC Strategic Plan, those objectives that related to services and supports.

And the idea of this report, it's a very large report. It's over 400 pages, and so what we were attempting to do was with all of the State-specific information, create a document that's easily digestible and try to organize it in a way where people can get the information that they want, whether, you know, they were interested in everything, or there are specific topics that they wanted to look at.

So we were mindful of that, and at the same time, we wanted to develop this comprehensive document because, you know, prior to this, there hasn't been sort of a compendium of information across the States.

So we're trying to broadly target the audience for this report. It has a couple of different purposes and goals, which again I'll get into in a little bit. So, first and foremost, people with ASD and their families, the advocacy community, and then policymakers at the Federal and State

level, as well as the research community.

So in addition to -- so here are the guiding questions, this is about as much as I'll get into methodology, that L&M used in their interviews with State representatives in trying to find out what's available, how is it delivered to people, and where's the funding for these programs because, of course, sustainability is always an important question for funding.

So to get into what each State profile looks like, each profile is about 10 pages. So this slide and the next slide break down how the profile itself for each State is organized. So the first part talks about who -- who they -- who L&M talked to at the State level, how many folks. And then there's the next section that talks about State bills and legislation and insurance regulations which provides a context for the information that comes later on what's available. Kind of the political climate, you know, where States have made progress.

And with the insurance regulations, it gives information on whether the State has an insurance mandate to target autism services or whether

there's, you know, what kind of equity is in the State between mental illness and medical illness. And also just to point out for those who are interested in the insurance mandate information, there is an appendix in the report that lists every State, you know, where they are at the time this report was developed.

And so, that right now this is a static document. The original intent was to create a document that could be updated if funding were available. Right now, that's not a possibility. So the way you could look at this report at this time is kind of like it's a point in time of information, and so it's a starting point.

Regardless of how you want to look at the report or what kind of information you're looking for, it's a starting point of where States have gotten to up to that point in time, which is about 2012. A little bit of information from 2013.

Okay. And then there's a section that talks about -- that's specific to Medicaid home and community-based services. I'm not going to talk that much about the services themselves because John O'Brien is going to talk about that later

this afternoon. But what it outlines with each State is the kind of Medicaid home and community-based services that they have available.

And we decided to go broad, and there's a list of all waivers or all programs that they have that are home and community based. And then we highlight those that are ASD specific or those that target perhaps a broader population, like intellectually disabled, that could potentially serve people with an autism spectrum disorder.

And in the highlights, we talk about all the services that are available, what the target population for that specific waiver or program is, and that's hopefully to help family members and advocates who are trying to -- who are trying to sort through what's available in a State. You know, where can they start? Where can they begin? What's the possibility of receiving services at home or in a community-based setting?

And then there's a highlight of State services and supports, and then there's targeted areas on early intervention, school age children and adults, you know, topic areas that are of -- that receive a lot of attention and resources at the

State level.

And then, the later part of each profile, the States were asked what kind of systems tracking information was available, and just to point out every profile is organized the same, but what information is available really varies based on where the State is in addressing each of these areas. So where there isn't really any information, that is -- that's acknowledged.

So systems tracking, I want to point out real quickly, systems tracking and workforce development and corrections, these three particular areas, the least amount of information is available, which points to the fact that with limited resources, these particular areas you don't see as much trickle down -- trickle down funding available for these resources.

But where there is information, it's very interesting to see what States have been able to do. So, in addition to being able to see kind of across States where there are gaps in data, you can also see where States have been able to make progress.

For transitions and coordination of services,

it looks at two different transition periods from early intervention to school, and then from school age to employment. And it talks about what resources are available, what agencies are involved in those resources. And then the profiles end with talking about any long-term plans that a State may have to expand supports and services for this population.

And then there is also -- there are resources at the end of each profile. Mostly you have links, URL links. So if you're looking for resources or if you're looking for where do we get the information for the report where perhaps you could find more updated information, that's all in the report.

So I was talking a little bit previously about service and support caps. So in putting this report together, and this is from observation, just from looking at all of the information that was there, there's a few service and support gaps that kind of popped out, which I'm sure many of you are already familiar with.

One of which is there is a lack of ASD-specific services for the adult population, and

States struggle with options for individuals who are already on program waiting lists and -- but still need resources and supports. Provider availability and access depending on the State, I mean, I know that's a problem for many States. And then supports for seamless transitions and also best practices across the lifespan, which I know from hearing some of the research this morning there are efforts to try to address that.

And then the last gap that kind of was a red flag for us is the insurance mandate barriers. There may be mandates, but the way they're designed still may create barriers for folks to receive services.

So, you know, with all the different eyes that may be looking at this report, there's a few different ways, these are just some suggestions of how folks might be able to look at the report.

You might be interested in a specific State and what their services and supports are, what the legislative climate is like. You might want to compare States that are similar, whether geographically or by population or politics or, you know, what have you. And then you may want to

look at, compare, you know, what supports and services are available across States to see where some States may be stronger or where other States are making inroads.

And then -- and then also there's an opportunity for States, you know, for States looking at this report to see where there could be improved coordination across the State systems of care. And it also provides an opportunity for States, if they so choose, to -- just to pick up the phone, which a lot of States communicate with each other anyway, and kind of share ideas and see where they could help each other advance the services and supports for the people who live in their State and local communities.

So since this is such a large report, it's not available in print. It is available online on Medicaid.gov. And the link is here.

And so, for people who are -- who don't necessarily want to see -- want the huge 400-plus page file, there are regional -- there are regional, I guess, volumes. I don't know if that's the right word. But there are regional reports that kind of organize the States by -- more so by

U.S. Census, as opposed to the HHS regions because since that probably makes more sense to most people reading the report.

So if you wanted to look at smaller files, those are available upon request. You can contact me to get that -- to get those files.

And if after this -- after today's presentation, if you have any particular questions about the report, you can go to this link. And if you want -- if you want more detailed information about methodology or the data tool, the data collection, the questionnaire that was used in talking with the States and interviewing the States, that's all available in the appendices of the reports.

And also one of the other appendices lists all the different ASD-specific HCBS waivers that are available by State. And also keep in mind when looking at this report and looking at the programs that are in there, that since that time, States could have new programs, additional programs.

So keep that in mind that it's not a be all, end all. It's a starting point for people to find information and resources.

Thank you.

Dr. Insel: Okay. Thank you.

Let's open this up for discussion. Idil?

Ms. Abdull: Thank you very much for presenting this.

I have to tell you. I've read all 400 pages, maybe twice. And I want to see if you can talk about -- and I don't know if people saw this last letter from Cindy Mann -- in particular about the EPSDT benefit. So it says that it is to prevent -- it's for preventive, diagnostic, and treatment of services for low-income families, for low-income children, adolescents, and their families.

And so, if autism is considered to be a medical diagnosis, and a lot of times we can use the EPSDT to diagnose, but not necessarily to treat. Particularly if you need early intensive behavior therapy or early intensive developmental therapy, a lot of States say that they're not able to do it because that's not part of the EPSDT when it was written decades ago.

So what do you -- how can you clarify that, and what can States do so that we are not asking every State to either apply for the 1915(i) or put

a State plan amendment to the Medicaid. Is there a way for children if you're low income, if you're diagnosed with autism, if your doctor prescribes whether it's ABA or another early intensive therapy, then this would pay for it?

Ms. Bowen: That's an excellent question. And actually, one of the afternoon speakers, Melissa Harris, who is the Director of Benefits and Coverage in Medicaid, she is specifically going to be talking about the bulletin that just came out yesterday.

And she'll be calling in. So she's not here now. So if she doesn't address your question, I would encourage you to bring it up again this afternoon.

Mr. O'Brien: I think, for a point of clarification, when we did this report, it really was a snapshot in time. And most of what States were doing at that particular point in time were covering these services through our other types of authorities, our home and community-based service authorities.

Some of them included some of our research and demonstration authority through the 1115 program.

Some of it through some of the ways we can cover additional services through managed care. What this didn't include was the services that are typically included in State plan services because there really wasn't much that we could decipher in the time we did the survey.

So I think what Melissa is going to talk about today is how that memo that you have in your packet actually increases opportunities for States to be able to cover services under our regular State plan authority and not just necessarily through some of the more traditional authorities that this report cover.

Ms. Abdull: Could I -- could I just follow up with that, John? Because you and I have had a lot of conversations about managed care versus fee-for-service Medicaid. Because managed care is usually for lower-income families are automatically given into managed care, which is an insurance company says we're going to manage the care of these children.

And then they negotiate with the State Medicaid agency what rates they're going to pay, what services they're going to cover, so on and so

forth. Whereas, the fee-for-service is usually for children who have disability, such as autism, but then are from higher-income families and then --

Mr. O'Brien: Well, and Idil, I think we've had this conversation.

Ms. Abdull: Yes.

Mr. O'Brien: We can continue to have it.

Ms. Abdull: Yes.

Mr. O'Brien: I think that may be true in Minnesota. That's not necessarily true across the board. Who States put into managed care really varies.

Ms. Abdull: By State. Correct.

Mr. O'Brien: By State. What we're seeing, though, more and more is that States are beginning to include more of the Medicaid population, including the expansion population, in managed care.

So, you know, I realize that there has been issues in Minnesota, and we're still trying to address those issues between managed care and fee-for-service.

Ms. Abdull: Right. So --

Mr. O'Brien: But it's different, depending on

where you're -- where you're at.

Ms. Abdull: No, no, no. No, I understand that, John. I understand that it's different for each State. But what I want to make sure that CMS does is that it doesn't discriminate the haves -- the services and the interventions that the haves versus the have-nots get in Medicaid.

I think it is cruel for low-income families to be discriminated against in Medicaid. So I want to see if I can get some assurance from you or somebody at CMS that irrespective of whether the State puts their low-income kids into managed care, that the services are the same. The rules are the same. The pay rate is the same.

And the reason I say the pay is that if I'm a provider, my job is to stay in business. So if I get Michael Smith with higher fee-for-service from higher income, and if I get Michael Smith from lower income who has managed care, but the rate for managed care is going to pay is maybe $50 for an hour. The fee-for-service is $80. I'm going to take the $80 kid.

And so, I would like a system where CMS says we're going to make sure the quality is the same,

the rate is the same. In other words, that a lot of these insurance companies are blood-sucking companies. I think we all know that.

And so, what they do is they negotiate lower rates for lower-income families who are not always going to complain or not going to sue the State. And so, you know, I just really would like the CMS to make sure equality is the foundation.

Mr. O'Brien: Well, and there are certain rules, statutes and rules that do require that what's being offered on the fee-for-service side is offered as part of managed care. In terms of rates, that's a whole different story.

And you know that is what it is as it relates to managed care. The companies do have the leverage to increase rates for services that they want to promote or to keep rates the same or to, in fact, decrease rates based on a variety of different factors.

So there are some things that we've got in place that are addressing some of your concerns, Idil.

Ms. Abdull: I know. I appreciate it. I thank you. I just -- I really want to just reiterate

that if we're interested as a nation in addressing health disparity in autism children, we have got to make sure that Michael Smith that's low income and Michael Smith that is high-income family are getting equal access at least under Medicaid.

Mr. O'Brien: Well, and I think part of what we're going to talk about this afternoon is that memo --

Ms. Abdull: Is that. Okay.

Mr. O'Brien: -- that's in front of you, which I think is an important memo, and it's important for folks to understand how that's going to increase access to certain services.

Dr. Insel: So we'll table that, and we'll hear more at 3:00 p.m. or so. David?

Dr. Mandell: This is a ton of work. Congratulations on putting something so massive together.

I've not read it as carefully as Idil probably has. But I am very interested, and I have sort of three related questions that I'm wondering if you could touch on? One is are there any models of excellence? Do you learn anything from reading this report about what specific States are doing

that is creative, that we could think about as a model for other States?

Specifically, are there ways that States are leveraging Medicaid dollars, especially in some of these other systems? So in partnership with education or in partnership with early intervention that we could think about expanding.

And is there any thought given to what these findings mean within the context of Medicaid expansion under the Affordable Care Act and what might happen to Medicaid as a payer for autism services under that expansion?

Ms. Bowen: Those are all excellent questions. The focus of this report was more of a compendium. It was not -- it was to gather -- it's truly a resource document. It wasn't meant to evaluate services. It was to get as much information as possible from each State.

It's kind of up to the user of the report of how they want to look at that. You know, you could potentially -- from looking at different States, you could potentially pull some best practices. We're not making that kind of evaluative comment on what's out there.

That's kind of maybe next steps if someone else wanted to take that step. It really is a -- truly a resource document. It kind of helps if you have questions, you can get some information that's available and then kind of decide how you want to move forward with that information.

And this did not -- this specifically did not address Medicaid expansion. The study was prior to that being implemented and wasn't really the focus of this report.

Mr. O'Brien: So, David, to answer the expansion question, which I think is a really good question, I think it's helpful to remind folks that most of the expansion efforts are really for adults that are, you know, above 18 or 21. And so, I think that the real question is for those individuals, what's the benefit package? What makes sense, above and beyond what the State is typically offering?

And most States are usually using their Medicaid program as their basis for offering coverage for the expanded population. But States have the opportunity to do more in those areas, as they do with the regular Medicaid population. So

are there additional services that States should consider, and then what are those services? And then having a conversation with State Medicaid directors about those additional services.

Dr. Insel: Jose, last comment.

Dr. Cordero: Just a quick question. Great that this is a lot of work is being done in terms of the 50 States and D.C. Is there any plan to include the territories like Puerto Rico, Virgin Islands, and others?

Ms. Bowen: At this time, there is not additional funding to update the report, and that is something that we would take into consideration if funding ever became available to look what we could do in that area as well.

Dr. Insel: Okay. Well, thanks very much, Sonya and John. And this is something we've talked about in the past. So it's good to hear the state of the State report. I'm sure there will be questions that will come up later this afternoon in reference to this as well.

We've earned our lunch break. Although we're running quite a bit behind, let's plan to take 45 minutes instead of an hour and reconvene at 1:00

p.m. I think you know there's a cafeteria on this floor just around -- down the hall and around the corner.

And we'll get started with public comment at 1:00 p.m.

(Whereupon, the Committee recessed for lunch at 12:15 p.m. and resumed at 1:00 p.m.)

Dr. Insel: Okay. Let’s reconvene. It’s 1:00 and this will get us back on schedule. It's fine if some of you brought your lunch back to the table and make sure that those members of the Committee who are joining by phone are back on the phone.

[Pause]

For our new members, an important part of each of the meetings is the public comment period. We're going to start that now, and we ask people who are making public comment. I think we have six today. We have 30 minutes set aside. So that's 5 minutes per person. To the extent possible, it's really important if you'll confine your comments to that window of time so that it doesn't put a squeeze on people later.

The first comment is from Wendy Fournier.

[Pause]

Ms. Wendy Fournier: Okay, and my slides? There we go. Thank you.

I'm here today to give you an update on autism and safety, specifically wandering today.

Autism-related wandering has resulted in another 27 fatalities since last year. Based on our data at NAA, there have been at least 67 U.S. deaths since we first brought this issue to IACC back in 2010.

This is a timeline that shows the work that has been done to date on the wandering issue. We've been working on this since 2008. I want to highlight that there is a PSA campaign that's going to be starting very soon. We partnered with the National Center for Missing and Exploited Children, and these will begin airing nationally probably by the end of the month.

I also want to acknowledge the extraordinary work and leadership of Lori McIlwain, co-founder and executive director of NAA. Without her, none of the work on wandering would have ever happened.

I want to go over some trends that we're seeing in wandering. We're starting to see more

cases of bolting. We document bolting cases when it's an individual suddenly becomes overwhelmed or frustrated and quickly leaves their environment, cases similar to Avonte Oquendo that you may have heard about in New York.

We believe that there are probably multiple triggers that can cause a fight or flight response and that research is needed on this topic.

We've also started seeing a greater percentage of cases that involve older kids and adults going missing. These cases don't receive the sense of urgency that cases involving young children do. It's easy to assume that they can take care of themselves, but many function at the level of a young child and are at great risk of harm.

This slide represents a total of about 413 wandering cases that have been reported since 2011. You'll see 2011 on the bottom, working up to 2014, we are half way through the year. That's represented up on the top.

This includes both lethal and nonlethal cases. Children age 10 and under are shown in red. Ages 11 and up are in purple. And you'll note an increase in the percentage of incidents that are

involving older children and adults.

This graph shows cases where individuals did not survive. There's a dramatic shift in the age of those who are dying. In 2011, which is shown at the bottom, it's clear that children 10 and under were at the highest risk of death, and that is no longer the case.

When we combine all of the cases together, both lethal and nonlethal cases, you can see that while fewer young children are dying, the number of deaths in the older group, the older age group is increasing. The blue and red here represent children 10 and under. The red cases were lethal outcomes, and the green and purple show kids ages 11 and up to adulthood, with the purple showing an increase in fatalities within this older age group.

Keep in mind that we're only half way through 2014, and we are working on breaking down this information further. So we should have more information for you.

We know that wandering affects 49 percent of individuals with autism. We now need to ask why. We believe that many incidents could be prevented

by addressing co-occurring medical issues that affect personal safety, specifically communication-related disorders.

This is backed up by the Interactive Autism Network study data on why parents think their children attempt to elope. We believe that many of these cases could be prevented with an effective means of communication.

Approximately 40 percent of people with an ASD are nonverbal. These individuals are not able to ask for help if they become frightened or lost. They're also unable to communicate their wants and needs, which could be triggers for wandering and elopement.

We went to the National Institute on Deafness and Other Communication Disorders Web site. Their strategic plan notes because effective communication is needed to get aid in life-threatening situations, loss of communication can put people at risk for compromised physical safety and survival. We'd really like to see the data on this, and if there is no data, we need to get it.

We also would like to know if there are any autism stakeholders involved in NIDCD workshops or

workgroups. Auditory challenges are one of the most common conditions that we see in individuals with autism, and it's something that NIDCD should be aggressively working on to improve the lives of those who suffer from it and to keep them safe.

Communication is essential for safety, and we believe it is medically necessary for every person unable to effectively communicate to be provided with assistive technology. Many families are unable to afford communication devices and are unable to get them through their school districts or health insurance. Would a hearing-impaired person be denied hearing aids when they could so significantly improve quality of life as well as personal safety?

NAA is working with IAN, the Interactive Autism Network, on a follow-up study to the wandering research that was published in Pediatrics in 2012. We're designing this study to look at auditory sensitivities in relation to elopement and personal safety.

Unfortunately, unlike other hearing disorders, which have specifically designed technology to assist affected individuals, our children's

symptoms are commonly dismissed as part of autism, and no options for relief for this co-occurring medical condition are offered.

I recently had to leave a small family get-together because my 14-year-old daughter couldn't handle all the voices and the noise. She also couldn't stay and enjoy her eighth grade dance with the rest of her classmates. We've been searching for technology to help our kids with sound sensitivities, and we found nothing.

I'm reading from this slide. It is well known that the use of directional acoustic sensing and hearing aids can be a very effective means of reducing the influence of unwanted background and acoustic noise. Where is this for our kids with autism?

In hearing aids, it is highly desirable that the size of the device be cosmetically acceptable.

Dr. Insel: We're going to need to --

Ms. Fournier: I'm almost there.

Dr. Insel: Thank you.

Ms. Fournier: This is what our kids get. So while issues like hearing loss and tinnitus are addressed through advanced technology and medical-

grade devices, our community is left to wear bulky earmuffs from Home Depot designed for construction workers.

It is not acceptable for families to have to create their own makeshift resources as a way to keep their children comfortable and safe. This community needs safe, effective, medical-grade technology that addresses auditory challenges.

We've just begun to look at these possible causes for elopement, but research is clearly needed, and a medical model needs to be established through NIDCD under the advisement of HHS and this committee.

I will leave you with this list of things that we all need to be working on -- research to discover the underlying causes of elopement, establishing a medical model, and data coordination between agencies to collect data on wandering incidents, triggers, and possible root causes that could lead to further research toward prevention of these incidents.

Technology to assist in wandering incidents based on the unique medical needs of our children. We need to keep them safe. We need FDA oversight

on the GPS tracking devices that are popping up and making wild promises. We need AAC devices to be available as medically necessary and covered by insurance companies. No one should be denied a voice.

We need resources for families from their physicians, schools, social workers. We need swimming lessons desperately and hope that these will be covered under ADA Title III. And finally, we need training for caregivers, school administrators, clinicians, law enforcement officers, first responders, CPS workers, policy guidance from the Department of Education, which we have asked for and hope to see soon, to prevent wandering incidents from our schools.

I had to fly through this. Obviously, I have a ton of information for you. I also submitted written comments. I would really appreciate if you would look at it.

Thank you very much.

Dr. Insel: Thank you.

We're going to move on to Eileen Nicole Simon.

Ms. Eileen Nicole Simon: My comments have only to do with brain damage that impairs language

development. Language is the distinguishing feature of the human species. Failure to acquire language is a neurological disability, not just a difference.

A name other than autism should be used to describe children who have trouble learning to speak. Perhaps developmental aphasia?

The cause must be looked for in the brain. Complications at birth are documented in the medical records of many children who have trouble with language development.

My son Conrad had to be resuscitated at birth. Before we had heard of autism, we were worried about the -- his language development and his hearing. An article on asphyxia at birth in the Scientific American appeared shortly after Conrad's diagnosis of autism with pictures of damage in the brain stem auditory pathway.

The auditory pathway, this seemed to explain Conrad's problems with language and his hearing. Conrad died at age 31 in a group home from a prescribed overdose of thorazine, 500 milligrams 3 times per day.

I put up a Web-site in Conrad's memory 14

years ago and immediately received many email messages asking how soon after birth his umbilical cord was clamped. Clearly, it was clamped before he was breathing, and resuscitation efforts seemed interminable before I heard his first weak cry.

Since the mid-1980s, clamping the cord immediately after birth has become a standard protocol whether or not breathing has begun. This is dangerous and now rightfully controversial.

Thank you, Doctors Batra, Crandy, and Guttmacher, for your discussion of my comments in April. Can we discuss this further? There are no health benefits from clamping the umbilical cord.

Thank you.

Dr. Insel: Thank you.

Next person for public comment is James Williams, and I note you have multiple pages. So just hope you can hold this to 5 minutes.

Mr. James Williams: Good afternoon, IACC. Thank you once again for welcoming me to give another public comment.

