U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

INTERAGENCY AUTISM COORDINATING COMMITTEE

FULL COMMITTEE MEETING

MAY 9, 2006

The Committee convened at 8:50 a.m. at the National Institutes of Health, Building 31, Rm 6C10, Bethesda, Maryland, Thomas Insel, M.D., Chair, presiding.

PARTICIPANTS:

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

DUANE ALEXANDER, M.D., National Institute of Child Health & Human Development (NICHD)

JAMES BATTEY, M.D., Ph.D., National Institute on Deafness & Other Communication Disorders (NIDCD)

ELLEN BLACKWELL, M.S.W., Centers for Medicare & Medicaid Services (CMS)

KATHRYN CARBONE, M.D., U.S. Food & Drug Administration (FDA)

JUDITH COOPER, Ph.D., National Institute on Deafness & Other Communication Disorders (NIDCD)

JOSE CORDERO, M.D., M.P.H., Centers for Disease Control & Prevention (CDC)

DENISE DOUGHERTY, Ph.D., Administration on Health Research Quality (AHRQ)

LISA GILOTTY, Ph.D., National Institute of Mental Health (NIMH)

BARRY GORDON, M.D., Ph.D., Johns Hopkins University School of Medicine

LEE GROSSMAN, Autism Society of America (ASA)

JAMES HANSON, M.D., National Institute of Child Health & Human Development (NICHD)

DEBORAH HIRTZ, M.D., National Institute of Neurological Disorders & Stroke (NINDS)

GAIL HOULE, Ph.D., U.S. Department of Education (Ed)

LARKE NAHME HUANG, Ph.D., Substance Abuse & Mental Health Services Administration (SAMHSA)

ALICE KAU, Ph.D., National Institute of Child Health & Human Development (NICHD)

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

AUDREY PENN, M.D., National Institute of Neurological Disorders & Stroke (NINDS)

CELIA ROSENQUIST, Ph.D., U.S. Department of Education (Ed)

JON SHESTACK, Cure Autism Now

BONNIE STRICKLAND, Ph.D., Health Resources & Services Administration (HRSA)

SUSAN SWEDO, M.D., National Institute of Mental Health (NIMH)

LUCILLE ZEPH, Ed.D., Center for Community Inclusion & Disability Studies

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PROCEEDINGS:

Dr. Thomas Insel: Good morning and welcome to the Interagency Autism Coordinating Committee meeting. We have a pretty full agenda and a rather short day, because a number of people want to leave to go to an event in New York that's this evening, so we'll jump right in. I thought given that we do have some new faces around the table, it would be good to start with a round of introductions and I'll just start with the person to my left.

Dr. Susan Swedo: Good morning. Susan Swedo from the NIMH and I'm the Chair of the NIH Autism Coordinating Committee.

Dr. Jose Cordero: Good morning. I'm Jose Cordero from the Centers for Disease Control and Prevention.

Dr. Audrey Penn: Good morning. Audrey Penn, NINDS, here for Story Landis.

Dr. Deborah Hirtz: I'm Deborah Hirtz, NINDS, representative to the NIH Autism Coordinating Committee.

Mr. Jon Shestack: Jon Shestack, Public Member of the Committee from Cure Autism Now, father of a 14 year-old with autism.

Dr. Bonnie Strickland: I'm Bonnie Strickland

representing Merle McPherson from the Health Resources and Services Administration.

Mr. Lee Grossman: Lee Grossman, President and CEO of the Autism Society of America and a dad of an 18 year-old with autism.

Dr. Kathryn Carbone: Kathryn Carbone representing Dr. von Eschenbach from the FDA. I'm the Associate Director for Research at the Center for Biologics.

Dr. Celia Rosenquist: Celia Rosenquist, National Center for Special Education Research.

Dr. Lou Zeph: Lou Zeph, Director of the Center for Community Inclusion and Disability Studies at the University of Maine, which is Maine's University Center for Excellence and Development Disabilities and also the guardian of a 32 year-old with autism.

Dr. Denise Dougherty: I'm Denise Dougherty. I'm the Senior Advisor for Child Health and Quality Improvement at the Agency for Health Care Research and Quality, part of HHS.

Dr. Barry Gordon: Barry Gordon from Johns Hopkins, but here is a public member and the parent of a 14 year-old with autism.

Dr. James Battey: Good morning. I'm Jim

Battey. I'm the Director of the National Institute on Deafness and Other Communication Disorders, and also the Chair of NIH's Stem Cell Task Force.

Dr. Larke Huang: Hello, I'm Larke Huang. I'm the Senior Advisor on Children in the Office of the Administrator at the Substance Abuse and Mental Health Services Administration.

Dr. Judith Cooper: Good morning. My name is Judith Cooper. I'm with the National Institute on Deafness and Other Communication Disorders and I serve on the Autism Coordinating Committee for NIDCD.

Dr. Cindy Lawler: Cindy Lawler from the National Institute of Environmental Health Sciences. I'm the program representative for the institute on the Autism Coordinating Committee, NIH level.

Dr. James Hanson: Jim Hanson. I'm the Director of the Center for Developmental Biology and Perinatal Medicine, the National Institute of Child Health and Human Development, and I'm also representing Dr. Alexander, who will be here a little bit later.

Dr. Alice Kau: I'm Alice Kau, program staff from NICHD. I sit on the Autism Coordinating

Committee for my institute.

Dr. Lisa Gilotty: Lisa Gilotty. I'm from the National Institute of Mental Health. I sit on the Autism Coordinating Committee and I'm here today for Ann Wagner, who is the Executive Secretary of this Committee.

Dr. Insel: I'm Tom Insel the Director of the National Institute of Mental Health and I have been asked to Chair this particular Committee. So with that as a charge, let me say that what we have done, for those of you who are new to the Committee or who are sitting in for someone else. In previous meetings, we have often taken about 10 or 20 minutes at the outset to just update on recent scientific advances or events within the field that we think people need to know about.

I think in the interest of time, what we will do today is probably a little bit different. We'll start off with just a quick roundtable to get updates from each of the agencies. Before we start that, I wanted to mention that in November we will be facing the three year anniversary of the Autism Matrix, which was something close to a strategic plan for autism research and we were hoping to use a good part of the November meeting to update you

on progress on that document.

The way this was originally structured, for those of you who weren't involved at the time, was that it was in three groups. It was sort of short-term, 1 to 3 years, middle-term, 4 to 6, and then 7 to 10 year goals for autism research and they were then staggered by the degree of risk or the degree of difficulty in getting those particular goals done.

So since we will be at the end of the short-term part of the matrix, we thought this would be an opportune time to look at what's been accomplished and also to ask the question of whether we need to do any mid-course correction for the 4 to 6 or the 7 to 10 year time frame.

Any questions before we move on to talk about that?

Mr. Shestack: So that's going to be an official recommendation of the group that you reconvene the original panel, some additional stakeholders and have them produce a short report or evaluation of the NIH progress towards the road map at the three year point, with recommendations for reevaluation or restating goals?

Dr. Insel: So Jon, you're making this as a

recommendation that what we do is use the November meeting to report out on an assessment of progress on the matrix, based on reconvening the original group along with some additional stakeholders and hopefully do that in August, September, then use the November meeting, essentially, to report on that assessment?

Mr. Shestack: I was thinking of a short report and a long frank discussion that would be my official recommendation.

Dr. Insel: Okay. Unless I hear any dissent about that, the recommendation, we will take that to heart and we'll plan to convene the original group sometime late summer, early fall, so that by November, by the November meeting, we'll be ready to provide a short assessment, sort report out on what the findings are, any recommendations for a change at this point in the out-years of the matrix, and then we will open up this meeting to considerable discussion about where we are at.

Very good, any other general issues before we move into the reports from each of the agencies? Okay. Then we're going to start with -- well, the way this is on the schedule, Bonnie, I think you are up first for HRSA. And the way we have done

these have been to -- I'm not sure if you were here at the previous meeting, but so you have an idea --

Dr. Strickland: I do.

Dr. Insel: -- just kind of get people up to date.

Dr. Strickland: I do. I'm buzzing here. I'm not sure how to deal with that, but I assume it's not going to interfere with my update. Well, let me go down to the seat where apparently I'm supposed to be. Okay. I knew I was sitting in the wrong seat. Well, there's a reason for that, I realized that Ann is 10 steps ahead of me. She has already got a place for me at the table.

First of all, let me tell you that Dr. Merle McPherson, who is the HRSA representative to the IACC, has accepted a detail to the HHS Office on Disability to coordinate the 9th International Congress on Serving Children and Youth in the Community. And that's going to happen in December. And we weren't quite sure how to deal with her representation on this Committee, since I understand the Office on Disability is also being added to this Committee.

So what we came up with is that between now and December, I would be the HRSA representative to

the IACC. Merle will be the representative from the Office on Disability. But she couldn't be here today, so I really am sitting in both seats today, both representing her as well as HRSA.

For those of you, new to the Committee or attending the meeting for the first time, I probably should give you an update on the Services Subcommittee. That committee was put together two years ago and Dr. McPherson has co-chaired it during that time with Sybil Goldman from SAMHSA. Sybil has since moved on as well and Larke Huang has taken her place.