Today, I come before you to talk about another issue that to me is pertinent related to people with autism, and that is employment. Based on my

experiences and the experiences of people with autism I've met, I have concluded that there are multiple barriers to employment with autism and that these barriers need to be addressed in order for individuals with autism to succeed in the work world.

First thing I think that is important for us to understand is that the world of work and the world of school are two very different environments socially. When I left high school, I discovered that although high school gave me knowledge that helped me in my work, the social skills I needed to survive in the work world were very different than the ones I needed to survive socially with my friends in high school.

But ironically, teachers would often judge my social aptitude based on my social successes with my friends in high school.

Second, there are many indirect workplace requirements that exist in a workplace or career that we don't always talk about when we discuss what is required to start a career. Here are two main examples, sensory requirements and social requirements.

Many careers and many jobs involve working in specific workplaces that have sensory requirements in a social culture. And our academic programs might give a person a degree for a job but doesn't necessarily train them socially to adapt to that culture or tell them, okay, here's what you have to cope with sensory wise in that work environment.

And as a consequence of this gap, I have met many adults with autism who have gone through school, gone through higher education, and then discovered they don't have the social skills or ability to function in the job environment they studied for. In fact, I have met quite a few individuals with autism who actually have to change their career path because they discovered they couldn't function in the sensory or social environment without struggle.

Finally, and this relates back to my comment in April, there are health barriers that can exist to employment. In April, I talked about biomedical struggles, and I've actually met people with autism who have a hard time holding down employment. Because they can get sick so often,

they often find themselves not -- find themselves unable to maintain a job physically. They're just too sick to work.

And oftentimes, we don't always talk about that in discourse regarding employment. We don't always realize that some adults and some people with autism can be too sick to work because of biomedical issues. Because oftentimes when we talk about biomedics, we're talking about it related to children. But children with biomedical issues grow up to become adults with biomedical issues.

Finally, one thing we also need to discuss regarding employment is the difference between employment and living wage employment and also the difference between employment and independence. Employment and independence are two different things.

You can be employed, but not necessarily independent. And sadly, in our economy, we're living in an age when a lot of employment that people with autism are taking is not always living wage employment.

In fact, in many parts of America, you actually can make more money off an SSI or a

disability check than actual employment. In many places, employers will not give a person a living wage. But SSI and disability will.

Therefore, in my opinion, the following questions need to be asked when we talk about employment and autism. How do we find employment that enables a person with autism to live independently? If an individual with autism is pursuing a specific career, how do we prepare them for those social and sensory requirements?

And if welfare in some context provides superior supports to adults with autism and conventional employment, how do we challenge this perverse incentive? How do we teach employers to stop undercutting that market with wages? How do we convince employers to do as Barack Obama said in the current State of the Union, pay their employees more?

The answers to these questions are probably different in different parts of the U.S., but I believe that these are the questions we need to ask ourselves to help people with autism find employment in society. I shall also now close by quoting Rachel Silverman, another self-advocate

with autism, from a portion of a paper that we co-wrote.

"I am perfectly healthy, educated, qualified, and capable of working. My language skills include full fluency in Spanish and intermediate reading proficiency in Russian. I have a master's degree in taxation. I don't need or want a six-figure income, particularly since I am childless and not interested in motherhood. But I know that I don't belong on welfare and that I deserve to be financially self-sufficient."

Thank you.

Dr. Insel: Thank you.

We're going to move on to Tara McMillan.

[Pause]

Ms. Tara McMillan: Good day. My name is Tara McMillan.

The reason why I'm here is because my son has autism. More specifically, he developed encephalitis through a set of vaccinations he received as a baby.

How do I know this? Because my son's medical records tell me that he was injured after every vaccine he received. It was only after I read a

book about one mom's account of mercury poisoning did I think to investigate for myself exactly what happened to my son and how he lost all verbal communication skills.

I went back through my son's records and noticed what no doctor even cared to look at, a pattern of illness after every injection. This showed me that correlation does mean causation.

If you're going to inject your body with heavy metals, animal DNA, and unidentified viruses, something bad will happen. This is not rocket science or anything that requires a Ph.D. It's plain and simple common sense.

The rise of autism continues to skyrocket. Why is this? It doesn't take a meta-analysis to figure it out. Nothing has been done about the use of dangerous vaccines on our perfectly healthy children.

Our babies are born with normal Apgar scores and above average. When they receive their vaccinations, soon after they regress and get sick. By now, I would think someone would come after the leader who is accountable with handcuffs. After all, I think that you have

ignored all the stuff that we are talking about.

As a parent, I feel that you need some time locked away in a jail cell for obstruction of justice. Sorry, I lost my place.

You have not done what you have the power to do. You have not heeded the concerns and pleas of parents. You have not seen what vaccines do to our kids.

Vaccines for what they really are -- you have not seen vaccines for what they really are. They are a train wreck, and our kids are on that train. More kids are being injured every day because people who have the power like you failed to do anything, anything about vaccines, which include the schedule, safety, and surveillance of those who are injured.

There is no path of recourse, no plan of compensation for our injured because vaccine makers are not liable for injury or death. They are free to kill and maim as many as they can without oversight. Doctors ignore parents when children get sick, regress, and become brain injured. We are left dealing with this injury on our own.

There is little, if any, help from doctors. They simply tell us it couldn't possibly be the vaccines. Vaccines do not cause injury or a high fever or even screaming for hours because that's normal.

You may think you are free to do anything you want, but one day you will have to answer for what you have failed to do. If you don't have time in jail, I know it would be a hard thing to live with having injured children with autism on your conscience.

Dr. Insel: Thank you.

[Minor's name withheld]?

[Minor's name withheld]: Hi. My name is -- Hi. My name is [Minor's name withheld], and I am 12 years old. My brother [Minor's name withheld] has autism.

I really don't remember Isaac having autism. I just remember him being like the cutest baby ever, and I remember him -- I remember asking myself why can't my brother talk?

Now that I am older, I understand why. When I finally got that picture in my head, I changed my entire perspective on life. I was only 3 when

Isaac was born. So as I grew older, it was difficult. I remember him banging his head on the wall, screaming, hanging on the stairway ledge, pulling our hair.

In a way, it made us stronger, but sometimes it tore us down in ways that I can't explain. I would cry at night, begging someone to change him and to make it different. But I woke up, and nothing had changed.

My dad is in the Army. So we moved around a lot. I remember telling my new friends that my brother had a condition called autism. They would ask why, and I just couldn't explain it because I didn't know why.

They would say I'm lucky because I'm home-schooled. But I told them over and over again that I would do anything to get away from my home and the chaos that went with it.

As I grew older, I started to understand and go to conferences with my mom. And the doctors there would talk about vaccines, and moms and dads would talk about vaccines and how they hurt their kids. And my mom would talk about it all the time at home.

So I was snooping in my mom's closet, and I found my brother's medical records. And as I was looking, I found -- I found that when my brother was only 17 months old, he had 10 vaccines at once. That, I believe, caused Isaac's autism. I believe vaccines caused my brother's autism.

If you do not believe me, you can look for yourself. I don't know how you sleep at night just thinking about all those kids, not just the autistic, but their siblings. They need your help. I need your help to just look into the vaccines and look and see if they are really the things that are causing autism.

You are just sitting there saying no when there's kids out there that really do need your help. Please just look into the vaccines to see if they are really the reason. Why are you holding back when we need your help?

Are you scared? If vaccines are really harmless, then why don't you look into it if there's nothing wrong? I don't -- I just don't get it. I can't get that into my head when I -- I need your help. Helping my brother, make sure that he's safe.

You don't know how hard it is just making sure my brother is in the same room as I am that he hasn't run away or something like that or that he's safe.

Please just if you won't do it for me or other people, do it for yourself.

Thank you.

Dr. Insel: Thank you.

[Minor's name withheld]?

[Minor's name withheld]: Hi. My name is -- my name is [Minor's name withheld], and my brother had a vaccine reaction when he was 17 months old. I was 6 when it happened. So I don't remember it that well, but it affected my family tremendously.

After 7 months of [Minor's name withheld]'s vaccine reaction, my little sister [Minor's name withheld] was born. And if my mom hadn't stopped the vaccines, shots, after his newborn shots, she would probably have been worse off than Isaac is.

I know after this you will just continue on to the next person, and you won't even think twice about what I'm saying now. And you're going to ignore more and more people as they talk about their real lives because these are real lives. The

things me and countless others are telling you about are real lives. They're not made-up stories. You can't just pass them along.

You need to think about someone other than yourself. You can make a difference by saying a sentence. You can change lives by doing this.

Before my brother's vaccine reaction, he was a normal kid. Afterwards, he lost the ability to nurse. He couldn't even crawl or sit up until he was 2. Now he still can't talk, but he can ask for things by pointing. He taught himself to read.

Before my mom found out about the vaccine reaction, we were constantly eating junk food, and I had psoriasis all over my body from wheat allergies. Now we eat a box of macaroni once a month. We eat salads for lunch. I no longer have an allergic reaction to wheat, and we are a mostly gluten free, organic family.

If my brother never had autism, I wouldn't know half the people I do today. So, in a way, I'm thankful for my brother's autism, but it is not a gift. And I will be glad when I can hear my little brother talk to me like a normal kid.

So please don't just ignore the people talking

to you today and do something about it. My brother is now 8 years old, and he still can't talk.

Thank you.

Dr. Insel: Thank you.

We've got a few minutes for discussion of public comment. We've heard about wandering and as a communication problem about the possibility of auditory pathway damage and even potentially from clamping the cord, issues around employment and in particular the need for both sensory and social transitions, and then from a family that's been struggling with a child who they feel had a vaccine reaction causing autism.

John?

Mr. Robison: I think that having had an exceptional number of young people come here to address us, I think it would be fair for us to answer these last two comments to say that we have invested significant amounts in studies of vaccines, and they have not led to a constructive answer at this point. That doesn't mean that things may not change in the future. But it has not been something that's ignored.

And I would also like to say, because this

regression thing comes up so often as if it is a new topic, that one of the great surprises of my education about autism was reading the original papers of both Dr. Kanner and Dr. Asperger and discovering that both of those doctors described regression in autism and the autism clusters that we talk about as new phenomena today in families 100 years ago. These were families who had reached adulthood in the 1930s.

So I would want the young people who are here to know that we are not ignoring these questions, and I think that I could speak for all of us to say that if we could help young people who cannot speak today to speak, of course we would want to do that. I think that that's a goal any of us could embrace, and for myself, I try and apply my very best thought to how we'll answer this question.

But it is -- it is, unfortunately, not so easy as look at a vaccine and come back with an answer in 5 minutes. It's just not.

Dr. Insel: Idil?

Ms. Abdull: I want to first thank all of the public members that came. It takes a lot of

courage to stand there, especially when you are teenagers and you talk about your brother. And you know, in Minnesota, at least in the Somali community -- and I'm no scientist, so I speak this just as one parent -- when you hear something so often, you think it's true.

So there are so many people that have said it's vaccines, it's vaccines, vaccines. And so many Somalis then didn't vaccinate, but I've seen families whose first child got autism and then said, oh, we're not going to vaccinate the second or the third. And then the second and the third got autism even though they didn't get vaccinated.

So I'm not a scientist, but I don't know if I want to say for sure if you don't vaccinate your children, they're not going to get autism. They are in the Somali community. There are families that have five children, the last four were not vaccinated, and they still have all autism.

So I will leave that to the scientists, and as John has said, there's been a lot of studies. I think maybe what makes parents and siblings mad is the fact that we don't know. So if you don't know what the environmental trigger is, you want to

blame or you want to assume that it's something that you're being repeated so often.

So perhaps if we can figure out what the environmental trigger is and whether it's the pesticides or whether it's something else in the environment that also maybe has some brain or genetic component, I think it might ease all the frustrations that we get from the public comments.

And the other comment I wanted to talk about is the wandering. I think that we have to address somehow. And I know that there has been a bill that was introduced in the Senate by a Senator from New York, Chuck Schumer.

Yes, I think he introduced the bill. It doesn't have a lot of coauthors, but hopefully, somebody in the advocacy level can move that whereby we try to figure out because wandering is dangerous.

I think my son is a bolter. He wanders. And he has one of those devices that track him after I heard it from Wendy, actually, one of the public comments she made. And he's only one of eight in the whole county.

And so, if there is a way to make sure that

these children are safe, and if it's medically necessary, I would really urge parents to get a prescription through your pediatrician. And I know it's tough, but you can fight CMS and you can fight Medicaid and you can fight the insurance company to provide it.

You can even fight the Department of Education to provide it because if the child is not safe, then there's really no point in anything else. You have got to make them pay for it. And sometimes it's a few hundred dollars. So sometimes I would just collect the money, get donations.

But don't leave it just until something happens. Fight, and get the -- call me even. I will personally help you if you are not able to get a GPS tracking service system, even just to train the police in your country. I will personally help you because I've been able to do it in my little county that I live.

I've been able to make this as a political issue. When people want to run for office, we would say are you going to make sure that if you become the governor or if you become the mayor, you're going to train the police force to be

responsible for this, and we put them on the record in Congress. And I think, as parents, we just have to take small leaps in making sure that our children are safe.

And the last one is the employment, and I know this is the last full IACC, but I'm hoping maybe the next cycle we can get people from the Department of Labor and really address the employment. Because these children will become adults, and then what?

If they're not able -- a lot of these people are highly educated. But if there is -- if they're not getting employment because the place is not socially appropriate, or they don't understand the social cues, if the place doesn't have -- my son would be overstimulated here. All these cameras and all these lights, all these people.

And I think the Americans with Disabilities Act would have to come in. Because we want to make sure employers are providing employment to people with autism in an environment that is friendly to their sensory needs and to their social needs.

So I would urge at least, please, Dr. Daniels, the next -- first meeting of the next cycle, we

need to get Department of Labor and make sure that there is training and that there is outreach and there is awareness for employers to make sure that people with autism are employed and that they're not running away because they have social problems or they have sensory needs.

Thank you.

Dr. Insel: Other comments, questions? Lyn?

Ms. Redwood: Hi. I also want to thank everybody who submitted public comments, written public comments and oral public comments. And thank you for coming and giving this committee your advice.

I want to let the public know that I don't sleep at night and that I sincerely, from the bottom of my heart, listen to all of your comments. And it disturbs me that this committee has not been able to provide answers.

And this disease, this disorder, whatever you want to call it, this epidemic is just so overwhelming on so many different levels. I feel that we need something more than an IACC committee that just meets four times a month to address the unmet needs of services and unemployment and also

what's causing this epidemic.

I think all environmental factors need to be studied, whether it's early cord clamping or Tylenol exposure. And vaccines, there should be nothing off the table.

I want people of the public to know that years ago when I first joined this committee, I tried very hard to get vaccines included into the strategic plan as an area of research, and I was successful only to have the Committee come back the next month and vote those initiatives out of the agenda. I do not think we have done due diligence in looking at vaccines and identifying the subset of children that are more vulnerable.

We've done a great job at doing population-based epidemiological studies. But those are not going to detect a subset of the population like the Hannah Polings and children that are more genetically vulnerable to injury. And we really, really need to do that.

I'm sorry. I apologize that I personally feel as though this committee has not been a success in that we have not done our duty to try to get answers for the American public. So, for that, I

apologize.

Dr. Insel: Anshu?

Dr. Batra: Yeah, I'd like to thank everyone who spoke. It's not easy coming up, making the trip, and speaking, no matter how old you are.

You know, as this is our last meeting, you know, I would urge at the next session to, again, have -- since Ms. Simon has repeatedly brought this to our attention in terms of the cord clamping, I think it would be, you know, in our best interests for, you know, the public to have someone from the American Academy of Obstetrics and Gynecology come and just let us know what the procedure is and how things have changed over the last few decades so that we can have a better idea about this particular issue.

And you know, Mr. Williams, you know, thank you for bringing up the employment issue. I mean, it's becoming -- it's such an important issue, as our children are aging into young adults and adults, and as we're getting them ready for life. And I speak for myself as a parent of a 17-year-old who is not going off to college, and we are looking to help him develop work ability skills.

And I so appreciate your insight in terms of the skills you learn in high school are so different from the skills you need out in the real world. And so, thank you.

But you know, I -- again, that's another area I think we have to, you know, as we move on in this committee to really focus on, you know, the transitioning of our young children to adults into the workplace and what the needs are and how we need to focus our energies to help them be successful in that -- in that area.

And again, I think the issues around, you know, the etiology of autism again goes back to really the importance of helping us identify the different subtypes. And because, as Dr. Amaral mentioned, there is not one autism, there is autisms. Many, many, many, I think.

And as a pediatrician, as a mother, I -- you know, I am at a loss when families come to me, asking me what to do because I don't have a lot of tools in my toolbox to help advise them. I am flying by the seat of my pants, and we need to help identify these subtypes so that then we can better tailor the interventions for better

outcome.

And so, a glimmer of hope this morning, Tom, when you mentioned the science update was there is, you know, some nice emerging information on potential biomarkers, looking at, you know, at four for potential identification as well as monitoring therapies. So I know we have a lot more work to do, and so, you know, thank you for coming out and speaking to us and letting us know.

Dr. Insel: Jan?

Ms. Crandy: I wanted to applaud the family that came up here and spoke. And when one of the sisters talked, it definitely made me remember when my daughter was diagnosed and how my other daughter felt. And I'm sure there was lots of resentment growing up and how important family health is and that we really need to be addressing the whole family.

All of my family is -- I would -- not all of them, but half of them work in the field of autism now because autism touched our lives. But I have a daughter that very much resents everything about autism, and now she's just had her first son, and he has signs of autism. And how that just

continues to impact the family and the family health and seeing her struggle with denial now and not wanting that to be part of her family anymore.

So I really hope that we also can look at the family unit as a whole. And good job, girls, on your testimony today.

Thank you.

Dr. Insel: Geri?

Dr. Dawson: Well, I just wanted to commend the National Autism Association for their leadership in the area of wandering and elopement. And Wendy, I thought that was an outstanding presentation, and it just reminds me that, you know, this was an issue that actually Wendy came and presented on here, and the IACC, you know, took action.

We actually have made some progress in this area, and I just think it's so important for the next committee to continue to identify issues like this one and continue to work on this one. In fact, I think Wendy did a beautiful job on that last slide with several kind of multi-pronged approach to addressing wandering that had everything from resources to science to data. And continue to identify some issues like that where

we can see some real successes, put a stake in the ground, you know, make a difference.

So I really hope the next committee just continues to identify some issues like that, that we can make progress on while the science sometimes can be so painstaking and take so long.

Dr. Insel: Other comments? Walter?

Dr. Koroshetz: Yeah, I just had a question in terms of the communication devices. Do they go through FDA approval process if they're medical devices? Do we know? Does the FDA regulate those things?

Dr. Insel: Tiffany, I think, is on the phone. She's our FDA rep.

Dr. Koroshetz: Tiffany, are you on the phone?

[No response]

Dr. Koroshetz: Does anybody else know whether FDA regulates these kind of medical communication devices?

Dr. Tiffany Farchione: Hello?

Dr. Insel: Right. We can hear you. Go ahead.

Dr. Farchione: Oh, okay. Sorry. I've been listening on the Webcast, which has a little bit of a time delay. So sorry about that.

I'm not sure about the communication devices. I'm not sure how -- whether that has been called as medical devices. So that's probably something that (inaudible comment) medical devices. And since I'm on the drug side, I don't actually know a lot about how they define things.

Dr. Insel: So last thing before we tie this up. There were some specific questions from the -- from Wendy about NIDCD and the stakeholder involvement. Judith, any comments about that?

Dr. Cooper: Well, we haven't had many workshops lately within NIDCD that focused on individuals with autism and communication disorders, although we did do and at that point we did have a stakeholder, a parent with a child with autism, when we focused on minimally verbal children with autism. And that sort of started our whole activity of trying to do some initiatives and increase awareness.

But that's really the only workshop we've done in recent memory that's focused on autism.

Dr. Insel: Okay. Unless there's anything else? Lyn?

Ms. Redwood: Tom, I hope with the next IACC

that the services and safety subcommittee will be reestablished, specifically the safety subcommittee because there was a lot of good work that happened when that subcommittee was functional. So I'd love to see that happen again because it is still completely unacceptable that our children are wandering and dying.

Dr. Insel: Well, on behalf of the Committee -- Larry? Go ahead.

Dr. Wexler: Just to comment a little bit on the wandering. My suggestion, if the Committee or the external organizations here are looking for a response from, for instance, the Department of Education, that it not be expressed as an autism problem, but as a child problem, especially in schools.

Because in preschools and early elementary schools, they're children, you know? And they may not have a diagnosis, or they may have a differential diagnosis, or they may have a diagnosis of intellectual disability. But the kid dies just the same.

So to make it a little more universal would probably -- not that I'm lobbying for any of this,

of course. But if you were to make it more universal, you might receive a more positive response because when you narrow the focus, there's always a counter to the narrowed focus, as opposed to from a policy perspective if you're talking about children, you're talking about children.

And it's hard to argue children. So just an observation.

Dr. Insel: Okay. We're going to need to move on because we're going to get behind again on the schedule. I don't want that to happen.

But I do want to thank all of the people not only who gave oral comments today, which can be very intimidating. So I would certainly applaud your bravery. But also we got 50 pages of written comments, which I want to make sure people have taken a look at. And they cover some of the same areas, but also a number of other areas.

And as Geri said, it's often been the public comments which have provided the agenda for this committee, if not in the same meeting, in future meetings going forward, and we will take these all under advisement if, in fact, there is a new

committee with the potential for reauthorization.

Before we go on, we had tabled approval or edits to the minutes from this morning. Can we just take a moment, and if you've had a chance now to look at those, get any comments about them. And if there are none, ask for a motion to accept as is.

Dr. Koroshetz: I make a motion to accept the minutes.

Dr. Insel: Okay. All in favor?

[Show of hands]

Dr. Insel: Any opposed?

[No response]

Dr. Insel: The minutes are accepted, and we will move on to the next session, which has to do with the update on the SUCCESS Project. This is one that you asked to hear about at our last meeting, and we're delighted to have Laura Carpenter from Medical University of South Carolina.

Dr. Carpenter is a graduate in psychology from UCSD, got her Ph.D. in clinical psychology from the State University of New York at Binghamton. Completed her internship and postdoc at the

Medical University of South Carolina, focusing on neuropsychology and ASD.