But that committee, that subcommittee is comprised of all of the service agencies represented on this Committee as well as interested private/public members, including Lee Grossman and Lucille Zeph, and we worked together for the past two years. And a year ago, we completed a services road map, which is now on the IACC website and there for you to review. After we completed it though, I mean, it's quite comprehensive and, obviously, there were not resources for everybody to take on all of the road map, and so each of the agencies identified a piece that they felt that they could undertake with existing resources and

that's what we have been doing for the last year.

I should say before I leave the topic of the Services Subcommittee that we have rotated the leadership of the subcommittee and Gail Houle, who is not here yet, but I think will be here, and Lee Grossman have agreed to co-chair the subcommittee for the coming year, with the promise that it's a one year rotation.

For HRSA's part, we agreed to convene an expert work group to look at the health aspects of getting services to children and youth on the spectrum with ASD. To do that, we convened an expert work group and we have been working with them over the past year to put together a set of service guidelines for the health profession, for the medical home as we referred to it, the primary care provider for children and youth working with other aspects, other elements of the system.

The idea is to get all of the pieces working together. Our focus happens to be health, because that's what we do. But to get the health care system working together with education, with social services, with the subspecialty providers to create a comprehensive system of services that would facilitate kids getting from screening to

identification into services into adulthood without huge interruptions in services and assuring quality in the services they receive.

That document is now in its preliminary draft. We will be meeting with the expert work group in June and again in August. We anticipate that it will be completed by the next meeting of this Committee and will be released about the same time as the American Academy of Pediatrics policy statement and tool kit on ASD. So we are really looking forward to that.

I see in the packet that CDC has a fact sheet on the latest prevalence estimates from the National Survey of Children's Health. I expect that Jose will be talking a little bit about that, but I would like to say that HRSA's Maternal and Child Health Bureau supports that survey financially and we'll also do so in the future, and we also have the National Survey of Children with Special Health Care Needs, which we also cosponsor with CDC and those data should be out next spring.

So, essentially, what we have, at this point, are data every two years on children with special health care needs and children in general and part of which is a prevalence estimate and description

of impact of autism and other children with special health care needs on this -- well, the impact of the system on children with special health care needs and children with ASD.

So with that said, I'll close and turn it back to Tom.

Dr. Insel: Great, thank you. Questions or comments for Bonnie before we move on? Okay. Let's go to the -- well, I'm not sure if anyone is here from the Administration on Children and Families? Do we have? Merle is going to be representing? Not here? So let's move on to Denise, Agency for Healthcare Research and Quality.

Dr. Dougherty: Okay. Thank you very much. The Agency for Healthcare Research and Quality, we have nothing to specific to report on autism. However, we have some exciting new programs that I think will be of interest to people in this group. One is the Effective Health Care Program in which entities, people, individuals can submit ideas for topics for comparative effectiveness.

So using the easiest example, two different drugs for depression, for example and there is actually a draft report out now for public comment. So there are a lot of opportunities, I think, as

effective treatments come down the pipe to do comparative effectiveness studies and we're doing that for Medicare, Medicaid and SCHIP Program priorities.

The other big activity that's part of the Effective Health Care Program is also a big contractor report with guidance on setting up registries that will facilitate effectiveness research and comparative effectiveness research.

So I think that will be useful for tracking children with autism and then also seeing effectiveness research when such research cannot be done using the standard RCT, so it can be done over time.

And I think that's about it.

Dr. Insel: Great, questions or comments for Denise? Everyone know what effectiveness research is? Maybe you should say a word about what that means.

Dr. Dougherty: Okay. Effectiveness research is the kind of research that's done after say a drug or a device or a behavioral intervention has been shown to be efficacious with one of those small very controlled trials that carefully select the patients. Effectiveness research takes the next

step with those efficacious treatments and researchers, whether those treatments actually work in a broader population, in a different or in a broader array of settings than the small rigorously controlled settings that the efficacy research takes place in.

So we have -- effectiveness research gives us a better sense of the scope of how drugs, devices, interventions work than the efficacy trials do.

Dr. Insel: Thank you. Okay. The Department of Education, so, Gail, you're on.

Dr. Houle: Good morning and thank you for having us as usual for the IACC meeting. We have been, in a lot of ways, maintaining our efforts in the area of autism. One of our new focuses that we're putting some much needed resources into is in the area with the Office of Special Ed Programs in the area of technical assistance provision. And to that end, as a Federal Agency, we don't provide technical assistance generally at the local level.