She's an associate professor of pediatrics in the Division of Developmental and Behavioral Pediatrics at MUSC, and her clinical interests include ASD, neuropsychological assessment, and applied behavioral analysis. Her research focuses on issues related now to the epidemiology of autism, which is the topic that led to this presentation.

Welcome.

Dr. Laura Carpenter: Thank you. So I'm here today to talk about the South Carolina Children's Educational Surveillance Study, or SUCCESS. It's a screening and assessment study aimed at understanding the epidemiology of autism spectrum disorders.

A study like this couldn't be done without a huge team of people, and these are most of my team. Missing two people. We also have a wonderful external steering committee -- Michael Rosanoff from Autism Speaks, Cathy Rice and Marshalyn Yeargin-Allsopp from the CDC. Young-Shin Kim is one of our consultants, and we have many community

partners that you'll be hearing about.

So my research team is very interested in understanding autism spectrum disorder prevalence. And the reason that we're so concerned with understanding prevalence is that understanding prevalence is critical to understanding whether or not we're equipped to help everybody who needs help.

So unless you know how many people are out there that need help and what their characteristics are, you can't begin to equip yourself to provide those services. So we defined prevalence as the total number of people with autism in a population divided by the total population.

But everybody here knows that that number will change dramatically based on how you define ASD, and that's not just how ASD changes based on DSM-4 or DSM-5, but it's also how we as a community are changing how we view ASD symptoms.

And it also changes based on how we look for cases of ASD, so how ASD is measured. And we're very concerned with regardless of what methodology you're using, who's going to be represented in

each study and who's missed?

There are many ways that you can look at prevalence. So you can do surveys where you call people and say how many people in your -- you know, is there anyone in your family who's ever been given an autism spectrum disorder diagnosis? You can do registries where each time someone is diagnosed with autism, they put themselves onto a registry.

You can do administrative counts where you look at how many children are receiving educational services for autism or medical services under a 299.00 code. The challenge with those first three methodologies is that they all require a prior diagnosis, and I think we all recognize that autism is both under diagnosed and late diagnosed.

So if you're looking at, say, a population of 5-year-olds, you know that there is a group of kids who simply aren't going to have a diagnosis yet.

An alternative to these methodologies and the one that is the most widely known in our country is the CDC ADDM Network, which uses an active

case-finding approach. So I assume most of you know the approach, but just as a quick primer.

Basically, in the CDC ADDM Network, we choose a specific population of children. We look at all their educational and medical records. We look for information related to autism, and then we have trained clinician reviewers go through those records and assign whether or not the child is actually a case of autism. In the CDC ADDM Network, a child is never formally evaluated by the ADDM Network. They're evaluated by community providers.

An alternative to that approach is what's called population-based screening and assessment, where you actually go into a population, you try to screen the entire population for autism, and then you assess those kids who are at risk for autism.

In the past, when we believed that autism was a very, very rare disorder, this methodology didn't make sense at all. But now that we know that the prevalence probably hovers somewhere in the 1 to 2 percent range, now this is becoming more of a believable and achievable methodology,

and that's what I'm going to be talking about today.

This study has kind of a unique history. It's really a partnership among many groups. So I have been working with the CDC for many, many years on the ADDM Network, and as you know, we recently reported that 1 in 68 children have an autism spectrum disorder. But in 2011, Dr. Young-Shin Kim did a study that was a screening and assessment methodology in South Korea where she reported that 1 in 38 children have an autism spectrum disorder.

So Autism Speaks became very interested in understanding that difference, and they are funding our study, and the goal of our study is really to conduct a screening and assessment study in the same population of kids that are also under surveillance by the CDC so that we can understand who is missed and who is not missed in each of the methodologies and how that prevalence might change based on how you measure it.

So the study is being funded by Autism Speaks, but we also have partnerships with the CDC and then, of course, with our community.

Our study addresses IACC Question 7, which is

what other infrastructure and surveillance needs must be met? We have three main goals. We want to calculate the prevalence of autism. We want to compare DSM-4 to DSM-5 in our cases. And we want to compare our findings to those using the CDC methodology.

So I'm going to talk about each of these stages individually, but just so you have an overview, our methodology involves screening all children born in 2004 residing in a specific study area. It's 8,500 kids. We conduct diagnostic assessments for those who are at risk for ASD, and those assessments are offered both in English and Spanish.

We calculate our prevalence, and then we compare our prevalence to the CDC prevalence in the same area, and we're also looking at diagnostic classification according to DSM-4 and DSM-5.

This is a study that's been underway for about 2 1/2 years. The first phase of the study, the screening phase, is almost done. It will be completed in fall of 2014. The evaluation phase will be completed in winter of 2015. The clinician

review, which is part of the ADDM methodology, will be completed in the spring of 2015, and I hope to be able to come back next summer and tell you some results.

So let me tell you about our little corner of the world. So this map is a map of South Carolina. The yellow portions are the portions that have been monitored by the CDC since 2000 for the prevalence of autism. The three counties in blue are those being focused on specifically for the SUCCESS study.

That three-county area is a very diverse area. We're a 32 percent black population. We have lower ethnic diversity, only 7 percent Hispanic. We're very economically diverse. So we have 33 percent of the schools in our area have Title I status, which basically means that they have a large percentage of low-income students.

Although it's a small area, we have some very urban pockets, and we also have some very rural pockets, which has been a really big learning experience for our team because you have to use very different strategies to reach those two populations. We also have a high rate of

illiteracy, and I'm going to talk about that more in a minute because it's definitely presented some challenges for our methodology.

So in Phase I of our study, our goal is to screen all the children born in 2004 living in our study year. We chose the Social Communication Questionnaire, which is a 40-item screener for autism that's completed by the parent, and we are distributing the questionnaire to families through all the schools in the area, as well as our home school associations and at community events.

The screening process is extremely labor intensive. So we have to get district-level approval for each district. Then we have to get school agreements. Then we have to have teacher meetings.

And then, from the family's perspective, on the right-hand side of the slide, the family first receives a letter of introduction. Then they get the actual screener. We have a waiver of informed consent. Then they get a postcard reminder.

And then about a month after this initial process, anyone that's not opted out or participated gets what we call a "last chance"

letter, where basically we talk more about autism, and we appeal to sort of their volunteer spirit. And we get about a 10 percent bump at that point. So that's an important component to the study.

We've completed 106 out of the 134 schools in our catchment area. So we feel like we're doing really well. There is also three virtual schools that operate in our area, and we're partnering with them right now.

And we have 25 home school associations that are active in our area, and we're trying to work with all of them. This is a population that's hard to reach. So you really have to work hard to build trust.

I'm just going to present some interim data on our response rate. We're getting about a 51 percent response rate at this point. One of our big concerns is making sure that we're getting good responding from both our minority and our majority participants, and this can be really hard to evaluate.

So, on this slide, I'm showing, you know, that we definitely have differential responding by race or ethnicity, but I'll draw your attention to the

missing information. So we have 1,500 kids with no racial information and 3,000 kids with no ethnic information. But based on these preliminary analyses, we implemented a number of interventions that I'll talk about in just a minute to try to improve our minority responding.

In the long run, once our entire study is going -- is done, we're going to be able to compare our responding to the actual population because this is a population-based study. And in that case, so far, it's looking at little bit better. But of course, we're not done. So our study area is 32 percent black, and we have 28 percent black participants.

So we don't have to worry about missing information as much when you're using a population-based study. So we're very hopeful that in the long run, we'll have a good representation. But in the meantime, what we've done is we've really stepped up our community -- visibility in the community.

So we attend community events. We attend back to school nights. We attend first day festivals. We attend any children's festivals, and we have

all these signs up.

Interestingly, in South Carolina, we also have some schools that are predominantly African American, and so that's presented an opportunity for us to provide special interventions at those schools that you might not be able to do in 140 schools, but you could do at 10. And so, I have a postdoc that's been in charge of those efforts, and she's done a great job and has gotten some really good responding using that -- using some special interventions. We call them the pizza party interventions.

So just real briefly, on the first 3,000 kids in our study. So all our kids are about 8 to 9 at this point. Well, no, some of them are turning 10 this year. And on the SCQ, a score of 15 and above is considered to be at risk for an autism spectrum disorder, and about 7.5 percent in the general population of kids are falling at risk for autism spectrum disorders. And of course, that is the group that we're most interested in doing our clinical evaluations on.

But we're also interested in this group of kids that are sort of we call it our elevated risk

group. They're falling between 9 and 14, and we know that there's going to be some false negative screens in that group. So we're also taking a sample of that group and bringing those kids into the clinic for an evaluation as well.

We chose the SCQ because we believed that it was the best screener available, and I still believe that. But we definitely are seeing some issues with the instrument. So if you look at who's most likely to come out at risk for ASD, boys are more likely to come out at risk than girls, which is good because boys are more likely to have autism than girls.

But on the other hand, nonwhite children, Hispanic children, and those attending Title I schools are also more likely to come out at risk. And I mentioned earlier that we have very poor literacy in our area. And we are working on a hypothesis right now that that's affecting performance on the SCQ, which can be wordy.

And so, over the last month, we happen to have done a ton of our Spanish evaluations, and we're definitely seeing a lot of false positives in that -- false positive screens in that group. And a lot

of it has to do with overly literal interpretations of questions or maybe not understanding subtleties even when the questionnaires are administered in the native language. So that's something that we're going to be able to investigate more when the study is over.

So in Phase II of our study, we'll be doing the clinical evaluations. We're bringing in 100 percent of those at risk for autism. We're finding that about 50 percent of those people invited to the clinic actually agree to participate, and we do have very good minority participation in this phase of the study. And then we're also bringing in 20 percent of those with elevated SCQ scores.

Our evaluations are all done by doctoral-level clinical psychologists with extensive training in autism. It's about a 3-hour assessment battery. We really worked hard to keep it, you know, just at or under 3 hours, and we felt that anything longer, families wouldn't want to come in.

The child gets the ADOS-2 and the Kaufman Brief Intelligence Test. The parent completes a DSM neutral parent interview. This was a huge

challenge, an unexpected challenge for our study. So most of the available interviews out there are based on DSM-4, at least when we were deciding this study.

And because one of our interests was comparing DSM-4 and DSM-5 diagnoses, we couldn't use a DSM-4 focused interview. So we worked really hard to come up with a DSM neutral parent interview, and I think we did a good job.

We're also using the Children's Communication Checklist because one of our interests is the social communication -- is social communication disorder. And there's just not a lot of instruments available right now to help evaluate that. We're using the Vineland, and then we have parent and teacher forms for the CBCL and the SRS.

So we've completed 75 out of what we anticipate to be approximately 300 evaluations for our study. So I just want to spend a couple minutes talking about community-engaged research. I think it's the wave of the future, you know, especially in autism, now that we're able to look at larger populations of kids. But it definitely has its own challenges.

It's really important to start at the top, meaning that if you can get approval from your State Ed Department, from your superintendent, from the diocese, from whoever is very high up, everything else runs much more smoothly in your study.

We have gotten a lot of practice at using the foot in the door technique, if anyone remembers that from Intro Psych. So, basically, you ask for something small to get started, and then you make your true request.

So when we first started the study, we would send principals these long emails asking them what we wanted them to do. And most of the time, they would say, yes, this is so exciting. We really want to participate. And then every once in a while, a principal would just say no, and we couldn't afford for that to happen because we really have to have every single school participate in order for this to be an effective study.

So now we call the principal's secretary and say, "Can we meet with your principal and ask his opinion on a study that we're doing?" And that

gets our foot in the door.

You'll see we had a -- we had an ad agency come up with our logo and our marketing materials for the study, which I think was critical. You have to have professional materials and strong follow-through. You know, this study is the most important thing in the world to me, but I recognize it's not the most important thing in the world to everyone else.

So to the extent that you can really look professional and have strong follow-through, it helps with your community support.

When you're doing a really large study like this, you have the opportunity to actually pilot materials and incentives in a way that you could never do in a small lab-based study. So we were able to design the study in waves, where we completely completed one screening wave before moving on to the next out of six waves. So we were able to then be reactive and make changes to our materials and our incentives to improve our response rate.

The corollary to that is that that is a ton of IRB work, and if I could go back and redesign the

study, I would probably give myself 50 percent effort just to deal with the IRB. Every time you add a new site, every time a site wants something tiny changed on a consent form or on a material, that's another IRB amendment. And when you have 140 sites, that's a lot of work.

My community advisory board is amazing, and I would never do another study without having a board. I think having a community advisory board in place at the time you're designing the study so that it's appropriate for your community makes so much sense, and then that group of people is invested in your research and your success, and they'll do everything they can to make sure that it's successful.

You have to hire people with good social skills and consider barriers specific to your community. So I hadn't anticipated the barriers of particularly our rural communities, where they have a hard time getting parents to school for any reason. And then years ago, Dr. Landa gave me the advice to be very visible in your community.

We never turn down an opportunity to give a talk in our community, to show up at an autism

walk, you know, to help with a run, and so I think we've gained the trust of our community for that reason. And I think that's helped us to be successful.

This is a newsletter that we recently put out, and we're planning on continuing to put out just to keep our community partners engaged so that we can continue this line of research.

I want to close just with some reflections about screening and assessment studies. There are some real strengths to this methodology. The most obvious one is that diagnosis is confirmed using gold standard assessment tools and highly trained clinicians.

You don't have to have a prior diagnosis of ASD, and I think the biggest strength of this methodology is the richness and depth of information that you can get about your cases. It's really only limited by your imagination and by what you think your participants will be willing to do.

We're not collecting biological information in this study, but I think in the future, it would be really amazing. The level of phenotypic

information that you can get about participants, family information, it's really unparalleled with any other methodology.

On the other hand, I also want to acknowledge some limitations of this type of methodology. First of all, your participation -- your results are only going to reflect who participates in your study, who chooses to help you with your research, and that's going to be affected by a lot of factors.

First of all, how do you market your study? If you market it as a study about child development, there's a lot of people that just aren't going to be interested or not have the time to help.

If you market it as a study about autism, there's a lot of people who will be frightened or there's people who will just think it doesn't apply to them because their child already has a diagnosis of autism. Or they know 100 percent for sure that their child doesn't have autism. So they think it doesn't apply.

This second bullet point I really want to highlight because I think, you know, the future of this line of research is serial assessment in a

specific community. So if we want to understand how autism prevalence is changing, doing serial screening and assessment studies is really important. But it's important to understand that who participates in your study is absolutely going to be affected by the attitudes towards ASD in that community.

So parental awareness of symptoms is going to change how parents observe their child's behavior and how they're able to report on their child's behavior, how they're going to answer questions to you. Beliefs about whether a diagnosis of autism is likely to be harmful or beneficial to their child is going to change who's willing to help with your study, and that's going to absolutely change your results.

And beliefs about what ASD is, is going to change your study. So there's no way that you can do a study in a vacuum. You know, any -- any methodology is going to be reactive to these sort of environmental changes.

The last bullet point takes me a little afield from what I was just talking about, but I want to make the point because I think it's an important

one, and I'm realizing more and more how important it is. My study is focusing on 8-, 9-, and now 10-year-old children. And it's fascinating to look at the differences in DSM-4 and DSM-5 in this age group, but it's not going to be easily translatable to infants and toddlers.

So I think the issues and the difficulties in applying DSM-5 to infants and toddlers are real and exist, and I think a lot more research needs to be done in that specific population. So this study is not going to be the end all and be all in comparing DSM-4 and DSM-5. But I think we're doing a great job with school age kids.

And I was told to leave 5 minutes for questions, which I think I've done.

[Applause]

Dr. Insel: Thank you very much, Dr. Carpenter.

Questions? Jose?

Dr. Cordero: Thank you for that presentation. Very impressive what you're trying to do. I think this is something very important in terms of understanding what ADDM Network and the process is actually capturing.

I have a couple questions. A, you're using a

screening tool, and can you tell us a little bit about the sensitivity of that screening tool? Number two, you have about 50 percent participation rate, and then how do you go about figuring out those that did not participate and how different or similar they are to the participants?

Dr. Carpenter: So I'll take your second question first because that's a little easier. So when the study is all done, we will be able to compare participants to nonparticipants because we've actually been given quite a bit of information about all of the children by our partner schools.

You saw there was a lot of missing information, but there's also a lot of information available about -- about the children who chose -- families who chose not to participate. It was one of the real boons in this study that we do have that information available. And so, we'll be able to make those corrections statistically.

The SCQ I think, in my opinion, it's the best available screening instrument out there for school age children. It's not perfect, and there

are some efforts underway to improve it. I think sometimes the language can be -- it's not always maybe vernacular English, and there's probably ways that it can be improved, based on the age of the child.

So, right now, it's aligned to age. The cutoff is the same whether you're 4 or 15. But I think it was really the only choice that I could have used for this study.

Dr. Cordero: Any sense of what's the sensitivity?

Dr. Carpenter: I don't have those numbers off the top of my head.

Dr. Insel: Idil?

Ms. Abdull: Thank you for that presentation. I was wondering, you had said that the number of Caucasian families and the number of minority families, you were having trouble with the minorities, even though the person conducting the translating was a person of color or minority. And I was wondering, is that correct? Did I --

Dr. Carpenter: For the Spanish-speaking evals, yes.

Ms. Abdull: Yeah. And so, I wonder then if you

took into consideration because just because you translate a word from English to Spanish, or English to Russian, or English to Somali, for that matter, it doesn't -- it's different. So it's not so much that the translation is wrong. It's a lot that the question of the testing.

I've seen a lot of the autism diagnosis and autism questions. They're not really culturally appropriate. So a lot of things I wouldn't consider autism in America would be considered an autism symptom.

So I wonder if you notice that, and if so, if you're notating so that could drive future research to making sure that the tools and the resources that we use to diagnose and the questions that we're asking parents from different cultures are appropriate.

In other words, we're not just translating information, but we are creating testing methods and tools that is culturally appropriate for that community. Even African Americans is different culture than Caucasian Americans.

Dr. Carpenter: Yes. Yes, all excellent points. And it's not what we set out to do with the study,

but we're just getting so much data that's going to be so useful.

When this study is over, we should have 4,500 completed SCQs in a general population sample, which is an amazing opportunity. And I want to clarify that the problems that we're seeing, the false positives that we're seeing are at the screening level, not at the diagnostic level.

And so, we have some kids coming to the clinic that we just say how did this child ever get into our study because they seem to have no symptoms of autism. And just anecdotally, I can tell you what I'm seeing is some overly literal interpretation of some of the questions on the screener. The problem does not seem to be at the diagnostic level, though.

Dr. Insel: Question about at the end you brought up the idea of looking at changes over time, and that's clearly of great interest. And the Committee has talked about trying to get those kinds of numbers. And while I think all of us assume that there's been an enormous true increase in prevalence, there are still those who would argue that this is diagnostic drift or something

else around better detection.

What would be the barrier to doing what you're doing in the very same population except taking people who were born in 1984 instead of 2004?

Dr. Carpenter: So our -- I mean, using 1984 specifically as a birth year?

Dr. Insel: Or you could just choose some range of adult -- this was done in the U.K. recently, as you probably know. And surprisingly, the prevalence is about 1 percent in adults when they went door-to-door, when they were expecting that there would be a huge difference between the adult prevalence and the prevalence in children.

So this comes to the fore because you've already got a population that has been followed through the CDC ADDM Network. You're doing a real population-based study, which is fantastic. And then the question would be could we get some picture of -- of adulthood, and whether the same population, I don't know how you would do it, but that's what I'm asking if --

Dr. Carpenter: Right. Well, that's why I asked if you were interested in 1984 specifically. Because those are -- you know, the methodology

that we're using involves partnerships with schools.

But you know, I've thought a lot about what sort of the ideal, the dream study would be. And I wonder, you know, there are problems with doing -- with doing multiple birth cohorts over time because what we all think of as autism as a community is changing, and it's changed dramatically over the last 10 years.

And you know, one approach would be to do this same study, but do it -- at the same time, take 3-year-old, 6-year-olds, 9-year-olds, you know? And that way, at least what we're calling autism it's static for that point in time.

Now, of course, then you have cohort effects. So rather than doing, you know, 8-year-olds in 2012 and then 8-year-olds in 2014 and 8-year-olds in 2016. So both methodologies I think have their strengths and weaknesses, and I'm still thinking about my next steps.

But I do -- I do worry about the way that not just the public is changing how they think about autism, but how we as a scientific community are thinking about autism. And it's changing, and

there's no way you can deny that, and that's going to affect any type of prevalence study that you do over time.

Dr. Insel: Coleen?

Dr. Coleen Boyle: Just in response to you, I mean, the challenge I see with trying to do that 1984 cohort is that there's no institution that sort of surrounds them that you could actually tap into. And so, it would be harder to really feel like you have made a complete, you know, essentially census of the occupational, the potentially educational wherever within the community.

Dr. Insel: So we do something like the NSDUH study is basically, you know, not whole population, but it's population sample, asking about substance abuse and soon be asking about mental disorders. Is there any real barrier to just putting in eight questions that would be screeners for autism, and you'd get a sense of what the rate is in people in their fifties or forties or thirties. To see whether there's any sense of a real --

Dr. Boyle: I mean, I think that's a great

idea. We do that with children at the National Health Interview Survey. So there are questions within that context. Not so much just questions about autism, but there's a screening questionnaire that's part of that. So, yeah, we could definitely do that. This is not the same as clinically evaluating.

Dr. Insel: Yeah, so --

Dr. Boyle: So, again, you're getting different kinds of information.

Dr. Insel: So, but that's what I like about this study, besides the acronym, which is probably the best acronym ever for a research project.

Dr. Carpenter: Thank you.

Dr. Insel: Is the -- is that you really are going very deep into those kids who screen positive. So, I mean, a 3-hour work-up is very significant. You could do that in the NSDUH study if you had people consented to be contacted. You could go back and out of your 60,000 or 50,000 come up with a 500 that you really want to look at to see whether they would meet criteria.

It just seems to me that whenever we talk about prevalence, we're talking about children,

and I'm not sure, having just heard from John earlier about how most people with autism are over the age of 18, why nobody has bothered to figure out a way to look at the prevalence among adults. It seems like that would be useful to know.

Dr. Boyle: I mean, I think it would be terrific.

Dr. Insel: Geri?