But what we are doing is developing some interactive web tools that will enable states and regions and professionals and parents, to some extent, to access a matrix, an interactive matrix of Federal Office of Education technical assistance

resources. And for example, you can go to the matrix and you can put in autism and you can put in your region or your state and the matrix will allow you to interact and pull up a list of all the technical assistance providers that we fund in that area who are working in the field of autism and also some information on where to contact them and what they would provide to you as a user of the matrix or a technical assistance consumer.

So that's one of the things that we have been working on over the past several months. And I'm hoping that in the Services Subcommittee today and this year we'll be able to talk more about training and technical assistance and how we kind of link that at the federal level to the practitioner level. So this is one tool that we're working on to do that.

We're continuing our training efforts and making plans to actually have some announcements in the near future to continue the professional development work that we're funding in the field of autism. And we also have the Institute of Educational Sciences that has announced an RFA for a center in autism. So that's available on the Department website and there may be a

representative coming to this meeting and so may be able to get you a little more detailed information on that RFA.

But if you look at ed.gov, you'll be able to access that information now. Thank you.

Dr. Insel: Thank you, questions or comments for Gail? I think I skipped CMS. I'm sorry.

Ms. Blackwell: You did.

Dr. Insel: Well, we'll go back.

Ms. Blackwell: Well, I was late, so I deserved to be skipped. I'm Ellen Blackwell. I'm with the Centers for Medicare and Medicaid Services. I neglected to introduce myself, because of my tardiness. I also have a child with autism. I'm here today to talk about what's going on at CMS and it's a very busy place, so I'll try to talk fast.

Just so you get some idea of the scope of what we do, we're serving 8.4 million people with disabilities, that group accounts for 44 percent of our total Medicaid expenditures, which was $102 billion in 2003. Right now, everyone in our building is preoccupied with the Deficit Reduction Act of 2005. I'm sure some of the other agencies here have also been touched by provisions in this Act and we are rapidly writing regulations that

follow from the DRA.

Many of these might impact people with autism. I'm going to run through them very quickly and I will mention the sections, in case members in the audience are interested in looking further into these. Section 6041, 42 and 43 are big sections. They allow states to impose premiums and cost-sharing on certain groups, including prescription drugs and emergency room co-pays. This is pretty new for us, so states can do this through their state plan amendments. We have some states that are already participating in this option.

Section 6044, this is also a big deal for people with autism. It allows states to provide coverage. We call it the "benchmark provision." The health insurance coverage has to match Blue Cross/Blue Shield, federal insurance coverage. Under this, if states elect to put up a population into this provision, they still have to provide wrap around coverage for children ages 0 to 19.

Typically, we would provide any Medicaid covered service for this group up to age 21. However, if a state does take this benchmark coverage, it drops their EPSDT coverage to age 19. We have three states that we approved recently,

Kentucky and West Virginia, they have submitted state plan amendments that put benchmark coverage in place, Idaho, I was told yesterday, has an amendment pending.

Section 6052 redefines Medicaid case management. We provide a lot of case management services for people with autism in schools through service coordination and other entities. There has been a lot of confusion in the past about what is Medicaid case management. Basically, it allows people to gain access to needed medical, social, educational and other services. So that provision will further define through a regulation that we intend to publish in July what Medicaid case management is as it differs from regular case management that might be provided through other agencies or entities.

Section 6062 allows families with incomes up to 300 percent federal poverty level to purchase Medicaid insurance for their disabled child. Previously, families and individuals had to meet certain income qualifications, so that's a big provision.

Section 6063, again, this one is kind of interesting. It's a five year demonstration project

that will allow some states, we have $218 million, 10 states we'll be looking and taking children who might be institutionalized in what we call psychiatric residential treatment facilities. Some folks refer to these as residential treatment centers. To be licensed under our rules, they have to fit into this box, Psych under 21 Facilities. And we'll be looking at the cost associated with keeping kids in the community and institutional costs.

Section 6071 is called "Money Follows the Person Rebalancing Demonstration." It's a five year program, $1.75 billion, that looks at transitioning folks from institutions to community settings and states will receive additional Medicaid funding in addition to their regular statement match, which typically hovers from around 50 to 78 percent to participate in this program.

I'm going to skip one section, which is my favorite, for a minute. Section 6087 allows self-directed personal assistance in the state plan. It allows people to exert choice and control over their own services.

And Section 6201 talks about additional federal payments for hurricane-related

demonstrations and I know we're going to be having a presentation on that today.