Dr. Dawson: But you would have to use an approach where you have a broad screener followed up by diagnosis. Because, you know, there are so many that weren't diagnosed. And so, if you asked, you know, how many people have a diagnosis, then there's going to be fewer people because people were less likely to have diagnosed and picked up on autism historically.

And so, you'd have to have some kind of broad screening questions that have to do with social ability and so forth and then do the diagnostic assessment.

Dr. Insel: But that's how we do population-based epidemiology and psychiatry.

Dr. Dawson: Right.

Dr. Insel: We do a broad screener, the CD. We

capture -- and it turns out only 30 to 40 percent of people ever have gotten a diagnosis or ever been -- about 1 in 4 has ever gotten any kind of treatment. And of those, only about 1 in -- you know, about 30 percent have gotten reasonable treatment.

So, so it's not that different. It's just that autism, for some reason, has always been assumed to only -- only -- we're only interested in the children, and yet, as John points out, we just haven't taken the time or really made the effort. And I was just thinking about this here because you've already got a population you've defined. But it would be much harder, I think, to figure out how to do that in a select population.

NSDUH is already zip code-based and is worked out for the whole country. David?

Dr. Mandell: You could probably do 1996, even if you couldn't do 1984 because you have the -- because they'll still be relatively close to school age. But I think one of the things that distinguishes it -- and your data on the SCQ is fascinating, and even your clinical observations of these folks I think are so critical. We don't

have a good field-based screening instrument for autism, or rather, we don't know if we have a good field-based screening instrument for autism.

And so, even if you think about some of the other disorders, we've given up trying to do field-based assessment of schizophrenia because we have lousy agreement between any of our field-based agreements -- measures and a psychiatrist determination of schizophrenia.

And so, we can do substance abuse, and we can screen, and we can do depression. And we can do ones where we have good concordance between the screening instrument and a clinical diagnosis. I think if we want to move into this area, it sounds like these SCQ data will be extraordinarily valuable in trying to move us towards having that kind of instrument where we could feel comfortable putting in 8 to 12 questions in a survey and feeling reasonably certain that we've gotten a highly sensitive and relatively specific population -- or sample for a second wave.

Dr. Insel: This would be a great question to put to Cathy Lord, if anybody happens to see her later this afternoon.

[Laughter]

Dr. Insel: So we may put you on the spot later, Cathy, to comment on this.

Sally?

Dr. Burton-Hoyle: I think that if you went to who applied -- filed for unemployment and went to State voc rehab programs --

[Audio disturbance]

Dr. Insel: Hold on a second. Let's see if we can figure out where --

Dr. Burton-Hoyle: I think if you went to State voc rehab programs who had tried to open files and you went to who had filed for unemployment, I think that would be a good broad-based way to find adults who had --

[Audio disturbance]

Dr. Insel: Wow. Okay. Last couple more comments. Matt?

Dr. Carey: I had kind of -- when she was speaking, I had kind of the same questions you were having about how would we apply this to adults as well? It's a big question that's always been on my mind.

I think it's one we're going to have to -- you

know, with Autism CARES Act, I think it's one we kind of have to be thinking about, right? There's a whole section here on demographics we need to know.

But just from my own perspective, getting that information is also very critical because that starts getting us really focusing on that population, knowing that population. Right? As a parent, what I need to know is what worked for kids who are like mine 20 years ago, 30 years ago? What worked, and what didn't work?

So, you know, I would personally rather learn from them than have the next generation just learn from me, right, just to be very selfish in that perspective. And right now, we don't have that data. We don't have that population to really study in adults, and we're not doing it.

So, you know, we're not going to get those answers in time.

Dr. Insel: Anshu?

Dr. Batra: Thank you, Dr. Carpenter.

I had a quick question, which I think is actually very important. Can you clarify what you meant -- what you said about the diagnoses made

for a school age child within school age years versus prior to that made more from a medical standpoint as a toddler versus the school age diagnosis of autism?

Dr. Carpenter: Yeah, so --

Dr. Batra: Because that's a very, very important distinction.

Dr. Carpenter: So, you know, this study, one of the parts about this study that I love the most, because it's my interest area, is the part of the study where we're comparing DSM-4 to DSM-5 criteria. And the study has gotten a lot of attention for that reason because people are very interested in how prevalence might change based on which criteria you use.

But truthfully, now that I'm -- you know, first of all, have been using DSM-5 criteria clinically for a while, and also we're 75 evaluations in. I'm seeing that there's a lot more concordance in DSM-4 and DSM-5 in the school age population than I think there is in the babies. And so, I think there's, you know, the criteria, they still need to be evaluated for the infant and toddler group.

I just wanted to make one more comment also about the adult, the adult surveillance. The oldest ADDM kids now from the CDC study, from the year 2000, are now entering their twenties, and actually, the oldest MADDSP kids are even older. So that was the Metropolitan Atlanta study started in 1996, and then the larger ADDM study started in the year 2000.

And so, I think specifically at our site, and I imagine other sites might have the same plans, we have a lot of plans for finding out what's happening to that cohort now. You know, the kids that were born in 2000, you know, we have a pretty good sense of what the prevalence was from that birth -- sorry. They were born in 1992. It was the 2000 study year.

We've a pretty good sense as to what the prevalence was, and now we want to know what the young adult outcomes are in that group. And so, we'll be able to say with a little bit more certainty what their needs are and what services they're accessing. So there is some opportunity within the existing ADDM framework to follow-up on what's happening to these folks in adulthood.

Dr. Insel: Coleen, we'll give you the last word, and then we're going to have to move on.

Dr. Boyle: I just want to plant a seed out there. So when we first -- our first study was actually done in Brick Township?

Dr. Carpenter: Right.

Dr. Boyle: And it was about the same size as this cohort, about -- if I remember correctly, about 9,000 children. It was 3- to 10-year-olds, and it actually used a screening and a records-based methodology. And obviously, those children are now young adults. So some investigator wants to actually go back and -- or contact and look at that community. It'll be a great -- a great study.

Dr. Carpenter: That's a really good point. All right. Thank you, everybody.

Dr. Insel: Well, thank you. John, do you want to make a final comment?

Mr. Robison: Yeah, it's actually not about this, Tom. It's about our previous issue.

Dr. Insel: So why don't we come to that right after the break? We'll give people 10 minutes.

Mr. Robison: We'll come back? Okay. All right.

Dr. Insel: And then we'll start with you when

we return from break. But it's -- I have 2:30 p.m. Let's start again at 2:40 p.m., and we'll begin after John's comment, we'll begin the discussion of trajectories.

(Whereupon, the Committee members took a brief break starting at 2:30 p.m. and reconvening at 2:40 p.m.)

Dr. Insel: So before we start the session on trajectories, which there's a lot to talk about. So I want to get moving pretty quickly here. John had a comment that he wanted to make, and Walter is just coming back in. So, Tiffany, in terms of FDA regulation of devices?

Dr. Farchione: Right. So, in the first place, even though an assistive communication device would help with, you know, autism, they wouldn't consider it a medical device being regulated by FDA because it doesn't actually affect the functioning of the body.

Dr. Insel: Interesting. Okay. Thanks for that FDA --

Dr. Farchione: It took a little bit to track it down, but --

Dr. Insel: Yeah.

Dr. Farchione: -- [Inaudible comment]...regulations are a little convoluted.

Dr. Insel: Right. Okay. Helpful to know. John?

Mr. Robison: Yes. I received a couple of requests, actually, to acknowledge the written comments. We did talk about the importance of the comments, and I think that a couple people raised the question how do I know if I send a written comment in to IACC that it goes anywhere other than the trash?

And first of all, I would say in my time of service on this committee, many people have written me and said, "I'm John Smith, and I wrote a comment about whatever, and I wonder what you thought about it." And I have never once had somebody write me about a comment where I couldn't find it in my packet here.

I'd just like to name the people who have sent us comments for our consideration. We've heard from Joseph Jason, Maria Ferreira, Martha Moyer, several comments from Marian Dar, Dawn Loughborough, Michael John Carley, Shawn Swain, Nydia Olvera, Dr. Kathleen Levenstein, Anne Jakus, Caroline Rodgers, Eugenia Ramsay.

We have four comments, I believe, from Eileen Nicole Simon, who also stood up and addressed us in person here. Carol Fruscella, James Blanco, Heather Price, Pam Rockwell, Portia Iversen. Pardon me if I pronounce some of these wrong.

John Best. Mr. Best has the distinction of being the only commenter who had profanity redacted from his submission. Even though I could handle it, maybe some of us can't.

Chanda Jackson, Lea George, Melissa Schneider, and Carolyn Gammicchia. The topics of these comments range from criminalization of young people on the autism spectrum, and some of you know my own son had trouble with that. So, believe me, that's close to my heart.

Awareness of autism, various suggestions about causation, talk of vaccines, mercury. A number of indictments of our failure individually and collectively on the IACC, plus our collective failure for the United States Government and the National Institutes of Health.

We have a question of ABA and civil rights. We have an announcement of a blog post. We have a proposed content sharing partnership, and we have

some other stuff that I would say is strange. But mixed in there, we have some -- we have some very serious thoughts. We have some people who've thought long and hard about comorbidity and issues like that.

The criminalization issue is a very serious topic, one we need to do more about, and we have some very thoughtful comments on awareness and other things. I haven't read them all yet, but I will read them. And I hope the rest of us do, too. And I just wanted to take a moment and let any of you folks out there who have sent us these comments, I wanted to at least give you my own assurance that I read every one of them, and I believe many of my fellow Committee members, too.

Thank you, Tom.

Dr. Insel: Thank you, John. Lyn?

Ms. Redwood: Just real quick to follow up on that. I know we've had this discussion several times about putting the comments up on the Web site. So I just wanted an update on that, and also to say if anybody who submits public comments would like for those to actually be made public, they can email me at lyn@autism.com, and I'll make

sure that those get up on our Web site.

Dr. Daniels: Still in progress. We'll update you as soon as we find out something. I think in the interim between committees, we should have some time to get this all worked out, and hopefully, by the time the next committee starts up, there will be a database on the Web site where you can access everything.

But in the meantime, if somebody needs to access particular comments, you can always write and ask for them.

Ms. Redwood: Will that be retrospective, Susan, for the comments that have been received for the past 7 years?

Dr. Daniels: It will go back to the beginning of the IACC since I've been here in 2008.

Ms. Redwood: Thank you.

Dr. Insel: Jan?

Ms. Crandy: Susan, would it have been possible if the person that writes the comments gives permission for it to be posted? Would that help us legally to be able to post it sooner?

Dr. Daniels: It would. But we already have thousands of comments. To go back and get consent

for each one would really be a big project. So we're not going to be able to do that. So we're going to go through other channels to try to get it all worked out.

Ms. Redwood: If we could also get the comments earlier, we would have a chance to read them before the meeting. That would be really helpful.

Dr. Daniels: We try to keep the deadlines as close to the meeting as possible so people can submit. In the past, when I first started, we tried to put the deadlines a week and a half before the meeting. We got a lot of complaints because people don't really think about the meeting sometimes until it's very close.

And so, we try to give them every opportunity to put in a comment, and that's why you receive your packets when you do. If the Committee wants to make a decision that you're going to close the comment period earlier, the Committee can make that decision. But just judging from complaints that we've gotten when things closed early, I would say that, and just the fact that we receive comments really up the last minute.

And we usually do even accept them a day or so

past the deadline if possible just to make sure, as much as possible, people are having the opportunity to comment.

Ms. Redwood: Maybe we could get them in installments then? So the ones that are submitted timely or earlier we could actually have, and then at the end. Then we wouldn't be getting a packet of 60 pages.

Dr. Insel: You mean for the next meeting?

Ms. Redwood: Yeah.

Dr. Daniels: For us to prepare multiple packets per meeting would really increase the workload for us, and also it would make it difficult for the database because the way they're going to be parsed in the database is per meeting.

Mr. Robison: Can't we just have like a box people check when they send in a written comment to release it, like a commercial operation would do?

Dr. Daniels: I don't think that there's any simple way for everyone to get access to an NIH email account like that. So this is really -- as far as I know, it's the most efficient way for us to share it while protecting privacy.

We also are required to redact everything before you receive it. And so, that also takes us time to go through and redact each comment.

Mr. Robison: I guess that was my question. Couldn't somebody waive privacy and redaction so that we offered somebody the opportunity to send a public comment in that was -- or send a comment that was private to us, but also they could just waive all that, and we could post it immediately and not have to worry about it.

Dr. Daniels: If there were a way to waive all of this and just go around the current Government rules for privacy, I would love to do that. But unfortunately, I like my job here in the Government, and I want to keep it. So I try to follow the rules. Unless I get permission from higher up not to follow the rules.

Ms. Redwood: Susan, could we just back it up 24 hours where at least we get them 24 hours before the meeting? I mean, that would give me enough time to read them.

Dr. Daniels: We would need to close the comment period earlier to be able to do that. We did have a holiday weekend this past weekend. So

on Friday, our staff was not working. So we had to get the comments earlier, and then we did redact them.

[Pause]

Dr. Insel: So let's move on to talking about trajectories. This came up at the last meeting as a topic that you wanted to hear about, particularly with respect to regression. We've got three speakers, and I'll just introduce them as they come up.

Dr. Audrey Thurm is a staff scientist in the NIMH Pediatrics and Developmental Neuroscience Branch. She is a licensed child clinical psychologist who specializes in ASD and other neurodevelopmental disorders. Trained at DePaul University and Boston Children's and did a postdoc at Hopkins.

She's been at NIMH since 2002, first in the extramural program, but since 2006 in our intramural program working with Sue Swedo and others on the – in the autism program there.

Welcome.

Dr. Audrey Thurm: Thanks to you for inviting us, and thanks to my other panel members, and

happy to be here.

I also wanted to add to my introduction that I'm also an aunt of a child with autism, who I went through the process with of the unfolding and diagnosis. I've been in the field for a long time. So thinking about regression and trajectories of onset of autism has been something that many of us have been focused on for a long time.

And even though this is a very nitty-gritty title and talk about how we really can define and measure and try to classify regression, actually a better title came from one of the IACC members, which is coming closer to describing the variable onset pattern in autism. And that was a paper by Geri Dawson, just to acknowledge that a lot of people in this room and researchers around have really spent a lot of time trying to unravel this in many different ways.

We've already talked today about really the importance of onset trajectories and thinking about this idea of "regression," and we'll unpack that quote as we go, as really essential for learning about the etiology and interventions and when and how you can intervene.

So I'll just get to my take-home messages before I even start, which is that this term "regression" is -- is loaded and has a lot of terminology related to it. And we need to sort of think more about the term we're using and then how we measure it to drill down.

So regression, as has been pointed out today, a lot of things sai have been pointed out today, which is great. So I'll try to go fast. Was used from the very beginning from Leo Kanner. If you go back to the 11 cases, in the third case that he described, it was a child named Richard whose mother described, "I can't be sure when he stopped the imitation of word sounds. It seems that he has gone backward mentally gradually for the last 2 years."

She said that when he was just approaching the age of 3. So it sounds like right around 12 months something changed for him.

And this description, I think, is very helpful because, first of all, it talks about language as being the first thing described as a loss. Although if you listen carefully, she talks actually just about the imitation of words, which

is already talking about the compounding of the language-word development and the social because, really, imitation is the social piece of it.

And then she also talked about it being gradual, and this sort of insidious where it's really hard to pinpoint the exact time and place for some of these kids.

On the other hand, regression is also a term used very, very widely in psychiatry and neurology for a lot of things. And I'd just point out a few examples here that it has been used to discuss the significant decline in previous diagnosis childhood disintegrative disorder, certainly in mitochondrial disorder where kids can be, you know, 10, 11, 12 years old, and all of a sudden have a very significant sharp onset of major, major loss of motor skills and other things, specific epilepsy syndromes and other neurologic problems in general.

And just pointing out related from our DSM-4 category was Rett syndrome, in which regression is one of the key features, and we should kind of stay tuned to Rett syndrome as learning more about regression since animal models have been starting

to try to crack at this.

And now that we are getting genetic diagnoses of Rett syndrome very early on, I just saw a study that came out looking at early onset of delays in children with Rett syndrome even before this regression occurs for those children.

So I'll start with sort of where we were. What we were doing for a long time was we were doing studies where we categorized groups of children as either having regression or not having regression, sometimes based on totally unstructured interviews, and then more recently based a lot on the diagnostic interview that was done, which most often has been the Autism Diagnostic Interview.

These studies, I'm not going to get into them too much because they are extremely variable in how they define regression. For a long time, it was only language regression. It was really only word loss and more like phrases that were used. And then, more recently, several studies have started to bring in at least some social loss, although some of that has been very specific.

And as you can see, there were very variable results when -- this is only looking at behavioral

outcomes. There is a much longer literature that has looked at other types of outcomes, including medical. Just in terms of very either cognitive or ASD symptoms, as you can see, there are definitely reports of worse symptoms in children with that categorically defined regression versus not, and as well as studies that showed autism symptoms being worse, but not necessarily cognitive skills. And then several that did show no differences.

I didn't put on here, but there was one study that did show actually higher skills in children with regression. So it's just been all over the map, which has really led us to say what are we doing here? Are we defining this in an appropriate way?

So, generally, those studies found about 25 to 30 percent of children having regression pretty consistently across the board, although it started to change when social loss got included in the definitions.

At the same time, we have very luckily been able to start conducting the baby sibs and other at-risk studies that have allowed us to look prospectively at infants, and you're going to hear

a lot more about that this afternoon. I'm just mentioning it in the sense that it has helped us in learning about a trajectory where we're certainly seeing that early delays are apparent, and more and more we're seeing maybe not diagnostic, but things that are occurring at 12 and 6 months that we can start to identify.

And that there are trajectories that we really want to look at, and these trajectories that have included delays as well as worsening. And social communication skills have really been the focus of these studies. So they have led us to now think about the sort of decline in a more general way.

And that raises many, many questions. But some of them are really if there is this regression, what is the pre-loss development like in children? How frequently, you know, is this development normal? And what is the timing of this kind of loss, and how does it fit in with a general onset of autism?

So several studies in the early 2000s started to look at this. Again, we didn't have a lot of the data we have now prospectively. So Geri Dawson and others painstakingly went through videotapes

after children were categorized as regressive or not and did start to see that even though they had been categorized as regressive from interviews, that they could see some delays early on. And so, these studies just talk in different ways about how delays were seen.

The last study -- last story I want to mention because it was the first that I could find that actually included the idea of pre-loss skills in their definition of regression. A lot of the other interviews that had been done really just talked about did your child lose these skills?

Of course, you had to have a skill to lose, but it didn't get into the details so much of when did your child develop skills? How sort of constant these skills were, what they were, and what was developed?

Again, a lot of the questions were more, you know, did your child lose language? Did they lose social skills? Really hard for parents sometimes to think about specifics there without hearing them.

So Sally Ozonoff and others took a first stab and saying, okay, maybe it's not just regression

versus not. Maybe we need to divide it up a little bit better, and you don't need to pay attention to the details here because some of them are ADI numbers. But what these studies did was look at trying to break it into at least four groups.

So that there would be a group where there was no regression. There were very early symptoms, although this was defined as parents being asked in hindsight were there symptoms before the age of 12 months? So it's pretty crude, but again, that upper quadrant being children who really had no regression. They were really delayed from the beginning or had symptoms of autism.

The lower quadrant being kids who no symptoms were seen even on hindsight before 12 months and a regression either in language or in social was reported. And then a middle two groups where one there was delays, but there was also loss. And another group that was plateau. Again, we're still working on retrospective parent report here, but we're trying to divide it a little bit more.

So a few studies were done using these methods and these were some of the studies that also didn't find differences so much in outcome. And we

know even from asking these questions that we really want to dig deeper into what the skills were because parents do have a hard time with these.

So what we tried to do in a study where we were specifically looking and trying to be able to categorize children with regression versus not was just to do the best we can with retrospective parent report.

We're not going to start from scratch with infants, and we've heard the difficulties in doing that. So we really wanted to just dive in as much as we could, using retrospective parent report by really digging into what the skills were. This has been done in a few other studies, too.

So we did an additional very long interview in addition to the diagnostic interview that asked very specifically about -- about 20 skills, but we really focused on 15 skills. Did your child develop this skill? At what age did they develop it? How consistent was it? If it was words, was it meaningful, spontaneous? Were they doing it in multiple settings? How long was that skill there? And then was that lost?

We thought this was the best way without having going through videotapes or, again, doing it prospectively that we could try to look at breaking up this loss into very specific ways. We gathered data on 244 children, and again, about 175 are considered ASD.

We did have 46 children that had developmental delays that were not autism, and we had 31 typically developing children in the study. And we used this interview that I'm talking about, which we termed the progression validation interview.

And from this, first, I just want to show the differences in this, is just attainment now, whether children had attained these skills at all. They were from the ages of about 18 months to about 6 years old when we did these interviews. So we try to do it as young as possible.

And as you can see, luckily, you know, typically developing group, we see it. The developmental delay group, not everybody developed a lot of these skills. But in the autism group, just pointing out, I mean, very -- as you would expect because these are children with autism, that a lot of children did not develop a lot of

these skills.

So just showing you the lowest percentages here, again, what we would expect to see. Very low percent for very specific what we now think of as great screening questions really are markers of autism. So only 33 percent reported ever showing objects, and only 24 percent reported ever pointing to express skills.

So when we went through these and then we're only asking about loss when a skill was actually established, we did find that loss of at least one of these skills -- again, they had to have had it to lose it -- was reported in at least in 63 percent of the children with autism. So loss was occurring in most children with autism.

And so, pointing to express interest, even though it only was gained in 24 percent of the children, was also the highest reported loss of a skill—waving, eye contact. So, again, these were reported more than language, words as lost, but words were in there as well. And I think that's something just that we've learned more and more is that a lot of the loss is not necessarily language, but more of these more subtle social

communication skills.

And that the other thing we really did not expect, and it made the interview much longer, was that the skill occurred at different ages for different skills. Parents would report the loss of pointing was at 15 months, but the eye contact retained until 18 months. It was variable. All, you know, within this age range, but it was quite variable.

So this is the data when we just kind of look at it by skills attained over time versus skills that remain. So if you're on the line, you kept all the skills that you had gained. And this just shows you what we did not want to see. We wanted to see cut points where we could easily say these children would fit into a regressive group, and these children would not be in a regressive group and focusing on the autism group.