Section 6086, this is the one that's close to my heart. This expands access through the Medicaid State Plan option to provide home and community-based services without measuring people against an institutional level of care, which is required in our 1915-c Waiver Program. This is something new. We have to start operating this program in January of 2007. We are currently writing a regulation. Again, that's Section 6086.

If anyone has comments about this language in the law, please, send them to me at CMS. We are making great efforts to interpret the language and the law. The institutional level of care is removed. Instead, people are measured based on their needs. So there are some issues with this particular benefit, the way the Congress wrote it, that we are struggling with.

So we appreciate everyone's comments before we publish our interim final rule. We also have applications due on June 15 for our Real Choice Systems Change Grants for Community Living. This program has been in place since 2001. We have issued 297 grants totaling $240 million. They

facilitate life in the community for people with disabilities. They are on our website at cms.hhs.gov.

We also have a long-term care research study in place. Eight states are participating. We are looking at how they are rebalancing their long-term care programs to help people stay in the community. We have promised this Committee a promising practices paper that actually what we plan to do is put some information on our website about how our states are serving children and adults through our 1915-c Waiver Program.

We have right now. I looked at our data yesterday, 280 waivers in 50 states. Four of these are autism-related waivers, Wisconsin, Indiana, Maryland and Maine. Although, I personally don't like to refer to them as autism waivers, because we are also operating 87 waivers for people with developmental disabilities, 85 waivers for people with mental retardation, 6 waivers for people with mental illness and 49 other waivers.

Obviously, states that don't signify that they are serving people with autism may very well be states that are serving people with autism on one of these other waivers. So it's really hard to

pinpoint.

I'll talk for one minute about our Katrina response. We have another type of waiver called an 1115 Waiver that we used to provide emergency services to folks who were hurricane evacuees. That program continues through June 30th. As of March 28th, there are 32 approved Katrina demonstrations, 4 Hurricane Rita amendments. These continue health insurance coverage and abbreviated eligibility provisions that are typical to Medicaid, so that people's health care could continue even though they had to move to other states.

We have also recently granted eight states the authority to activate uncompensated care pools for payment to providers of last resort who assisted people affected by Hurricanes Rita and Katrina. So that's it for CMS. Again, anyone who has comments on any of these DRA provisions, you can send them to me. Look at the law. We are just like everyone else. We try to figureja out what the Congress meant and then write it up. And sometimes we struggle. The regs have to be in place.

Actually, we have to implement some of these programs before our regulations are issued. So, you know, whatever comments you have are very helpful

to us. They are going out in interim final form, which means that there is room for comments. And we're doing our best, but we're like everybody else. So send comments, please.

Dr. Insel: Well, thank you. That's quite a summary. I think in a previous meeting we heard how CMS is the single largest payer for autism services generally in the nation, but one of the things that you talked about here the 6086 section around home-based care.

Ms. Blackwell: Yes?

Dr. Insel: I think this group would probably be interested in hearing more about your vision of how that will roll out and how for instance, the assessment would be made of what could be reimbursed.

Ms. Blackwell: Well, it's an interesting benefit, because we offer some more benefits. Medicaid offers optional services under the state plan. But under our 1915-c Waiver Program, we can offer services like respi-care, enhanced personal care, environmental modifications, habilitative services that we can't offer under the regular state plan or that we weren't able to offer until Section 6086.

The other issue with the 1915-c Waiver is that people have to meet an institutional level of care; that is they have to be qualified by the state to be at a hospital, nursing facility or institutional care facility for the mentally retarded level of care. That is waived with the state plan provision.

Also in waiver, states are allowed to target particular individuals. As I mentioned, people with autism, people with mental retardation, people with developmental disabilities. But under this state plan option, we have mixed feelings about this, as we develop this reg. The Congress wrote this in a manner that does not allow states to target beneficiaries. So our thinking, at this time, is that the only way that states might be able to target a particular group is by offering a certain set of benefits.

So we have to define what those benefits might be and then states will have to choose benefits. For example, to target, I mean, I was thinking about this yesterday, people with autism, a state might want to elect services that are more typically used by this population. For example, respi-care, personal care, possibly habilitative services, possibly some behavioral services.

But I think of it as reverse targeting, because the only targeting allowed by the Congress is elderly and disabled. So states may tell us how many people they want to serve. Say it's a thousand people and they may establish waiting lists, but as soon as they do that, the cutoff cuts off. So, as I said, we're struggling to some degree with the language.

Under the C Waiver Program, states can say, okay, we're only going to serve people with autism. We're only going to provide that group with this set of benefits. But the people have to meet the institutional level of care versus the needs-based level of care. So it's been very interesting for us and we're curious to see how states will implement the benefit.