Although you do see -- you see a loss in PDD, and you do see a little bit of loss in the developmental delay group. But what we didn't see was this cut point that we were looking for. We were also surprised because, again, our materials did -- we were recruiting for regression in the

beginning, and we did not see many children who had gained all of the skills and lost them all. We saw one child where that was the case.

I mean, there were children who had gained a lot who had lost, you know, just a few of them versus quite a few of them, but we just didn't see the cut point. What we really saw over and over again was that this was continuous, continuous measure of how many skills were gained and a continuous measure of how many skills were lost. And they were independent of each other, and they were much more dimensional than categorical.

So, and this just shows over time the skills that were gained and then -- and then skills lost. And you can see, and you'll see trajectory data later this afternoon as well, showing that, I mean, overall, there is a dip as you would.

It's not just skills not being gained anymore in children with autism. There is definitely a dip overall, and you know, if you start to categorize those who lost more, you can see a much more downward spiral.

And that children—certainly children—in typically developing children from just a few

months of age bifurcate here, but children with autism start bifurcating at 14 months from the developmental delay group. And for the children with PDD, it's not until 18 months.

So when we're hearing and we're doing these interviews, we're hearing actually "my child started flapping around the same time" very commonly, and we're realizing that, yes, regression is not about starting skills. It's about losing skills. But we really need to make sure that we keep the beginning of other autism symptoms into the picture here when we're looking at loss and really thinking about trajectory of onset of autism symptoms versus this idea of just regression.

So using the ADI and a version that allowed us to ask about the onset of repetitive behaviors, we looked and we looked at the timing of the first loss that occurred for a child, again when the loss was variable over time, and we found that in 61 percent of the children, the repetitive behaviors that they reported actually precede, were earlier than the loss of skills. So the idea that regression is something that happens first

and then autism happens after is muddier than we thought.

Going the wrong way. So it just -- trying to picture this, I think it's really three or four dimensional rather than a one-dimensional idea of this regression being categorical that, I mean, this is how I'm thinking of it now that we certainly have the timing where things happen at different times. We have early delays occurring. We have loss occurring, and then we have development of interfering behaviors that all come together.

So now I'm going to talk about -- now that I just presented only retrospective parent report, I'm going to talk about some of the limitations of this that we've been lucky enough to be able to learn about now that we also have prospective studies. So I think we're going to hear more about this later as well that when you ask parents, even when they're 2 and this happened at 15 months, they have a hard time remembering, as we all do. I have a hard time remembering what we did yesterday.

We start to hear, "I'm really not sure about

the ages. I'm really not sure did he do this skill, you know, every day or was it just a couple times. I remember this one time. So I think he did it all the time," things like that. Because then when we ask later, we often get different stories.

So this, there were some studies that actually did ask at two time points and found up to 20 percent disagreement at those time points. So, again, now that we have prospective studies, we can start to look at the differences. And I was lucky enough to get data that is hot off the press from Sally Ozonoff at the MIND Institute, and we've been working together on this in a lot of ways.

But she has the prospective data where she's at seven different time points from 6 to 36 months been doing studies where she's using observation during testing to rate behaviors, social communication behaviors such as sharing, enjoyment, smiling, eye contact. And from these, she has done latent class and found two groups.

Again, the white line on the top is typically developing children. So they are having these skills and getting better and keeping them. But

within the children who end up with autism at 36 months, she has two different classes.

And most commonly was the class which was 89 percent of the children that by observation of examiners looking over time, they were declining in these skills, in these social communication skills that she was looking at.

She had previously done a study where at 36 months, she had done the Autism Diagnostic Interview and asked the question about regression, and most of the children who she found in this group who had undergone this decline, parents were not reporting a regression at all. So what she did in this cohort was she was able to ask the parents at each of these time points how they felt about these specific skills.

And when she did that, she had much greater agreement. So 71 percent compared to 89 percent now of the parents did report actually, you know, compared to how he was at 6 months, now at 12 months he's showing less of these skills. So there was much greater agreement.

She also noted that there were some parents who continued to report that their children had

lots of skills, and those children were also -- had autism at 36 months.

So with 30 seconds left, the concluding remarks are just that we really want to think about loss. There's no question that we're going to hear a lot more about the more we see in younger children starting. We're seeing this downward loss of skills, but the idea is whether we can think about it at all categorically or whether we have to think about it dimensionally.

And I will conclude there.

[Applause]

Dr. Insel: Let's hold off on the discussion until the third presentation. We're going to go on -- thanks, Audrey -- to Rebecca Landa, who I think is pretty well known to this group.

Dr. Landa is the founding Director of the Center for Autism and Related Disorders at Kennedy Krieger Institute and a professor in the Department of Psychiatry and Behavioral Sciences at Johns Hopkins School of Medicine. She's the principal investigator on a number of studies that you've heard about, even some today, including the baby sibs effort, where she's on the Executive

Committee for Autism Speaks.

She's a member of the Toddler Treatment Network and is a PI for one of the Autism Treatment Network sites and co-principal investigator for the CDC SEED study and many, many more. But she's really of interest today because of her work on trajectories and following kids longitudinally, and that's what we'll be hearing about.

Dr. Rebecca Landa: Thank you, Dr. Insel. And thank you so much for inviting me to be a part of this group.

I want to thank the NIH for funding this work and also Autism Speaks and the Karma Foundation. I have some data in here from those groups. I want to thank the families and children who devoted so much time to this, my wonderful staff, and Dr. Margaret Bauman, who was a PI for my first baby sib study.

This slide is just a quick public service announcement sort of thing that from the work with the baby siblings of children with autism, we've been able to develop for the Maryland Academy of Pediatrics this 9-minute tutorial that's on

YouTube. So it's free. And it has three sections that I've demonstrated two of them here. I'm sorry, one of them here looking at seeing social opportunity through play.

And it shows pairs of videos in each section. So there's a total of six different children, all 1-year-olds, with the first video showing a narrated video of a child who is not showing signs of ASD, but the other video is showing a 1-year-old who is showing signs of risk for ASD.

And one of the things I just want to point out here and maybe you'll see it in the videos I'm going to show you, that when autism first appears on the scene, it can look kind of subtle. It doesn't -- it's not like you pick up the phenotype from age 3, 4, or 5 and plop it down at 1. It looks a little different.

So I think of autism as a disorder of development where in most of the 6-month-olds, which is where we have most of our beginning data, things start off in general grossly within normal limits, and then there is a disruption in developmental processes that converge at different times in different ways to give rise to ASD

behavioral phenotypes.

Now we used a prospective longitudinal design, which is highly efficient. We study infants at high genetic risk for autism that is baby siblings of children with autism. And the risk controls where we can control the age of the time of assessment, the context, including things like the kinds of cues the children are getting, the amount of distractions, the camera angles, the difficulty of the task. Lots of things and also the types of tasks.

We -- these are the groups, and we've just added a pre-term group with my latest funding, and I don't have data on them right now. We know from my work and from the Baby Sibs Research Consortium that Autism Speaks supports for us to donate our data to a common database that about 19 percent of infant siblings of children with autism will go on to have an autism spectrum disorder, and another about a third will have milder, non-ASD related language and/or social delays.

These are the ages where our children are tested and the ages at which I'll be showing data today. The 10-month visit was added in my most

recent grant, and I'm not going to be showing data from that.

At 36 months, we classify children into one of three groups. Either that they have an autism spectrum disorder or that they have an intermediate phenotype. And for us, we've been defining that as a language and/or social delay, although there are other things that we could put in there. And then a group of "unaffected."

And when we began to look at our data, we had some surprises. First of all, and maybe you call me naive, but I'll admit maybe I was. I started this in 1997. So there is probably more than one naive person at that time.

But we really expected overt signs of atypicality by 6 months of age in babies who would go on to have autism. But that isn't really what we found. So I'm going to show you this video of a 6-month-old who went on to have autism, and his case is rather severe. And he's a teenager now.

All right.

[Video presentation]

Dr. Landa: Now mom has been playing this peek-a-boo game with him for a little bit. He hasn't

looked at her, and you can see she's shaking her head, and she's saying, "You're not even looking." So she turns to this little piggy game, and he's enjoying it. And he starts to smile, but he doesn't look at her at all through this whole process.

The other thing that we found in this little man when he was 6 months old is that he had this very repetitive raspberries thing going on. And he also had motor delays, and he was delayed in his babbling.

This is a child, and you're going to see more tapes of him. You'll see another tape of him at 14 and another one at 24 months, and this little guy did not -- we did not think that he had ASD early on, but he ended up with it.

And you can see, I mean, this looks pretty good. He's looking at his mom, and he's smiling at her. And so, you know, this is the kind of thing that we see in most of the 6-month-olds who go on to have autism.

Another surprise was that we kind of expected that there would be stability in ASD presentation, that you would show it early and you would show it

all the way through. There is a lot I'd like to say about this, but I'm not going to be able to tell you about it today. But we also thought we would see pretty typical development with a regression. And as Dr. Thurm sort of forecasted, that's not the typical picture.

So what we found, and this is now being replicated by most people in the Baby Sibs Research Consortium, is that there's a prodromal period to autism. And so, up at least through 6 months, behaviorally the children look on the surface to be functioning quite well. We do find that we have a group of children with ASD who manifest early enough for us to detect it at age 14 months, and they still have it when they're 36 months.

And then we have another group who we didn't detect it at 14 months, and I have to say we're pretty good at it. And only really sophisticated people do this testing, and then we -- the children ended up having ASD after -- at the third birthday and maybe even before.

But what we reported in a paper that we published in Child Development, actually, it came

out in 2012, is that language regression can occur in either of these groups, and it can happen over more than one of our age intervals. So it can be slow like Kanner originally presented.

Now Dr. Thurm already went through this. So I'm going to fly through this slide. What is regression? We're used to thinking of it as a language loss. But there is so much more to it.

We need to also be considering frequency of communicative use of words, frequency of social interaction, deterioration in the quality of social interaction, decrease in social responsivity, decreased diversity of behavior, reduction in the quantity -- or quality or complexity of play.

And what about the appearance of the atypical features? And so, the term "regression" has connotations that may or may not be helpful as we try to dig into understanding neurobiological mechanisms in autism, and yet we don't really have a better word for it other than worsening, which isn't so sophisticated, but it kind of does capture what we're seeing here.

So let me tell you a little bit of what we're

finding in the 6-month-olds, and this was another big surprise. The surprise was that what we see in almost all the children who go on to have ASD or social communication delays are motor delays. And most of those motor problems involve postural control.

We've identified those in 3-month-olds and in 6-month-olds, and then we just had a paper, Dr. Insel noted it this morning, come out looking at quality and duration of grasping.

And when we look at the early -- oops, I want to show you this video just really quick here. I'm going to make it fast.

[Video presentation]

Dr. Landa: This is the little guy. You're going to see him again at 14 and 24 months, but this is the pull to sit task on the Mullen. This is a really big drama case of head lag. But even the mildest head lag at 6 months is not okay because head lag isn't there anymore after 4 months of age.

And I am not saying that this is a marker for autism. I'm just saying it's a sign of delayed neurodevelopment, and we've got to pay attention

to it. If you have a family history of autism, it might take on new significance.

When we looked at self-generated postural control, postural shifts, at 3 months of age and 6 months of age in infant siblings of children with autism, we found that these are highly correlated with language functioning at 18 months. There is a growing literature on the relation between motor development and language and social development that's really intriguing, and so that these are not totally isolated phenomena.

This is in a paper that just came out in Child Development on motor system, and so what we did was we created this grasping or object manipulation composite from the items in the fine motor items in the Mullen Scales of Early Learning. And we found that the baby siblings of children with autism at 6 months, as a whole group, were considerably behind the low-risk group, but their overall Mullen fine motor scores were within normal limits.

And so, this is a point that I may forget to make later. So I'll say it now. Is that you can't rely on standardized tests at 6 months to identify

these problems. These are qualitative matters or frequency of occurrence matters.

It's not a question of can you do it once on this test and get your points, and this is look at grasping behavior that in 6 month olds, these are baby sibs of children with autism. These are low-risk controls, and this is them at 10 months in terms of their proportion of time grasping objects, and you can see they catch up.

This is not looking at quality of grasping. This is looking at quality of grasping. Okay.

I know I'm going fast, but this is going to be on the Web. You can look back at it later. And I just wanted you to get a mental image of what it looks like in some of the children who have the early manifesting ASD.

[Video presentation]

Dr. Landa: This is the little guy you saw with the head lag at 6 months, and this is him, and I'll just narrate with such a short video, but he's not engaging with the examiner.

He doesn't really have an understanding of what to do with the toys. And he's a bit more interested in the sensory properties of the toys

than in using them for more mature exploratory play or even functional play, which he should be able to do at this age. He's 14 months old.

Now this is the little man that you saw here, who was smiling at his mom during peek-a-boo. And here at this age, at 14 months, he was language delayed, but in this video, he just kind of looks a little shy. He's interested in the toys. He's doing these triadic gaze shifts back and forth from the toys to the examiner.

He's very high proximity to his mom, and he's doing this spontaneous -- spontaneous looking at people and smiling. And I'll show you him again in 24 months of age in a minute.

Now this is the little guy -- by the way, this little guy after 6 months, his mom, his parents put him in early intervention. He got physical therapy. Then he started in our intervention program at 14 months. This is him at 22 months.

And we hammer joint attention. But I just want you to see that he has come a long way, but I think you can still see the subtleties of the social impairment here. Yeah. So he still has autism.

And this is the little man who had the later emerging ASD. So he's having a hard time getting his attention, and he's mostly interested in the wheels on the car. So does he look different to you than he did at 14 months? He did.

Okay. So I'm going to tell you about some trajectories, and this is a paper that we published in Child Development, a different paper from the one that I just talked about. And we had 204 baby siblings of children with autism, all of whom had outcome classifications and 31 low-risk controls, and we tested the children at these ages. And so, I'm going to show you some graphs of three groups -- early manifesting ASD, later ASD, and non-ASD.

I'll be showing you raw score data from the Mullen Scales of Early Learning and also raw score data from social and communication behaviors from the CSBSDP. But this is not in the paper, but I wanted to show you what this looked like so that you could see what happens with their ADOS scores.

We know we're not supposed to give the old ADOS-G before 18 months of age, but with Cathy's blessing, we did give it at 14 months. But you can

see the expected thing happened, and that is at that 14 months, kids are getting some score on the ADOS, and it kind of normalizes by 18 months. And this is the group who did not have ASD, and you can see they just stay with a low score all the way through their third birthday.

Whereas, the later manifesting or the later detected group has this huge spike between 18 and 24 months into this is their social and reciprocal and social interaction score. It spikes and it stays high all the way through the third birthday, and this is the group that we identified at 14 months. And they stay high all the way through their third birthday.

Now what happened in receptive language? You can see that at 6 months, the raw scores for the three groups are quite similar. This is the non-ASD group. This is the later manifesting ASD group, and this is the early manifesting ASD group.

And the curves here in receptive language raw score are hugging each other up until 14 months, at which time the non-ASD group has the textbook spurt in language development that you read about,

and the later manifesting group did not have that spurt.

The early detected group starts to diverge from the other two groups between 6 and 14 months, and as a group, they show a virtual plateau, and then they begin to have growth, and they track this other group but don't cross over it. This is what happens with frequency of initiation of joint attention in the CSBS Developmental Profile, which is a play-based assessment. It takes about 20 minutes.

This is the early identified group. This is the later identified group, and this is the non-ASD group. And this is where kids had to spontaneously show or point things out during this interaction.

But here's the thing that relates back to what Dr. Thurm was saying, and this has to do with frequency of self-generated shared positive affect. And the later manifesting group starts out at a typical level at 14 months, but by 24 months, they're really taking a major hit in their frequency of occurrence of this. Whereas, the early detected group, they're not doing it. What

little bit they gain, they lose.

I'm not going to show these videos right now. I can come back later and show them if we have time.

So, oh, you know what? I think I do have time, actually. Oh, no, because I'm going to show you the latent class findings. Right. Sorry.

So one of the things we wanted to know is, well, we're creating these classifications ourselves of early, later, and non-ASD. But what if, we didn't tell the software, the statistical package anything. We just put the data in, and we let it tell us what categories of development we're getting.

And just like Dr. Thurm said, we need to be looking at multiple aspects of development at the same time. So we did this latent class growth curve analysis, and this is what we found. We found four different classes of development.

We found an accelerated class, a normative development class, a class that had early language delay with later fine motor delay, and then a group that was slowing across the board. I'm going to show you what these two looked like, but I

wanted you to see where the kids with ASD were distributed across these four latent classes.

And so, the early manifesting group, none of them appeared in the accelerated growth. A small proportion occurred -- appeared in the normative group. Now I will tell you that the normative group had a little delay in the beginning, but then they caught up, and so it wasn't too much to write home about. But if you're into nitpicking like I am, that might mean something.

But then we have the majority of these kids showing up in the slowing class. The kids who have later ASD, we have one child who was in the accelerated class, and then they were rather reasonably distributed equally across the other three classes.

These are T scores. That means that they're standardized scores, and the mean on those tests is 50 with a standard deviation of 10. And so, anything between 40 and 60 is within normal limits, but if you drop more than a standard deviation between two ages, it's a concern.

So this is that group that had the early language delay, and this solid line is expressive

language. The dotted line here is receptive language. And then you can see that by 36 months, we had this fine motor delay. It drops a little bit. It's around 37.

And this is what happened in the developmental slowing class. Now remember these are T scores. So you can't say this is regression, but some of these kids are having actual regression as well. And so, the first thing to do drop off is language, and then everything else drops off together in a synchronized fashion starting at 18 months.

So the risk period really is happening sometime between 6 and 14 months for this developmental trajectory of this group.

Okay. My time's almost up. This is a treatment slide that we published, and just to show you that in an RCT where both groups were getting an active intervention that was identical, except the blue group got an interpersonal synchrony curriculum overlaid on that, that we see that if we teach it, the kids get it.

So we can manipulate these core deficits early in development, and Dr. Dawson has shown this with

Sally Rodgers and her work as well. And this here is the typical rate of acquisition of initiation and joint attention in the 6-month period. So this is a pretty robust finding.

So, basically, I just want to say that connectivity in autism appears to be disrupted, and it seems to become disrupted over time, and this disruption seems to be time sensitive. And do I have time to show just a super quick video?

Okay. So I just want to show that this is a study that's underway, and these are 1-year-olds with autism spectrum disorder, and this is the little 14-month-old that you saw earlier.

[Video presentation]

Dr. Landa: And so, I'm going to talk over this. But this activity may seem kind of ho-hum, but this is the way we really teach these kids early imitation skills and event sequences and how to really organize themselves in their little worlds.

And this is a comprehensive intervention that really hammers the social cognitive and language components, but I just want you to see malleability when you get them when they're 1. Now

not every child is going to have this kind of response.

And then, just so that you know, there will be a couple more summary slides that are going to be on the Internet that everybody can go back to just to summarize the findings in the end.

Okay. Thank you so much.

[Applause]

Dr. Insel: Thank you, Rebecca.

Finally, Cathy Lord, who comes to us now from a new position as Director of the Center for Autism and the Developing Brain at the Weill Cornell Medical College in New York Presbyterian Hospital. And I'm not going to take more of your time to introduce you because I think most people here know about you and your many accomplishments.

Dr. Catherine Lord: While I'm doing this, I could talk about screening. But actually, it's right -- no, it's not here. Excuse me. Screening.

This is just jumping around so as to not waste time. But I think we don't have a good screener, actually. I think my answer is we don't have a good screener that's useful across broad populations.

I mean, I appreciate that the South Carolina group used the SCQ. I think there are real limits to the SCQ. Oh, all right. There are limits to the SCQ, and I think we do worry or I worry that it may miss more capable kids.

It certainly didn't work in Norway, just sending it out in a packet as part of the MoBa study, which is a population-based study. We had every Norwegian child had complex motor mannerisms just because, again, getting to cultural sensitivity, that people thought that was probably a good thing, when we were talking about odd mannerisms, but we didn't say that.

So there are all kinds of subtleties there. We've been working on a phone screener, which is very short and can be done by somebody who is not highly skilled. It takes about 20 minutes. Just, and it seems to work pretty well with school age kids, with parents of school age kids who don't have diagnoses necessarily.

It doesn't give domain scores. So we were sort of hoping it could replace -- some of you know the long ADI and the 3-hour interview, and we were hoping it could replace that. It doesn't. But it

does do a pretty good -- it has quite good sensitivity, not great sensitivity. Wait.

Quite good sensitivity, specificity separating autism from other kinds of disorders is somewhere around 65, 70 percent. And that's about as high as we can get. And I think that's probably better than some of the things like the SRS, for example. But it's, you know, not great.

So we're trying, but I don't think -- I mean, I think as Dave said, there isn't a really good thing we can just send out with eight questions that's going to pull up autism.

And particularly when we're counting, we have to have high sensitivity, but the problem is if you bring in 40 kids who don't have ASD, for every 2 that do, you've wasted a lot of time. So let us know if you're interested in this phone thing because we're happy to distribute it.

But I think we're still stuck, and you know, the neurobiological community has tended to say, well, then don't look at autism. Let's just look at whatever these things measure, but I think that gets problematic because I think you're filling in at different levels.

You have people with autism. You have people who don't have autism. You have a lot of the world who have other things. And when we get all of them mixed into an autism sample, it's very hard to know what we're getting. But that's my bias.

Anyway, back to regression, and I'm happy to answer questions about that later. I think I'm going to cut as we go because I think I have very similar things to say, as Becky said and Audrey. And I decide to have that cock-eyed title just because I thought by now you might be almost brain dead looking at all these slides.

I do have conflicts of interest in that I do get royalties from Diagnostic Instruments if I'm not involved in the project at all, and if I am involved in the project, I give them to a charity called Have Dreams. And I've had research support from many of the NIH institutes. So I have many people to thank here, as well as Simons Foundation, HRSA, Department of Education, and Autism Speaks.

So what I'm going to do is very quickly mention a few general issues very fast because I think they've already come up. I'm going to focus

on talking about a study we did where we followed 78 children who were referred to us under 15 months of age -- so that was as young as we could get them -- where someone was worried about possible autism.

So it's different than baby sibs because someone had to be worried. You'll see that not all the kids had ASD at all or actually any problems. And some of them were baby sibs, but we tried to see those kids as close as possible to once a month. So we wanted to monitor -- I mean, just as Becky was talking about and Audrey, we wanted to monitor going forward what happened to those kids.

Then I'm going to jump a bit and talk about factors that affect how parents and all of us describe our children in interviews because there are a number of very significant methodological factors that influence what we say when someone asks us did your child ever do this? How bad was it in the past?

And then I'll show you a brief video, just because I think the theme of all of our talks is really emphasizing the commonality of children losing skills, children with ASD losing skills in

that second year of life, if not before. And the fact that this happens quite commonly, and it occurs in the midst of many other things.

But there also are kids who have quite extraordinary regressions, and I don't want to forget those kids. They're not very common, but they do exist. And I think they're a part of the source of why we feel an urgency to do something about this.

So just to flash this by you, I think the idea that autism really is a term that describes people who have very basic difficulties starting early on in social, communication, and something about repetition or sensory responsiveness. But it also includes many, many other things, some of which may develop because of the difficulties in being a child or an adult who have these original deficits, and I'll just skip through that.

And also I think, as Becky said and Audrey, we're talking about both the diminution of social skills and communication. So we're talking about things that don't develop or don't occur as frequently. We're also talking about the presence of things that we don't typically see in ordinary

people or at least ordinary people of the same age. Because some of the things, like flapping, we do see in tiny kids.

So because we're talking about both of these things going on at the same time, knowing what's appropriate and what occurs in other kids at that time is absolutely critical. Because I could say a child is abnormal because he doesn't say hi to me when I say hi, but in fact, if he's a 14-year-old boy who doesn't know me, that is not abnormal.

Whereas, if I'm his grandmother, and he's 2 and he loves me, then that would be abnormal. So we've got to take context into account and context really changes a lot in those first few years of life. And they also differ across kids and families.

And I think Becky already said this, but just we're talking about a developmental disorder that not only changes as kids develop, but we think that disorder itself changes children's opportunities for learning. And I think one of the reasons why regression is such -- attracts so many of us, so how can this be happening, is to watch families struggle with "what is going on with my

child" when you have a child where everyone thought things were going just great, and then it becomes clear that it's not.

No matter how that happens, that's a phenomenon that families experience that affects how they interact with families and I think affects families for years as they remember that process of realizing something is not right, especially if things seemed very right early on.

So we had a study in Michigan where we basically ran around and managed to get pediatricians and anybody we could think of to refer 78 kids where someone was worried about autism. Now of those kids, some of them we never saw any signs of autism. So they're not on this chart.

There was a group that didn't look autistic at all. Now some of those kids had other delays, but no sign of autism. We tried to see them as close as possible once a month. The same person, the same examiner or researcher saw the same child every month because it turned out when we first tried this, it was just too tense for families to be coming in and say, surprise, this is who you're

going to see this month.

Every 6 months someone who did not know the child came in and did an assessment, did another ADOS, did a Mullen, did a Vineland, and gave us an independent sort of diagnosis. The other thing you should know is that I made these poor examiners every month make a guess or estimate how certain they were that this child would or would not have autism at age 3.

They hated this. But it basically ended up being a 15-point scale of "I am absolutely sure that this child is going to have autism at 3" to a 1, which would be "I am absolutely sure this child will not have autism at 3," and everywhere in between. So we can use that as a metric of the clinician's sensitivity.

What they did when they saw the child was they gave them the toddler ADOS. So the parent was present, and then we also asked the parent just to fill out a much less systematic form than has been discussed earlier where we just said are there any things your child learned this month, and are there any things your child seems to have stopped doing?

And what I can say, actually, was we only had three families who ever said their child was losing skills in this context, the way we asked it. So I think it goes back to the need to ask more specific questions.

You can see that our kids with ASD, and this was done -- this was based on 3-year-old diagnoses again by an independent person or a set of people. The kids were quite smart. So even the kids who had autism diagnoses in that day had a mean nonverbal IQ of about 80. There was a lot of variability, though. There were also kids who had much more significant delays.

But they were also, I should say, all walking. So they were all walking when we met them at whenever it was, but before 15 months. So, again, that probably determined some of what we're finding.

And you've been looking at trajectories all afternoon, but this just shows you the kids who never in all of these assessments, the average was about eight assessments. Some kids had 15, 20 assessments. So each red line is a kid, and on the left are the kids that no one ever said they might

have ASD. And then on the right, somebody at one point, it only had to be one, got into the right.

And you can see the shading of the standard deviations. These are ADOS scores. Higher is worse. But look at this. I mean, it's just all over the place. The good news is, thanks to modern statistics, we, too, like Becky, got four groups, and things then begin to make much more sense.

So you can see over the bottom right, 40 percent of the kids, remember, of that 78, had very low ADOS scores all along. We also have a high group, up in the upper left, who were persistently very high.

And then we have an improving group, which is really good news, which is 20 percent of those kids, their scores went down. So they moved from quite high ADOS scores to actually not out of the woods, but pretty low. And that's a significantly greater number than we find in all of our other longitudinal studies. So this is just between the ages of 15 months and 3.

But we also had a worsening group over on the right, and those are the kids, about 20 percent of the kids, their total scores went up—so about 20

percent. You can say, well, that fits with the old estimates of regression, except that their parents weren't saying they had a regression.

And then when you look at what the clinicians said, again, the clinicians were quite good at saying for the kids that were up -- these are the groups are defined by the previous category, by how they actually changed. And then this is what the clinician said about them.

So 15 is absolutely sure this kid's going to have autism. 1 is absolutely sure this kid does not have autism. And you can see top left of the severe group, the clinicians got it. They were very confident. Bottom, except for that one whoopee child that you see bouncing around there, he -- the clinicians also were quite consistent. But you also look at the worsening and look at the improving. The clinicians are just all over the place.

And if you take the mean, I mean, this is a good example of what statistics can hide, is if I just showed you the blue line, the clinicians are showing that the child is more likely to have autism -- or children. And here, they're showing a

little bit of less likelihood. But they're basically all over the place.

So one of the lessons we learned was that the clinicians aren't any better than the parents month to month at saying this child is getting worse or this child is getting better. And these clinicians love these kids. So I think they were not seeing what the data would have told them if they'd actually looked at the scoring. And they weren't allowed to.

So we didn't find differences in gender, although we had a small proportion of girls. So maybe it's there, and we didn't see it. We didn't find effects of ethnicity. The siblings tended to be less affected than the other kids, in part because we think their parents were saying I'm worried because I have another child with autism, and he does this quirky thing.

And there's a lot of change even between 30 and 36 months. You know, many of these kids, although they have ASD, they're quite smart, and it's really a different story if you're talking and doing all kinds of things at 30 to 36 months than a child who has significant other

disabilities like language delay.

But then, just to make this even more complicated, when we look at individual items on the ADOS, what we see are different patterns for different items. All those scores I showed you before were totals, where we just added up how many problems do you have? So a high score means more problems.

And just to make this thing harder on you, I flipped it. So going up is good here. So in the white group are the kids that never had an autism diagnosis and at 3 we thought really were typical.

In the red group are kids who had other problems, primarily language delays, but not autism. And in the blue group are the kids with autism. So over time, and this actually fits nicely with Becky's just video, the kids got better in joint attention, response to joint attention.

On the whole, everybody got better. The autistic kids didn't get quite as better as the typical kids, but everybody's score went up.

Similarly, in use of gestures, again, slower with the kids with autism and slower with the kids

with developmental delays, but everybody's score is going up. But we have very different patterns on a number of items, and this again fits very much with what Becky just said.

So the blue are the kids with autism. Remember, these are kids that people already were worried at 14 months or sometimes younger when we met them, but their eye contact is actually getting worse while everybody else's is staying about the same. Same thing with overall rapport, which is just a way of the examiner scores how hard did I have to work to keep this child engaged with me? So that's also going down for the kids with autism and actually going up for everybody else.

And then we have almost, we have a number of other places where things aren't quite that clear, but again, response to name went down a bit, level of engagement, and shared enjoyment, again fitting with what Becky said. So the common pattern, similar to what actually Audrey reported, Sally Ozonoff reported, was that most of the kids who got diagnoses of ASD at 3 showed decreases in these things.

But we have to remember that at the same time, some of them were showing increases. And so, that's why the totals didn't necessarily go down for all of them. They're getting better in joint attention, some of the kids. They're talking. They're doing all sorts of things even while their social skills are -- they're losing some social skills.

I'm going to come back to this in a minute, but just let me switch gears. So when people have used particularly the ADI, which I feel personally responsible for, but I want to say, I did not write the regression question in the ADI. And I lost the battle with the U.K. We've refought the Revolutionary War several times in revising it, did not win. But people have analyzed that data a lot, and the problem is that it sets the bar very high for a regression.

You're supposed to be using 5 words on a daily basis for 3 months in order to lose skills. And when we did a more detailed study, we found that the average child who lost words, which doesn't include everybody who lose other skills, only had 4 words or 3 words and often didn't have them for

3 months. They might have had them for a month.

I mean, we required a month because it gets so hard to know if your child said it once. So do you count it? But, so there are real problems with using that in the first place. But the miracle and I think this group actually cited Andrew Pickle's study as one of the seminal papers or maybe Autism Speaks, where he found that parent report of regression defined in this way was one of the most distinctive properties that kids with autism had versus kids with language impairment.

Now I think that's important because although I don't think that the parents are reporting what we're asking them, most of those kids I don't think had more than 5 words used on a daily basis for 3 months. It just doesn't make sense with all the other data we had.

There is something about being able -- knowing that your child lost social skills that I do think is really, really important. And what it means is that we're asking something, and people are telling is something important, but it's not really what we're asking them.

We do know that if you use reports of language

loss they're much more reliable. In our longitudinal study, the parents agreed with each other more often if there was a language loss and were more consistent from year to year. It's just a more clear phenomenon than social delays.

But that doesn't mean, as the other speakers have said, that the social losses and the other kinds of things are not really important. And then there are a huge number of factors that most of us do not think about in terms of interviewing families. And I jumped into interviewing just because I happened to be around when Michael Rutter was writing an interview. But there are many things I didn't know and lots of people don't know.

So let me just give you two examples. One is called telescoping, which is that the farther away you are from a phenomenon that you're reporting in time, the farther away, the longer ago it was, the more likely you are if there was a delay to report that delay as being later. And we can document that.

We have a longitudinal study where we asked people the same questions. We met them when their

kids were 2. We asked them the same questions at 5 and at 9. This is the same sample. So not adding in people who had later development.

And people who when we met them when their child was 2 said that their child started talking at 20 months, by 5 were reporting it was 26 months and by 9 were reporting it was 33 months. Same families.

That also happened. This is autism and developmental delay. So it's not a unique phenomenon to autism.

We also tend to round things up. We tend to say, oh, around 3. Or oh, around 2, which really gets to be important when you're talking about tiny differences in toddlers. We don't say 17 1/2 months. We round it up, and we associate it with specific events.

This just shows you, if each one of these curves is on the same sample, what families said at age 2, 3, 5, and 9. And again, you can see that their time, the number of people who reported their kids as having very late language gets higher and higher the older the kids are when they report them.

This is a phenomenon that happens with anything. If somebody asks you, I don't know what, how old you were when you -- especially if it's something you're delayed at. Like if you were late in riding a bicycle, and you remember you were late, it's going to move back.

Now it has to hit a point at some point where this can't go on, but it's really surprising and very predictable how people do this. And it means if you're interviewing parents of 10-year-olds, when did their child start talking, you're going to get later dates than if you'd met them when their child was 2 or 3.

In addition, if you ask someone how abnormal a behavior is now versus ask somebody -- so I'm asking parents of 5-year-olds how difficult are your children's social behavior? And we'll get one answer. If I ask the parents at 10 how difficult was your child's social behavior at 5, it gets worse.

Now some of that you could say I didn't realize how bad it was. But it keeps getting worse, and when you look at other people actually seeing the kids, they're not getting worse. So we

all move what we think.

I mean, memory is a constructive process, and it's not that we don't remember it. It's just that we rewrite it a bit.

In addition, how I ask you makes a difference. So if I first ask you what is your child like now, and I don't tell you I'm going to ask you in a few minutes what was he like before, you tend to say he was a little worse before, but not very.

If I ask you first what is your child like now and then immediately afterwards what was your child like before, you make him a lot worse. And I think partly maybe this is true, more true for Americans than other countries. We're just optimists. We always think that kids were worse, and they're getting better.

So when we compared, we have data, for example, on exactly the same questions for kids at 5 and at 10 describing 5-year-old, and they're worse. They're almost never better. They're worse at 10 describing the 5-year-old. And I can make you do that even within a 5-minute interview.

If I want to make your kid look really worse, I can set you up to do it. Not on purpose, but we

have to be very, very careful because people use these numbers to quantify severity. And I mean, you know, I am big believer in looking at behavior, but this -- this is going to probably drive the neurobiologists into even more fits of we need a biomarker because we've got to be aware of these things.

And this affects how we interpret changes in the past. Again, not specific to autism. So what I'm trying to mostly say is that we have to be very, very careful in looking at regression. I think there are real phenomenon of worsening. They have to take into account where the child is now.

You have to have skills to lose them. It doesn't mean just because you have a regression that you were perfect in every way before you lost skills. And when we quantify where you are, we have to take into account what are you learning in addition to what you can't do.

Because maybe if you're learning a lot, people don't see the things that you can't do. If you have a child who's talking incredibly well, but doesn't look at you, maybe the parents are less concerned about whether he's not looking at them

than they would if a child who is not talking.

On the other hand, I want to end just because I do feel like there are kids who have quite extraordinary regressions in autism. And they're rare. I mean, I was thinking about it just preparing this talk. I think I've seen eight of these kids.

Three of them had autism already. They were kids who had autism and language, and then had regressions where they stopped talking. It was horrible. And the other five, I don't know. I mean, I didn't meet them until things were already going wrong. But they do exist. But I think they're very, very rare compared to the more common phenomenon we've talked about.

So let me just show you this because I think we need to recognize what it's like for families. This is kind of long.

[Video presentation]

Dr. Lord: So this is a home movie that the mom brought me. Now Meredith liked things with sticks early on. You can see her with her toothbrush. So she responded to her name. No one thought this was particularly weird.

So "have a bite of this." Grace is her sister. She just said "delicious."

So she's coming up to 2. And she just started making these funny little sounds, and she got very interested in this little routine that went with the TV show. But nobody thought much of it. I mean, they were actually videoing it because it was so cute.

But then she gradually started talking less and less and screaming more and more, and she was very hooked on standing in front of the TV. She also got very interested in sticks and stick-like objects. And her family responded by trying to do music with her.

But she also was attached to a dried banana peel, which began to really make her mom worried. But I think it's interesting that they're just trying to make this into something like play. And at this point, the mom had taken her to a pediatrician who had said nothing was wrong. And they then videoed her. She's in her little dance class. She's now about 2 years, 3 months. And she was just totally uninterested. So you can see her in the back. She started playing what they

described as hide and seek, where she'd spend a lot of time behind the curtains.

And this is Christmas. And her grandfather just said, "You don't care at all about us," and this is the beginning of special Ed. So this is when we met her.

Now the good news is she did start talking about a year later. She is now quite verbal. She's doing well. She still has autism. But she's quite a bright little girl and can do all kinds of things. So she doesn't have, I think, the prototypic outcome that we worry about with these kids with very severe regression.

But I partly wanted to just stick up for the fact that this does occur. It's not the most common thing, and I think in for the DSM-5 group, and I think Audrey's group, when we've tried to look for families who have kids doing this, it's very hard to find them. I mean, they do exist. But mostly when people talk about regressions, they're not talking about this.

They're talking about those kids who stopped talking for a little bit, didn't talk that much, have less eye contact, and this gradual phenomenon

that's often accompanied by other things that are good. So I think we need to remember that we are looking at a moving target that is not just ASD, but a lot of other things.

We also are looking at strength. So this little girl had a lot of strengths at 15 months, at 2 years. She had a lot to lose. And a lot of other kids wouldn't have gotten to that point, and I don't know what that means. But there was a dramatic change in her.

For the other kids, I think it's equally dramatic if we quantify it, but it's very, very hard to do this without careful, well-controlled measures because there are so many things going on in parents' minds and even as somebody who sees the child once a month, what's going on in your mind. And we need to try to figure out what is it that's lost and also what's moving along in a positive direction.

So, again, we're talking about clinical variability perhaps related to etiology, but we don't know. And then we hope somebody is going to figure out what the brain mechanisms are.

So, again, just to summarize, I think most of

what we describe as regression is a common phenomenon that involves various skills with some things decreasing while often other things are increased. I think we have to be really, really careful about using parent reports because it's very hard to remember, and there are well-known phenomenon that make it more likely that we will see things that aren't there, and we just need more information, ideally prospective studies that look at behavior and then link it with biology.

And so, I had a lot of collaborators. This went on forever, these studies, and families have really stuck with us. This is my Christmas card from them, and just thanks to them and thanks to you.

Oh, and this is something else. Okay. Thank you. So we should --

[Applause]

Dr. Insel: Thanks. We want to have a little bit of time for discussion. We're running really late, but I do think there are so many issues that the three of you brought up, I want to make sure that the Committee has a chance to comment or ask questions.

John?

Mr. Robison: Cathy, I guess this is mostly directed at you, but possibly others can answer. I ask you first because you're kind of an authority on diagnosis.

So you've obviously looked at thousands of people on the autism spectrum, and you stated at the end, "I've only seen eight really serious cases of regression." And then you showed that video as an example. And frankly, I mean, not to be disrespectful, that didn't look to me like that striking a regression compared to other stories I have been presented as an IACC member.

How would you reconcile the stated extreme rarity of that, the 60-some percent that we heard about in the earlier studies that lose some skills during development, which makes it seem almost normal, and then the many statements of parents that we on the IACC have listened to as one parent after another has gotten up there where you are said my son at 18 months lost all his language, regressed totally, and they attribute it to vaccine, mercury, whatever.

But those things seem so totally at odds. How

would you reconcile that?

Dr. Lord: I don't know. I mean, I guess -- I mean I --

Dr. Insel: Cathy, can you use the microphone?

Dr. Lord: Sorry.

Dr. Insel: Thanks.

Dr. Lord: I think that my colleagues were a little bit worried that my showing you this video I would slant things, but it was a significant regression. I think that the parents just didn't keep videoing her when things were bad.

And so, you know, you saw a girl who was very interactive and talking and imitating and gesturing and playing with symbolic play, and then who was doing really nothing but hiding behind curtains and squealing. So it was quite -- you know, she didn't we don't know if she lost motor skills. I mean, we don't really know.

And actually, when I met her at I guess about close to 3, she -- her fine motor skills were actually pretty good. I mean, if you were patient and got her attention, I could get her to do quite a lot. But she was very, very autistic then, which she had not been, at least I would say from these

videos.

I don't know. I think that -- I think that there are losses. I mean, I do think that most kids probably who have ASD do lose some social skills and communication. I think that really happens. How it gets organized into parent accounts, I don't -- I don't know.

I think that -- but we also do know that the parents in our studies were not very good at precisely telling us when things happened. And you could see that the times moved back.

I also think that we know from memory that people tend to organize how you describe an event around other events. So it used to be when I started in this field that families often would say, you know, he wasn't -- you know, he was fine until I went in the hospital to have his baby brother. I came home, and he was never -- you know, he had changed radically.

Nobody says that anymore, you know? But it used to happen. Or we get on vacation, and I came back from my 3-day second honeymoon, and he was not the same. So that used to be very common.

And again, maybe stress, the stress of having

a baby brother or the stress of your parents leaving you with a babysitter makes things worse and parents see it with a different eye. But it is hard to reconcile. And I think for those of us who have been looking for these cases where they are well documented, I mean, they do exist.

I'm really -- I mean, I put here. But I don't think they're not the ordinary. They're not common. I mean, I think we can all attest to that. I think there is now quite a large literature of it's not common.

It doesn't mean that it isn't real or it isn't important, but it's not common.

Mr. Robison: Do you have a sense of how much regression is a bump in the road and how much is a permanent and catastrophic loss? I mean, you said catastrophic loss was really rare, but you have not yet spoken to how much of what's lost in regression ever comes back. Is that known?

Dr. Lord: I think a lot of it doesn't exactly ever come back. I mean, I think that's part of -- that's a very good point. I think that although, you know, on graphs, it looks like a little loss, it's not a little loss. You know, to go from

freely looking at people and smiling and responding in a nonverbal way and intending to communicate to not, is a big loss, even though it's only, you know, six ADOS items.

So I think that is -- I shouldn't -- I don't mean to imply that that's not catastrophic. I just think that it's gradual and it's not the same thing as what happened with this little girl I just showed you who had so many skills and then lost them. If she didn't have them and she'd done that same loss a year earlier, it wouldn't have looked -- it would have looked more like our graphs.

But the fact that she got into her 2s and was this very bright little girl and picked up all these good social skills for some reason makes it look more catastrophic.

Mr. Robison: Thank you.

Dr. Insel: Walter?

Dr. Koroshetz: Yeah. So I guess a question for the group. I was struck by the fact that if you look at the data in the different classes that you talk about, the thing that strikes you is the variability of the clinician examination is all

over the place.

So it seems to me the signal is this noise. That in these -- that that's really something not to be ignored. And it also brings up the question of these are, you know, these are snapshots in time, and so the noise could be that things are subtle and people are reacting differently depending on the clinician interacting with the kid.

But it could also be that, you know, if you had a more continuous measure that you could make significant improvements. And the movies are quite dramatic. So that my question is, I mean, is it maybe more important going forward to just hook up a camera in the house and do kind of an automatic or semi-automatic analysis of the kid's behavior integral over time, as opposed to these -- these kind of snapshots in time.

Dr. Lord: I think the hard thing there -- I mean, partly the clinicians' judgments were not good when there was anything subtle happening. But the clinicians are the people who did the ADOS. So where we have very neat graphs are also clinicians, but they're doing something where they

have 10 standard tasks, and they have to code those tasks as they go.

So live people can do this. It's just that even while they're doing that, if you ask them their conclusion, they say other things because they're in the moment. So it isn't that people can't do it. It's that people need guidance, and then you need context.

The trouble with putting a video in somebody's house is so many different things happen. I mean, you have to have standard context. If nobody tries to get a child to interact with them or if they are very skilled, like the little girl's parents getting out the sticks, you know, they can make things that are actually quite odd look not so odd for a while.