As I said, it's active in January, so we expect, as soon as we publish a State Medicaid Director Letter and a Template for the benefit, to start getting these in before we publish our regulation.

Dr. Insel: Ellen, let me just see if I can clarify one thing about what you have just said. At a previous meeting one of the points that was made by many people around the room, the coverage for

services that is available depends on where you live?

Ms. Blackwell: Absolutely. Well, to some extent. I mean, Medicaid guarantees a basic set of benefits under the state plan option.

Dr. Insel: So that's the clarification question.

Ms. Blackwell: Right.

Dr. Insel: So --

Ms. Blackwell: Everyone receives basic benefits through Medicaid. And then states are also able to elect optional benefits, mental health benefits that could impact children with autism.

Dr. Insel: So for the 6086 provision when that goes into effect --

Ms. Blackwell: 6086 is completely new.

Dr. Insel: So will that be dependent on the state deciding that yes, this is something we're going to cover?

Ms. Blackwell: Yes. It's an optional benefit.

Dr. Insel: So some states will have this and some won't?

Ms. Blackwell: Some states will not. We probably expect some states will not use this it's 1915-i in our statute, benefit at all. Many states

now are taking -- well, some states have taken their c waivers, the ones that target certain populations and benefits and are rolling them into managed health waivers called 1115 Waivers.

So we actually don't know. The fact that there is a limit to the targeting in some ways, you know, as I said, we have thought about it in terms of states being able to reverse target possibly by identifying certain services. But everyone in Medicaid gets basic benefits and then states elect to provide optional benefits. Our match rate varies. I believe right not it's from 50 percent to 78 percent in some states that have higher poverty levels, Louisiana, Mississippi, Alaska, those states tend to receive a larger match from the Medicaid Program.

But it does certainly vary from state to state. Different states operate, you know, different waivers that provide a whole variety of services and it does truly depend on where one lives. And advocates can always go to State Medicaid Directors and take a look at what's going on in other states. I think our Promising Practices website is pretty good. When we finally get these papers up there and take a look at the states that

are doing a good job, we plan to examine what those states offer in their state plans, what they offer in their waivers, what money they might be receiving through our grants and take a look to see which states are doing a good job.

And if they are doing a good job with people with autism, how are they doing it with Medicaid funding. So that's our hope.

Dr. Insel: Barry?

Dr. Gordon: Ellen, just maybe a big picture question. But what I understand of the Deficit Reduction Act, it involves a reduction in money.

Ms. Blackwell: You know, yes, Barry. I said yesterday, I have to go into this meeting and say with a straight face that we're going to reduce, okay, how much, $4.3 billion, but we're going to also do things for people with autism. And it does sound backwards.

Dr. Gordon: And what does the $4.3 represent percentage wise?

Ms. Blackwell: I don't know that.

Dr. Gordon: Approximately.

Ms. Blackwell: I don't know. I mean, our budget is huge. We're the second biggest budget in the country behind Social Security and ahead of

defense.

Dr. Gordon: Okay.

Ms. Blackwell: So, I mean, I guess --

Dr. Gordon: I think the --

Ms. Blackwell: -- conundrum here is that the premium-sharing provisions in the DRA are expected to reduce Medicaid expenditures, because people that have more money will be expected to pay more for their care. I don't know how it will affect people with autism. I guess it depends on what their income is and their earning power. Probably, I mean, most people with autism are on, you know, Social Security disability income. They are probably pretty low wage earners, so their cost-sharing -- you know, again, it's depending on what state people live in.

Probably, they won't be impacted as much, people with disabilities, especially severe disabilities like autism as some other populations.

Dr. Gordon: Can I ask another question?

Ms. Blackwell: Okay.

Dr. Gordon: Which is does this -- do you think there are opportunities then, like the provision you were talking about?

Ms. Blackwell: Oh, absolutely.

Dr. Gordon: That might allow more flexibility both on the state's parts and perhaps individual's parts.

Ms. Blackwell: Yes. And we're trying to be very flexible as we write these benefits to allow states opportunities. Often times where I work, I think states see us as obstructive and uncooperative and we're really trying to make sure that everybody follows the rules and everything is equal. And, you know, this is a great -- 6086 is a great option.

The demo that looks at psychiatric residential treatment facilities for kids and how we can keep them in the community, we actually already have some data and there are plenty of studies to show that there is efficacy and cost-effectiveness and also in terms of helping kids by keeping them in the community. But it's really great that the Congress passed this opportunity for us to share with states and perform our own research.