So I think we do have to have behavioral context, but we can't just have streams of video. But we can do a better job of quantifying what it is that we see.

Dr. Insel: Anshu?

Dr. Batra: Thank you for this wonderful presentation. For me, this was very meaningful because this is what I do, and welcome to my world

and how fuzzy it is.

And you know, I think the issue here is that you're talking about development, you know, and development is so multifaceted and so dynamic that you can't just pin it down to one area. As Dr. Landa mentioned, there are so many other moving parts, literally, that we have to take into account.

So you can't just make a judgment on simply just joint attention or eye contact or fine motor skills. You have to look at the whole picture, and very often, it is not quantitative. It is qualitative, and that's -- that's why I think, you know, we're sitting here scratching our head, even after a tremendous presentation.

And to what you described in your data is exactly what I see in the real world in my practice, and it is and there are some kids I can absolutely right from day one predict that things are not going to go well. And there are some kids that, you know, absolutely prove me wrong, and then everything in between is what you basically described.

And there is not one single thing that I can

identify as the key component, which is again why we need to go back and really -- really look at these biomarkers of these various different trajectories and to identify them.

And John, to your point, in my world, what I saw was pretty dramatic. And yes, you know, there is even more. I mean, in my over 20 years of practice and my own three kids, I've probably, you know, had at least 10 regressions, true regressions, some that were very dramatic, almost overnight. And some that were gradual like that. And it makes your heart stop, regardless of how dramatic or how because it is -- it is you know something bad is going on.

And it just depends again what the etiology is. Just recently, I unfortunately had to diagnose -- I diagnosed a little girl with Rett syndrome that I had been monitoring and following and then boom, you know? Three months after I had seen her last, she lost some skills, which is a big no-no in my world.

So it's just -- again, I think what you've identified is, again, it's very clear to me because it's what I see. But again, it's still

very fuzzy because we don't understand why.

And the last point is, Dr. Landa, you mentioned, you showed a video of this little boy. You mentioned he initially had adequate joint attention, et cetera, and then he was I think the one who went on to develop ASD. And just as an aside, you mentioned, oh, he had motor issues.

And again, I think we have to look at those kids a bit more because he definitely looked like he had low muscle tone and things that I think again are earlier in the developmental sort of -- in development. Verbal skills, language, communication skills are definitely later in the developmental -- I mean they're later comers.

And so, I think, you know, looking at some of those issues earlier on I think are going to be helpful to help identify the trajectories.

Thank you.

Dr. Lord: I mean, I think one of the things that's I don't know if it's unique about human beings because I don't know everything about all animals, but actually, we should have David comment about primates. But we can do so many things.

I mean, a baby is pointing, you know, shifting gaze, nodding their head, offering people things. I mean there are so many things this baby is doing, and they don't come in all at once. And so, that's part of why we're stuck, and that's part of where we need certain kinds of animal models and other kinds of animal models are not going to help.

Because a zebra fish is not going to do 10 different things, they can't do any of those things that the babies are losing. On the other hand, it may be the zebra fish's brain is going to resort in a way that will be relevant to that.

Dr. Insel: So we've got a hard stop at 5:15 p.m., and I know there are still some hands up. Let's go ahead and hear from Lyn and Alison, and then we'll need to move on.

Lyn?

Ms. Redwood: Hi. I'll try to be really quick. Audrey, I was sort of awestruck by your presentation when you seemed surprised that there was such variability.

And I guess when I look at that data, my thought is this is somewhat predictable if we're

thinking that 50 percent of autism is environmentally driven and that these environmental exposures are occurring at different times, prenatal, postnatal. There is different doses of exposures, and there's different sensitivities that we're going to see this across the board variability with regard to when children start manifesting abnormalities or injury and the level of that.

The other thing that I heard loud and clear was that we need biomarkers. And when these children, even though I'm not certain that I agree that it's a minimal amount. I know my son was one of those children that had a very dramatic regression. I think it's important to capture those kids at that time and study the heck out of them.

And I think if we start looking, as Anshu said, with low muscle tone, what's going on with their mitochondria at the time, what's going on medically with them and metabolically and with their immune systems, I think then we can capture those definitive biomarkers that we need. Because looking at the behaviors is a little bit late.

Something was happening prior to that time.

So that would be sort of my take-home message is that we really need to be studying these kids intently when we see those regressions.

Dr. Insel: Alison?

Ms. Singer: So my question was for Dr. Landa. You didn't say this specifically, but it looked like from the data, that the kids who were diagnosed before 14 months were more severe in their symptoms.

And I'm wondering if that earlier diagnosis meant they got into early intervention and whether because of that they were eventually able to catch up or make additional gains versus the diagnosed later group?

Dr. Landa: Thank you for asking that.

It is true that at 36 months, based on the measures that the Mullen, there is no -- they're not wildly different at 36 months from the kids who were the early -- the later diagnosed kids. And not all of those kids went into early intervention, because some of the families didn't believe us.

Because even at 14 months, it's even though

when you look at these graphs, it seems like, wow, they should be so dramatically different, and of course, they were enough different for us to see it. But I would need to look at those treatment data. I'm sure they're in one of my papers.

But I do think that that could have been one of the rescue things that helped those kids mount a strong developmental trajectory. So I think that's a good point.

Dr. Insel: Well, I think this has been a really good discussion. This came about because of the conversation we had at the last meeting, wanting to talk more about regression and trying to understand it. Clearly, it's complicated, but it's really helpful to have three people who've probably thought about this better than anyone anywhere to guide us in how we think about this going forward.

Let's give this group one last round of applause.

[Applause]

Dr. Insel: We really appreciate your coming to help us understand this.

We've got one final session before we stop at

5:15 p.m., and this is the round robin session, which we try to do as often as possible to hear from members of the Committee. Many of you have brought slides. Some of you have very, very long presentations, over 30 slides. We're just not going to be able to accommodate that in the time we've got.

So I thought it was important to hear from people who had come from outside. Let me ask the members of the Committee to see if we can consolidate what you were going to say and make these briefer than 15 minutes. If we each take about 5 or 10 minutes to summarize what you think the other members of the Committee may need to know, that should get us around the table so that no one has to be neglected.

So, Noah, you are first up.

Mr. Noah Britton: Thanks. I'll only take 10 minutes.

So everybody breathe…Stretch. You're awake. Come on, we're alive. Don't pass out on me. I waited all day, but I only had 3 hours sleep. So if I can be awake right now, all of you can, too.

All right, so those of you who know me,

obviously, I am a self-advocate, person with autism. I'm also a psych professor, and I've worked with a bunch of kids all over the spectrum, adults all over the spectrum, and I've done published research.

And what I figured -- oh, sorry. I don't know why that's there. That's better, just kidding.

Anyway, so this is based on what I've seen as best I can. I realize I'm in a room with a lot of people who only believe in published research from famous science journals. And I want to address this conversation more to people who understand the value of experience.

You know, I think Larry or Walter was it, who said that video is so useful, and I think that video is more powerful than any ADOS score we're going to find, convincing us of what actually is going on. So I want to talk to all of you who understand the value of experience and understand that reality isn't necessarily numbers.

There are some things in life that are so obvious that you don't really have to question them. You see them, you know? The sun might feel hot. Am I older than I was when I took this

picture? Is this dog actually driving this car?

As obvious as the answers to these questions are, what I'm about to say feels equally obvious to me and to a lot of us on the spectrum who aren't consulted enough during research that defines us. We do our own research, though, and I think maybe the most reliable source for anything about Asperger's is the Asperger LiveJournal page at this point.

I see stuff on there, hypotheses no one is testing, and it's all self-reported. It's all people talking to each other, asking, talking, listening, saying does anyone else do this? And having read hundreds of journal articles, I say this is the most reliable thing. The hypotheses there I don't see replicated in research.

So I'll briefly go over some stuff I've learned from seeing that and working with kids and being, you know, myself for 31 years. So, as many of you know, hypersensitivity is the big issue with a lot of the underlying symptoms. Hypersensitivity to sensory input, social interaction, and change.

So neurotypicals look at the sun and see this.

People on the spectrum look at the sun and see this. This is going to make you irritable. This is going to make you not want to go outside. This is going to make you change your mood in a room that's got overwhelming lighting.

Most of you know this already, but this underlies a lot of the inconsistently identifiable symptoms reported in research. I'm going to say those symptoms aren't exactly symptoms, but responses to this core hypersensitivity issue, and I think this is particularly relevant when explaining meltdowns.

So how does it feel when you're working intensely on something and someone calls your name? Someone interrupts you. This is how a lot of social interactions feel for us. Eye contact especially, you know, it's irritating. It's distracting, and this hypersensitivity to people increases our arousal level so much we're paralyzingly preoccupied by others nearby and have to flee until we can calm down.

I think this explains a lot of the executive functioning delay as well. You can't think straight when you're preoccupied by evaluation

apprehension, which many of us are when around people we don't know.

I read reports saying that we sometimes under-react to stimuli. I don't think this is due to an insensitivity but rather to being so overwhelmed by our senses that we can't react, like a deer in the headlights or because we've numbed our ability to respond to our senses because we know our reactions aren't acceptable to others, as I did many years ago. I think this makes me more tolerant and also less responsive to my feelings.

I think this general hypersensitivity underlying it is a delay in our ability to recover from the normal increase in arousal that comes from sensory input or the presence of others, which explains our decreased ability to process and respond to global rather than specific change, like changing your mood or changing your perspective so you can understand someone else's.

Or changing your activity, all of which require an all-encompassing internal change. This is what we really don't do well and underlies the meltdowns I had when my mom would surprise me after school with a trip to the dentist, or the

difficulty we have in processing and accepting criticism, which, again, we can be receptive to, but not until we've recovered from the disproportionately high emotional shock and the need to alter our entire perspective.

I think this explains our troubles in immediately understanding others' perspectives. You know, the theory of mind idea, which, in itself, explains why we don't care about your rules for grooming and other social norms, which I think has some benefits, but also obviously makes us less popular sometimes. And also explains our difficulties with multitasking and our superior ability to find flow and engage in work and continue for many hours on one task.

I think this is why we're so systematic in our thinking because it takes away the need to make quick changes, which are literally emotionally painful, and I'm sure many of you here understand what I'm talking about.

All of this supports the SHANK3 research that talks about the idea of, you know, indirectly decreasing the speed of glutamate transporters, overwhelming certain neural connections, and

failing to trigger others, and maybe this is responsible for our delay in long-term potentiation and weaker ability to learn implicitly or respond to conditioning. Sorry that was very dense, but the cause of autism would be.

Anyway, the only way I can process mental changes that life requires is by prepping myself. So I look at my schedule. I see my agenda for the day, and I start to get into the mindset I'll need to have for things like lecturing or dancing hours in advance. So by the time it happens, I'll be ready.

If I don't have this opportunity to prepare, I'm confused, delayed, and useless in this environment. Having a predictable schedule gives autistics the chance to get in the mindset needed for what we'll have to deal with later, making us more capable of handling spontaneity within that type of situation.

Based on those core symptoms and my intensive study of the most effective interventions, I suggest the following for interventions. Predictable structure, concrete explanations, and advance warning for all changes, as well as the

obvious things you have to do with everybody like showing genuine love for and interest in the clients, not judging their unusual outlooks or behaviors, and offering intrinsically motivating opportunities for mastery.

Whether your intervention is about teaching your clients improv acting, letting them play with blocks, or giving them cognitive therapy seems to matter less than including those other things, which people don't manualize because they seem to be too abstract, but they're so important.

Behavioral problems, anger, and poor self-awareness tend to naturally decrease in an environment that's designed that way but will increase if the subjects are exposed to treatment to try to push down those symptoms directly, like physical or emotional punishment, which obviously no one enjoys. And our hypersensitivity to conflict and interpersonal interaction makes punishment several times more painful for us than for typical people.

So we're not taught, but rather traumatized until we learn helplessness or try to defend ourselves by developing behavioral problems. This

is the sort of thing I don't hear said in the typically designed research.

I would like to make one addendum to my section of the 2012 strategic plan relating to treatment, which is that many poorly designed treatments can be very effective if implemented by staff who recognize the importance of these things. But if they don't intuitively understand this, these treatments are no more effective than those same people playing videogames with their clients all day. And that's one reason why I couldn't list any of those interventions as being effective in the 2012 strategic plan update.

Their published results alone aren't enough to satisfy the scientific criteria needed for effectiveness, though some do show promise. And I think this is because they're approaching things from the outside in, rather than accepting that if you want to help autistic people come into your world, you're going to have to enter our world first and help us grow from there.

So these are my sources. Any questions? Again, I tried to rush. All right, I'll let the next person --

Dr. Insel: Wow - that was great.

Mr. Britton: Thanks. Thank you.

[Applause]

Dr. Insel: Thank you so much. That was terrific.

Sally?

Dr. Burton-Hoyle: Okay. And I will, again, work to be within 10 minutes.

About this is -- we're going into year four of our College Supports Program at Eastern Michigan University due to demand of people saying we wanted our children to go to college. And even though there's lots of people with autism, there aren't any numbers specific to how many people are in college that are on the spectrum.

Some of it has to do with self-disclosure, and that ability or inability of parents to embrace and help their children understand who they are, and the strengths and skills that come with autism, as well as the needs. And what we know is that people don't struggle in college because of their abilities. They struggle because of the whole navigating the university environment.

We know that college success is possible with

the right supports, and the supports have to be respectful and much from what Noah was talking about. It's kind of honoring the disability culture of each individual and seeing what are their strengths? What do they like to do?

We are doing this at Eastern Michigan University, which is 23,000 students. And we've got, you know, every kind of program. And students come into our program. They're admitted into the university.

So this is not a getting ready for college. It's not, you know, there are different kind of certificate programs in college life sorts of things. When you come into this program, you are a student at Eastern Michigan University.

And our College Supports Program is an individualized and person-centered approach. We do person-centered planning after intake and records reviews and all that sort of things that is designed to support students as they transition to college and progress through graduation. Our students are between the ages of 18, and they come in, you know, at a traditional age.

And some people have completed a community

college program, and they've done that community college program, in a 2-year community college program, many times they've taken 3 or 4 years. So they might come in at, you know, at 20, 23, or something like that. So we've got quite an age group.

And some of the key components of our program have been in building an infrastructure to being an autism-friendly campus and honoring and not feeling sorry for, but honoring the culture of the disability. We have learned that the university community is defined by the student.

So when a student comes to EMU and they come into our College Supports Program and we've done person-centered planning, we do not try to make them do this or do that. We help them find and kind of craft what their strengths are, with an emphasis on the career planning that focuses on their strengths. And that's used quite a bit to help them in any kind of behaviors perhaps that might act as barriers.

We have done extensive training and workshops with our Board of Regents and every conceivable office on campus. The Admissions and Registrar and

the Food Service and every single RA in our dorm system has my cell phone number, which is very scary, so that in the middle of the night if they didn't know what to do, they would call.

And all of our students live in a room by themselves, and there are no special autism dorms or autism wings or anything like that. There are dorm rooms around the campus and based on accommodations that the disability resource center can approve. And they don't pay any additional money, too. They just pay whatever they would pay, a normal sort of price.

And then also we've what we do is that we hire mentors that are graduate students that provide how much ever supports are needed for that person to be successful, and it varies. And it varies from the mentor, you know, knocking on their -- the dorm room door at 9:00 and saying, "Come on, let's go to class," to meeting them in front of the building, to if they take notes and all that sort of thing, they meet after class and kind of go over things. But there is at least a daily check-in for each person.

And one of the things that at the university

level, faculty and people are understanding that this is beyond accommodation. So this is not just accommodations. That's a free service provided for that's a legal accommodation through Section 504.

This, families that apply and their children come in our program there are fees that they pay because we have to pay for staff to accompany them to do whatever sorts of things that are needed. Academic supports, organizational supports. We might help them set up their notebook. Visual support.

That all is done with the person so it isn't like that their dorm room is filled with, you know, Velcro schedules and things like that. It's all in accordance with what's going to help that student, help them with whatever their daily living skills.

A lot of negotiating, compromising because sometimes people get away from home, and they think I hate showers. I'm never going to take a shower ever. And that might sound great, but doesn't work well.

And so, we've done things like, okay, based on the person-centered plan, we know you love to

swim. And there's a rule at the swimming pool that says you have to take a shower after you -- before you get in the pool. So then it's like then they swim 5 days a week.

So, I mean, there's different sorts of ways that we work around the daily living skills. The social living again defined by them.

They had an open house called "fajita fest," and all the clubs and organizations are there, and the fraternities were rushing hard. And one of our students, they wanted him to go become a TKE. And so, all year long, his parents are fighting it. Everybody was fighting it. He's joining because he got a job this summer, and he's going to pay for it.

So the whole idea of self-determination. That's what he wanted to do. He wanted to be a TKE. His parents are like, oh, my gosh, what's going to happen here?

And then helping everybody get a job on campus is so important. And even if it's a 6-hour a week, 4-hour a week job, they've got somebody else telling them, hey, you can't pick your nose or, hey, you know, you need to use deodorant before

you come in here.

Or you can't talk on your cell phone. You can't text. Any of those sorts of things. It's somebody else doing them, and it's really quite valuable.

And then this next year we've got 18 students, and I think 13 of them are going to be in the dorm. So the residential life is going to be dorm intensive, where we're providing whatever kinds of supports are needed for them to be a part of the community.

And we have students that have written books, self-published books on Amazon. We've got artists. We've got musicians. We've got all sorts of different kinds of things that we support them in doing that they do as part of the university with the support of our mentors.

We have recreation groups. The student signs off on their FERPA, meaning that we -- I can talk to the faculty, and I can talk to the family, and the student, of course, is in full knowledge of this. There's nothing done like behind the student's back. Nothing, nothing like that.

Coordination with student's medical provider.

Some of them Skype with their psychiatrist or psychologist, you know, long distance, or we've set some up in Ann Arbor that they've seen those.

A student came in through our intake process, and he's fascinated with the Manhattan Project. We found a history professor who did his dissertation at MIT on the Manhattan Project. So getting the university, the faculty mentors, the community mentors, different individuals like that.

We start the school year off where I sit down with the faculty and the student, if they want, and we go over the syllabus and the accommodation letter. And that faculty member then understands that, oh, this is a person that if they get nervous, they're going to get up and they're going to pace. And then that's okay.

Or this is a person that they're going to doodle, and then that's okay. As long as faculties know ahead of time, we have not had one single problem, knock wood, in 4 years. So, and they understand that somebody is going to be with them, you know, some of the individuals.

We have to teach them how to use office hours appropriately, that they can't just go and sit in

the professor's office for all 3 hours, that -- and then we have lots of mid-term meetings and lots and lots of meetings. So there's lots of communication.

All of the students are on either Google Calendar or a daily planner that's hooked into me so that they learn how to plan so that like Noah was talking about, the consistent schedule. We had snow days. This year, Michigan had a bad winter.

So that what is going to be the back-up plan when the university is closed? We had 3 days off from school. So these were students, who didn't really care much for having a day off from school, but we had a plan in and different kinds of activities were done.

And I'll skip through here. Some of the evidence-based practices we use in our visual supports. We have social work -- social work, speech and language pathologists, and clinical psychologists that work with us on we've got different social groups, and social mapping is something that's used. Video modeling is used. I run a graduate program in autism, and all my students do various sorts of things with them as

well.

The video modeling is that, okay, what's the social problem you want to have help on? One young man didn't like that his face didn't move. That somebody told him he had a face that looked -- looked monotone. He wanted to learn how to smile and react because he wanted a girlfriend.

So we did video modeling on those sorts of things. So it's all chosen kind of by individual -- and develops scripts and recreation groups. We've got somebody that runs with the university faculty running group, you know? And some that run just with other students.

The prices range from all over the country. There's programs like this all over the country, some that aren't even affiliated like as being a university student, that are anywhere from $2,000 a semester to $40,000 a semester. Ours is approximately $5,000 to $8,000 a semester, depending on how intensive the supports are.

So they pay for this on top of their -- of their tuition. And then usually people who live in the dorms. There are scholarships, thank you, Autism Speaks. You have scholarships that many of

our students have applied for.

Vocational Rehab Services, I know in Washington, D.C., we've got two students coming that they're going to pay all the college support fees, and they call them MEP plans, but plan savings for college, those plans.

And also the way our Medicaid plan is written, focused on community, people that are CMH, community mental health eligible. There's a line item for community living supports that they're using to pay for some of their fees. So, and then this is a book written by the Autistic Self-Advocacy Network on navigating college.

So it's an important thing to know the difference between -- you know, there is community college, which is always, always, always the best way to start and just take like one class at a time. And then there is also like 2-year programs that just focus on daily living skills, and then there's like our program, which is a 4-year degree program, except it's probably going to be longer than that.

And then there's college internship programs. So this is that last Web site you can look at.

Then it goes State by State for various programs around. Okay?

Dr. Insel: Okay. Thanks very much.

Dr. Burton-Hoyle: Thank you.

[Applause]

Dr. Insel: Jan, we've got three more presentations. So --

Ms. Crandy: I can do it very fast.

Dr. Insel: -- I have to ask you to be quick. Thanks.

Ms. Crandy: I wanted to share with you about ATAP. It's Nevada's innovative approach to improving child outcomes. It's self-directed. It began in 2007 as a pilot. We've increased the number of children that we serve and the plan types. And we've set in progress measures, which I want to share those with you.

The program went into statute in 2011, became a permanent program. In 2013, ATAP received $11.7 million to be used over the biennium through general funds and tobacco settlement dollars. So we're not even touching Medicaid, and we need to expand how we're going to continue to fund so we can serve more children. As you can see, by 2015,

we're only going to be serving 572 children.

Our purpose is to eliminate or decrease the level of lifelong supports, and our priority is to improve child outcomes and support changes that make a significant difference to the family. We created the program to assist families with the expensive cost of treatment, and we provide a monthly allotment to help families pay for this treatment.

The monthly allotment pays for supervision and parent training and amount of treatment hours weekly. It's community based, and the parent and the caregiver is the driver of the program. They select the plan type and their provider and their treatment team.

And most of the programs are home based, although clinic-based options are available. The parent manages the budgets and tracks the treatment hours and approves payments online.

Our eligibility is they must be under the age of 19 and have a diagnosis or a special education eligibility of autism, but it must be accompanied with ADOS in the assessment report.