And our Real Choice Systems Change Grants, we just held a conference a couple of weeks ago and it is wonderful to hear state folks come in and talk about what they have done with even small amounts of grant money to help people stay in the

community, provide -- many of these grants provide information to families that have children with autism.

So I can urge everyone to take a look at our website, cms.hhs.gov. It's new. It looks really nice now. Press on the button that says Medicaid and go a little bit, dig a little bit deeper, because we do some really innovative things in addition to just administering a health care program for the poor and the disabled. And, of course, we have Medicare, too and I won't talk too much about that today.

But I told Lee yesterday if we had another meeting, we could make arrangements for us to do a presentation on Medicaid, because I think that many people don't understand our program. It's very complex. It's impossible even for people internally. It takes about five years to figure out how Medicaid works. And so I'll try to -- in a future meeting, I would be happy to do a presentation and try to explain Medicaid 101.

I talk fast as everyone knows, so maybe that would be very helpful to everybody.

Mr. Grossman: I just can't express enough how great it is to have Ellen on the Committee now.

There was a big gaping hole that was produced for lack of a great representative from CMS here in the past. And it's important that CMS is represented here, because it does take up a considerable -- it does represent a considerable amount of the monies that are spent to treat autism.

I'm curious how available is the data that CMS has? It seems as though because of the large population base that you're dealing with, that there may be some opportunities there for some amazing type of research or population studies.

Ms. Blackwell: Well, unfortunately, we collect data mostly based on services and not on diagnosis. So we can tell you how much Medicaid spends on personal care and how much Medicaid spends on home and community-based services, but it is really hard for us to break it down. We can tell you in the waivers, for example, the benefit people -- say there is an autism waiver, we can tell you how much a state spends per individual in the autism waiver.

And waiver states, essentially, have to meet what we call budget neutrality, which means they have to show that it is less expensive to keep a person in the community than it is to provide institutional care. We have that sort of data, but

we don't -- I mean, I have gone to our data folks and said autism and they just kind of squint at me and say well, we could run this or we could pick a state or we could try, but I haven't gotten anyone who said oh, yes, Ellen, I can get that for you right away.

Dr. Insel: So we have actually done some work around this. One of our grantees from Penn who has been working on this, what he is concerned about is that he can do very nice studies with Medicaid data locally. But there is no way to grasp the national picture, because when he goes to CMS, what he is told is well, you just have to go to each state and work with them and he doesn't want to go to 50 different states to be able to do this.

So there may be an opportunity in this to try to find a way to provide a national database for Medicaid recipients. It would be a fair amount of labor, but if you had a focus like this one area, there may be an opportunity to get something that would be very helpful to get us through the national picture.

Ms. Blackwell: Well, as I said before, I really struggled when I looked at our C Waivers to try to figure out how many of them are serving

people with autism. And it's just almost impossible, because many of these people have dual diagnosis, as everyone here knows. I mean a person with autism could be served under an "other" waiver and we would never know about it.

So I've tried to look at, you know, the numbers that we talked about earlier here, the numbers in the general population of people with autism, numbers of people served by Medicaid and run those sorts of really basic calculations. But, you know, I can go back to our numbers people again and beg and plead some more, but it's tough. I think we really have to look at services that might benefit people with autism and that may be as far as we go with Medicaid.

It could be behavioral health services. We don't know how much. I mean, as I said at our last meeting, Medicaid is a big supporter of educational medical services. Again, we don't know how much the Medicaid Program spends in school settings, because we don't differentiate by provider type. We only calculate by service. So it's really hard for us. States report to us quarterly on something called the CMS 64 form and it breaks down services into very general categories.

So it's tough. I mean, I'll make an effort, but it is really tough.

Dr. Insel: Well, I would second these comments. It's great to have you here at the table and we look forward to working with you. One of the things that this group can do offline is to provide some good dialogue and some good plans across agencies. And some of the things that you are struggling with, we know we have grantees that are struggling with the same issues. And it would be great to get you to struggle together, because you are on the inside of this and we may be able to get a better fix on some of the numbers.

At least, because we are very interested in how the services are rendered and how the money is deployed in different places. And just using the Philadelphia data for Medicaid recipients and looking at age of diagnosis has been very helpful in showing that there is a profound difference in ethnicity when you get diagnosed with autism.

Ms. Blackwell: Well, as I said before --

Dr. Insel: And that wasn't clear. I mean, I can't emphasize enough our early and periodic Diagnostic Screening and Treatment Program provides any state plan service to any beneficiary whether

or not it's in the state plan. So kids have this wonderful opportunity through EPSDT from the ages of 0 to 21 to receive any covered 1905-a service. Not respi-care, not the non-1905-a services, but EPSDT is a great program and possibly even under used in some states.