ATAP seeks to empower parents with the

knowledge through education and training to take an active part in their child's outcome. They're required to attend parent training monthly, and they're also required to do parent hours or to fund hours because the money that we're providing in our assistance program does not pay for all the treatment hours that are required in our plan types.

Providers are typically -- most programs overseen by a BCBA or a licensed behavior analyst, and the weekly treatment hours are delivered by behavior interventionists which receive ongoing training and based on each child.

I wanted to share with you the different variety of service plans. We have a comprehensive plan, a variety of targeted behavior plans, insurance assistance and collaboration because we want to utilize cost sharing. They are designed to support transition through the plan types. And the maximum length that a child can be in ATAP is 7 years.

The comprehensive plan, a child has to start before they turn 7, and it addresses skills across all domains on a daily basis. The maximum time

that a child can be in this plan is 4 years, and they have to average 25 hours a week of treatment.

Our targeted behavior plans are narrow in scope, and they address parent and caregiver priorities. Typically, it's crisis intervention, behavior management, daily living skills, functional communication skills.

The extensive plan, a child must average 15 hours a week, and typically, kids that are in the comprehensive plan transition to this plan.

Our basic plans, these are typically older kids and are coming in for learning iPad, learning how to use iPad skills. Typically, that's only for 1 year, and then they're exited from ATAP.

They can get back on the wait list again. A lot of parent training to make sure that parents, when they exit, they can implement and teach skills.

Therapeutic plans, most of our kids are receiving therapy through insurance plans. So not very many kids opt to choose this plan.

Social skills, we know this is important. We want our kids to be able to be employed in the future so kids transition through to this plan, or

kids that are higher functioning that start our plan, families elect this. They have to use approved curriculum, and it includes individual sessions and group sessions. But we require parents to enroll their child in an activity with typical kids so that the skills can generalize by the second quarter of the plan.

Transition plans, we really believe strongly in transition, and it outlines a systematic decrease in ABA treatment and supervision hours. And the last quarter is intended to only address increasing parents' capabilities.

Our insurance assistance and collaboration plan is designed to promote and utilize cost sharing. We help families pay for their co-pays or their yearly deductible so they can start accessing their insurance.

Our insurance mandate went into effect in 2011, and it has a cap of $36,000. So it's not going to buy research levels of treatment. Our plans, also we try to collaborate with other agencies. We have collaborations with one of our school districts. We've done pilot programs with them where they pay for part of the supervision

and part of the hours, and we pay.

Safeguards have been put in place by ATAP to ensure a child's treatment journey is guided by data-driven decisions. Some of those are listed here. Mandated reviews by our care managers, quarterly and annually. We have designed we call them our impact data targets, which is we assess annually on 64 targets, and we have an online data system to track these outcomes.

Other outcome measures at intake and at close. We do a number of assessments. We look at the Vineland, cognitive skills, language assessments. We do the PDD behavior inventory, which measures treatment effects. We look at kids, how they're doing in school, the difference. We also look at the parents. Are we making a difference in the caregiver?

And we have taken video on kids at intake and annually since 2007. So we have quite a large video library. Our annual performance indicators, those are called our ATAP impact targets. It's progress on 64 behaviors or skills. Eight of them are considered critical targets, which by having these targets; we are also driving the providers

to make sure that they're addressing them because they have to meet certain percentages of the targets and the critical targets to continue in the plan type.

The critical impact targets become a priority. The first five are parallel with our Early Intervention Services skill set data requirement, which we passed in 2011 also as a -- to start tracking outcomes coming out of early intervention. The other ones, all of these we believe are foundation skills.

These are a sample of some of our impact targets that forecast a decreased level of care after exit. And we also are really looking at the percentage of time in regular education, if that changes, making sure that if we meet all these targets, we know that the level of care that we have to help take care of them in adulthood will be decreased.

This is we're doing this pretty cost effective, I think. Our average cost in January was about $1,500 a month. This is our cost per plan type. So families can receive up to $2,000 a month on the comprehensive to do 25 hours a week

of treatment, and this kind of shows you how many plans that we are serving and the cost across the plans.

Know that kids, any functioning level across the spectrum we serve. I wanted to show you so you could see a breakdown of most of the plans that we're serving are comprehensive or the extensive plans. And this is a breakdown of the age of kids that we're serving in the program.

So this was -- our goal is to serve 307 kids by the end of June. I think we're on target to make that. But as you can see, the breakdown of the ages, I want to show you our wait list so you can see why we're not getting those little guys as soon as I would like to.

Five years is the longest time when we picked up kids. We look at this every single month. So the month that we picked up the child, he had been on the waiting list close to 5 years. Our average is 560 days. So it's a long wait.

These are things that we need to improve. The future direction is utilizing more pay sources to enable all children to have access to research levels of treatment.

Really wanting to -- and our State is looking at this. Our legislative health committee on healthcare just voted to support it in the legislation for 2015 Medicaid coverage for ABA in our State plan and removal of the statutory limitation of the $36,000 cap to get it in line with the Affordable Care Act.

Now that child outcome measures are established and being collected, additional funds are needed to fully evaluate and analyze program outcomes and long-term childhood outcomes.

Very proud of Nevada. I also shared a history of its commitment to a lot of bills that have been passed to make changes effective in Nevada.

So thank you. I appreciate you letting me share that.

[Applause]

Dr. Insel: Thanks very much, Jan. Actually, that's a great set-up for the last two presentations from Melissa Harris and John O'Brien.

Mr. O'Brien: Melissa, are you online?

Ms. Melissa Harris: Yes.

Mr. O'Brien: Great. So I think earlier we had

distributed and talked a little bit about the informational bulletin that we put out last night. So it is hot off the presses, and we thought we would use this opportunity to talk to the members of the IACC about what we're doing.

This is an important policy clarification that we've done as it relates to State plan services, and so I've asked Melissa Harris, who is our Director of the Division of Benefits and Coverage, to talk a little bit about what you're seeing in that informational bulletin.

So, Melissa?

Ms. Harris: Thanks, John. I'm happy to be here with you all remotely today, and I know we're pressed for time as well. So I'll make it really fast.

The informational bulletin that we issued yesterday was to describe the role of the Medicaid program in providing services to children with autism as a population. This will not come as any surprise to you all, but we have been contacted by a lot of States over the last couple of years, mainly as a result of court cases in which the States were being mandated to offer either a

service package generically to children with autism or, more likely, were being required to offer a specific service called applied behavioral analysis to children with autism.

And the courts were deciding that ABA services specifically were part of a State's EPSDT responsibilities. EPSDT, in a nutshell, is the requirement that children under -- individuals under the age of 21 in Medicaid be given any medically necessary service articulated in the Social Security Act at Section 1905(a). That lists all of the mandatory and optional services that our States should be offering in its Medicaid package.

Obviously, for an optional service, the State is in the role of decision-maker as to whether they offer that benefit to their adult population under -- or over the age of 21. For kids, though, if it is listed in 1905(a), it is mandatory to be provided to kids, regardless of whether it's provided to adults, assuming the child meets the State's medical necessity criteria for receipt of that service.

There had been a rather tortured history of

the role of the 1905(a) and the menu of services as it related to treatment for services that were really more characterized as learning a new skill or maintaining a skill. And CMS had really been part and parcel of that confusion indicating that the -- that 1905(a) really was not a good fit for habilitative services.

In reality, that's not the case. There are a couple of individual benefit categories in 1905(a) that have language restricting the scope of that service to restorative services. I'm mainly talking about the rehab category in 1905(a), which is the main authority used for the provision of substance use and mental health services.

But if you look at the rest of the authorities in 1905(a), there is no limiting language in the statute or regulations that say that services have to be for the restoration of a skill previously attained and then lost.

So we've really done a rethinking in a number of avenues, including with States as part of the Medicaid expansion conversation, how habilitative services as a whole fits into the Medicaid benefit package. And pretty quickly, once you start that

conversation, you end up talking about children with autism, ABA, other services for kids on the autism spectrum disorder, and where was CMS going to end up with that?

So you couple all those moving pieces together with an increasing number of court decisions that were saying I don't care where you cover it, but it is part of your EPSDT obligation, the time was really ripe for us to make some sort of statement about the role of EPSDT and the Medicaid benefit package as it related to this population.

We very intentionally did not call out a specific treatment modality for these kids as the service to be offering, even though ABA is the topic of a lot of the lawsuits and it's probably the benefit that is most understood by a lay person. Our goal was not to say we expect States to cover applied behavioral analysis. It's more like the expectation is that children with autism are a population that needs to have their service needs met under the State's EPSDT obligations.

ABA is one way to do it. We included a link to a report that the Federal Government had sanctioned a couple of years ago that spelled out

some other treatment modalities, and we certainly think there is a lot of room for the evolution of additional treatments to come on the scene that, you know, could be offered in addition to or instead of or in some sort of conjunction with ABA or any other kind of treatment.

So that the take-away message is not that there is any particular intervention that is mandated. It's more like this is the population of children that needs to be served through EPSDT including through the provision of services to address their autism spectrum disorder.

So States are going to need some time to digest this information and recognize that they need to implement services that they have not been required under EPSDT, and in fact, at sometimes, you know, have been expressly prohibited under EPSDT. So we kind of beg everyone's patience as the dust settles and States plan out their way forward.

But we really are interested in your experience as this guidance rolls out on the ground and any kind of fits and starts that you're seeing, or a State that you think is really doing

a good job at tackling this issue we would really like to hear about that as well.

So let me stop there, and I'm happy to answer any questions in the couple of minutes that we have.

Thanks.

Dr. Insel: Thank you.

Let's open this up for questions. Idil?

Ms. Abdull: Hi. Melissa, if you were here, I would hug you. Seriously and you would be the first CMS person I would hug.

[Laughter]

Ms. Abdull: And I -- no, let me finish. Let me finish because it is extremely painful when your child -- when CDC says learn the signs so you can act early, and then NIH or NIMH says to act early, get early intervention, right? And then you go to the Medicaid, which is CMS, and they say, oopsie, we don't pay for the intervention that we were told by the other departments within HHS.

So I have been fighting with a laser-like focus at CMS just to say, look, if the child has a medical condition, and if CDC and NIH and NIMH are telling families to get early intervention,

whether it's ABA or floor time or developmental or what have you therapy, I think we have to be able to cover it for low-income children. And so, I'm getting like goose bumps. I think I'm so done harassing Marilyn Tavenner and Cindy Mann. You can tell them I'm off their butt.

I think this is a really good day because it doesn't necessarily have to be ABA. I know Autism Speaks pushes ABA. But if we can get children get covered for what they need, whether it's habilitative or rehabilitative under EPSDT, for all the States. That way, they don't have to necessarily put up funding for the 1915(i) or additional funding for the 1915(c).

That is very difficult to get, as we found out in Minnesota, because a lot of States don't have the funding. So they didn't do it. The legislators just don't do.

But thank you so much. Thank you. You have just made my last day of IACC.

Ms. Harris: So I imagine this is Idil?

Ms. Abdull: Yes. Hello.

[Laughter]

Ms. Abdull: Hi.

Ms. Harris: Well, you know what, I'm glad to have the opportunity to speak with you. I know that you have been making the rounds because you've been experiencing things on the ground that didn't seem quite right to you for a long time. And that it's always frustrating when there isn't a straightforward path from the current operations to a future arrangement that really seems to be legitimate.

And so, you know, we know that this was not specific or this issue wasn't specific to any one State or any one parent, but yet, you know, the time where we can kind of continue walling off EPSDT benefit package for children with autism was really over.

And some could say that the groundwork for this document was actually the Affordable Care Act, when it put habilitative services front and center in the list of essential health benefits for use on the exchanges and for the Medicaid expansion population and immediately touched off conversations of what is that in the Medicaid context. And you know, we're going down this path with eyes open on the -- for the expansion

population. What about the traditional Medicaid population? And then further on, what about kids?

And so, we've been struggling ever since we were really made aware of the breadth of the essential health benefits menu with where to go next. And then, so you coupled that with the speed and the number of court cases that were happening, and it really, you know, begged the question of what CMS was going to say here.

So I appreciate your reaction to this. I hope -- our fervent hope is that this isn't just like guidance to be released as a subtle statement, but that it really does move the ball for kids and their families on the ground. And I can foresee States needing help in figuring out what services to stand up. You know, we don't necessarily want to see the world blanketed or the country blanketed with ABA specifically, but I think it's safe to say States are going to be receiving some pressure to stand up that benefit.

To the extent that any of you can help a State figure out what other interventions are around, ABA is fine to implement. But we really want to be talking about the universe of interventions that

have some -- some evidence behind it, you know, even in very small context that really does result in better health outcome for these kids.

ABA might be perfectly legitimate for -- you know, for the really young kids, and as kids start to age further, it might be less conducive to offer a particular service in lieu of a particular other one. So there's going to be all sorts of space for people to help States and help CMS, frankly. I mean, we never hold ourselves out as any kind of clinical expert in this field or generally. But to help us all figure out what makes the most sense and how a child-specific identification of services is really going to be the philosophy that carries the day.

And so, I -- I appreciate, you know, hearing your reaction to this. And we've had some other good reactions from stakeholders in the 24 hours or so since the guidance has been on the street. But we don't -- we don't kid ourselves this is going to be an easy lift, and so there's room for all of us to be kind of keeping the conversation going to make sure that movement is happening and, you know, everybody is kind of rowing in the same

direction to get from point A to point B.

So I appreciate what -- you sharing your reaction with us.

Dr. Insel: Noah?

Mr. Britton: Hi, Melissa. It sounds like this is a step in the right direction, and I really do appreciate the fact that now doctors aren't going to turn to illegally prescribing off-label drugs that will make the kids worse.

That said, I think now they're going to turn to prescribing ABA that's often going to make some of the kids worse, and I'm wondering is there anything that can be done to stop this being over-generalized? You know, obviously, if I were 3 years old and getting ABA, I would be 10 times worse off than I am now.

It may be effective for some people, but I guess what I'm wondering is do you have anything in place to stop this from being generalized? And also what can -- what would you need to be convinced to recommend other interventions that are more recent?

Ms. Harris: Let me take the second part of the question first. Typically, CMS hasn't had to issue

any kind of statement jumping on the bandwagon of a particular intervention. Now we've done it a couple of times before, once with assertive community treatment and once for peer support specialists. So it was basically saying be aware that these services are legitimate for coverage under Medicaid, and understanding that because of the EPSDT mandate, saying that really did indicate that it was an expectation that States would cover this under EPSDT.

Certainly, ABA has its supporters and its detractors, and we're a little hesitant to take a firm stance either way because it can be such an individualized determination of whether ABA would be the perfect intervention for one child, and even a child of, you know, the same age who's presenting with maybe slightly different symptoms, ABA would be less efficacious for them.

And so, I think, you know, to get -- kind of straddle both components of the question, you know, I think to the extent that a State proposes to us to cover in their State plan various interventions for children with an autism spectrum disorder, we're going to be hard pressed to say,

no, that's not appropriate for the children in your Medicaid program.

I think the entity that's really going to need to hear very loudly about the universe of interventions that are out there, including those that have been developed since the publication of the report that we linked to in our guidance, is the States. And they're going to -- you know, as they are crafting the services for this population, what they're going to know is have they been mandated by a court order to provide a particular service?

If yes, then they need to stand up that service. What else should be brought up as their menu of services for this population? If they haven't been mandated to do ABA or any other specific kind of intervention, what makes sense for them to add to their Medicaid menu, understanding that they could be asked about ABA by any number of stakeholders? Again, because it's kind of like the most universally known treatment, for better or worse.

So I think to the extent that there are other reports that have some evidence base behind them

to say even for someone that looks like this, you know, that this particular benefit has been proven effective, States are going to want to know that.

Because of the variety of individuals who would fit under that birth to 21 age span, you know, regardless of whether or not they have autism spectrum disorder or not, States always struggle with if they stand up a particular service under the State plan and it becomes a mandate under EPSDT, does that mean everybody from birth to 21 always gets that service?

And one of the conversations we've been trying to have with States without, you know, being all that formal about it is, you know, States, there is still room for some -- for some determination of what is going to make sense for a particular child, and it doesn't mean that every kid with the same diagnosis is going to have the same medical need for a particular service.

It's more like the State needs to put a system in place to be able to work with the care team and the individual child and family to say what makes sense for this child, and it might look very different for what makes sense for another child.

So understanding the universe of options available to a State under this heading of treatment for children with an ASD diagnosis is going to be critical.

So I wouldn't -- I would focus a lot of your attention on the States. To the extent you've got something that you want to share with us about another intervention so we've got it in our back pocket as we're talking to States about this, we're more than happy to take a look at it It's like I said. We don't ever want to proclaim ourselves as any kind of clinical expert, and we're advising States as they come to us to say help me articulate the kind of services you want to see in our State plan.

Dr. Insel: Melissa, we're going to have to adjourn in just a minute, and I want to make sure that John has at least one minute to talk about the waiver program. So we're going to have to cut this short. But this is a great message, and I think hard to imagine a better way to end this particular meeting until we hear from John about the waivers.

Mr. O'Brien: Yeah, I did want to mention that

at the end of the informational bulletin is a mailbox that if you have additional questions please feel free to email Melissa and staff your questions. Because as she said, we're learning as we're going along.

So some of what Melissa talked about is going to be available through the EPSDT program, but not all the services that people need, whether those are adults or kids, are going to be available through those different types of services that are in our regular State plan. And those typically then fall into our home and community-based services program.

We have three of those programs. They have kind of been built up, built on by Congress over the years, and so we did in the middle of January release some regulations which we think are fairly important regulations in terms of the way that we oversee that particular program and how States, more importantly, design their home and community-based services programs.

And the three parts of the regulations, and I'll send Susan the link to those regulations and to the summary of the regulations because those

two are several hundred pages long, are number one is that allows States to collapse their HCBS programs.

We have almost 300 home and community-based services programs, and therefore, you know, States are ranging anywhere from, you know, 2 or 3 to up to 10. And so, this gives them the flexibility, collapse the programs which help, in terms of managing the programs and also in terms of having some consistency of the experience of care that people who need different services get or have when they participate in those collapsed programs.

More importantly, the two other provisions are that we are very clear about what we expect both in terms of a person-centered plan and the person-centered planning process. We had some language in some of our technical guidance under the 1915(c) program. But now we have some clear language that is in regulation that sets forth what we expect are in those plans and how those are developed.

Last, but not least, and I think this is the one that has actually brought the most attention, was how we have defined the qualities or the characteristics of home and community-based

services both for where people live, but also what people do during the day.

And I would encourage you all to look at what those characteristics are. But for the most part, these characteristics are really focusing on ensuring that people really are integrated into the community and that for those facilities that are identified in the regulations, there are a number of facilities that are identified as institutions and, therefore, cannot participate in the home and community-based services program.

And then there are certain types of facilities that we have identified that may, in fact, have the characteristics of an institution, and it is up to the State to be able to demonstrate that those institutions or those facilities, in fact, are home and community-based services. Or they meet the qualities or the characteristics of those home and community-based services.

In order for States to be able to meet the requirements that are in the regulations, we are requesting that they do an environmental assessment of all the services, both residential and nonresidential service types that are in their

home and community-based service plans. And that they identify which ones fit nicely into home and community-based services, they meet the characteristics. Those that clearly don't and those that, frankly, might need some time over the course of the 5-year waiver period to transition to become either institutional or to become home and community-based services.

Those transition plans have to be put out for public comment. The States have to take those public comments seriously. We are going to look at those public comments so that we make sure that when we do approve a home and community-based services waiver that, in fact, those facilities that may have been identified either by the State or by consumers, families, other advocacy groups identified as not meeting those characteristics, that we have a clear path about how those facilities and, more importantly, those individuals that are in those facilities are going to be part of the State's transition plan.

So stay tuned. We are just now in the process of getting some of the first States' transition plans. We got a few early on, and we sent them

back to do their homework because we didn't feel like they had probably done the public comment process in a way that we thought was necessary and respectful.

Dr. Insel: So, John, if you can send the links to Susan, and Susan, you can send them out to the Committee, that would be a great thing --

Mr. O'Brien: Yep.

Dr. Insel: -- I think for people to take a look at and maybe even be able to provide feedback within their own States as well as to you.

Mr. O'Brien: Well, that's right. And you know, again, we're trying to keep States and we're trying through various consumer groups, letting those consumer groups know when those plans are -- transition plans are out for public comment because we want to make sure that as many people comment on transition plans so that we -- we know where we've got problems and where we don't.

Dr. Insel: So that's a great way that we can work together here. So if you can provide that, especially to the foundation and to the nonprofits who are around the table and who have people in all 50 States, that's a great way to get both the

clarification that Melissa talked about as well as the waiver changes. It's a great way to disseminate that. That'll be helpful, and then, hopefully, we can get some feedback.

Well, we have come to the end of a very long day. We started the day by introducing new members, and so it's a little bizarre to be ending the day by closing out this tenure of this really outstanding committee.

I want to thank all of you for your service, which has been extraordinary. We've had many, many meetings. We've taken on some tough issues. There have been moments of, I think, strong criticism about the Committee, but also moments of success. And we've heard some great science. We've heard a lot about the service needs.

All of you have been fantastic to work with, and it's been an honor to serve as chair. I am hoping that at this point we're hitting the pause button and not the stop button.

I think for the research folks, it's actually kind of a fast-forward button. As you might have heard or might remember from the last meeting, we have a huge number of RFAs around autism that are

just getting funded at this point. So the funding level continues to increase, not to stagnate.

And that will happen with or without the IACC. There's a real commitment to do more and to do better.

At this time, last thing I'd like to do is just to thank Susan and the OARC team for all that they have done to support us.

[Applause]

Mr. Robison: I think we should also -- you know, we should thank you, too, Tom, for your work being a chair. I think really you've done a very fine job.

[Applause]

Dr. Insel: Thank you.

Mr. Robison: The only thing that could make it better is if you had someone stationed at the door with $1,000 envelopes for us on our way out.

[Laughter]

Dr. Insel: We'll make a recommendation for that in the new legislation. Or lunch. It's actually easier to get the $1,000 than the lunch, as you probably know.

Dr. Koroshetz: I think a cure for autism.

Dr. Insel: That would help.

Thanks very much, everybody, and safe travels. And we will be in touch in terms of legislation so you'll know what to expect going forward.

(Whereupon, at 5:23 p.m., the Committee adjourned.)