So at least under the Medicaid Program, children are -- have excellent opportunities to get health care services.

Dr. Insel: Yes, I think what we keep hearing in this meeting is even when the payers are there, often the providers are not. And that's another -- we'll hear this from other people this morning, I think, but it's one of the big challenges is making sure that even when it can be paid for, there is someone there to give the service. And even in Maryland, which you mentioned is one of the waiver states, that's still a big challenge.

Ms. Blackwell: Yes.

Dr. Insel: We should move on. From FDA, do you want to get us up to date?

Dr. Carbone: My sympathies. I understand what it feels like to be a black box that nobody appreciates and under-funded. What I would like to talk to today is obvious. We would like to see more

applications for treatments and prophylactic treatments for autism.

I think that what our plea would be to get there would be one not of developing -- the matrix is an excellent outline. But what we often deal with is prioritization of what you solve on the matrix, because there are certain things that will get products produced faster and approved faster and tested faster than other things on the matrix. So I would encourage the Committee as they review this to keep an eye towards what is necessary and what is lacking to get therapeutics pushed through in a more efficient manner.

And in that vein, we do have, something unfunded essentially, opportunity within the FDA called the "Critical Path," where we work with others to educate them about these particular critical issues that may seem small and unexciting, but are holding up drug development and treatment development. If anybody wants to look further into that, there is now, in addition to the document describing it, a list of Critical Path and co-opportunities, which is a nice way of saying problems, that we would see resolution of these would be very helpful.

It's very general, but the list is revolving and it's an opportunity to push and try and move up on the priority list the autism relevant and ASD relevant areas. It's at www.fda.gov/oc/initiative/Critical_Path and there are three documents. The original document describing the Critical Path, the document describing the Critical Path opportunities listed and the actual list itself.

For example, biomarkers, clinical trial, endpoint improvements, case definitions, all these sorts of things would help in pushing better therapies through faster. We welcome collaboration. In fact, we have under the Office of Commissioners set up exclusively to deal with collaborations. Many of the Critical Path needs are known to us at the FDA and are known to industry, but many of the discovery scientists are somewhat unaware.

We have done some work over the last couple of years developing workshops with various NIH Institutes to educate both intramural and extramural scientists in these sorts of opportunities and the focus on getting drugs developed more efficiently and more effectively.

We have mechanisms to set up collaborations.

We actually like to serve as sort of the broker, if you will, the non -- the disinterested party being the FDA, the non-biased party to broker collaborations between academia, industry, sponsors and even ourselves, our own scientists to try and move these things forward.

So if anybody would like to propose or see some of these pursued, some possible partnerships pursued, feel free to contact me and I'll put you in touch with people in the Office of the Commissioner. And I think I'll just leave it at that.

Dr. Insel: Okay. Thank you, questions?

Dr. Gordon: As a physician, the Vioxx and related things have struck me as perhaps raising the bar too high. I'm not sure that -- have you, at the FDA, felt that drug companies might be less interested in pursuing secondary uses for current drugs, because of the liability? I mean, we're talking about potentially treating children over a long period of time and I can't imagine that it wouldn't put a damper on companies' enthusiasm for pursuing what is still a relatively small market.

Dr. Carbone: I think there is an issue that's pretty well-known with even studying licensed

pharmaceuticals for secondary indications, because it's often well-known that they are used for these purposes and there doesn't appear to be any strategic value to studying this, because we don't, the FDA, approve medical practice, we simply approve the medication is safe and effective enough.

Keep in mind that many medications are withdrawn actually by the company itself and not as an action of the FDA. And there are certain motivators there that are different. I think you are right in assessing sort of the environment of risk averseness and litigation prone problems. And I think that the more, in a way, sponsors can work directly with people who are interested in these therapies, is actually users of the therapies, and getting together these consortia, the more effective these -- we may have movement.

Dr. Insel: This is at a pretty early stage though. At this point, has the FDA ever received an application with autism as an indication?

Dr. Carbone: I would rather not comment in public about that right now. What I can do is work with the Center for Drug colleagues and identify the public information available and sum that for

you. Yes, I could bring something to the next meeting about that.

Dr. Insel: Okay. Alright, let's move on to NIH, Sue Swedo, report out.

Dr. Swedo: Hello. I have six items that I'm going to try and cover in our 10 minutes. The first is your rather hefty notebook in front of you. It is the May meeting and at each May meeting we present you with a portfolio of the grants currently being funded by the NIH. As you look through that, you will see that there is quite a bit of basic science that has direct relevance to autism in making discoveries in the neuroscience underlying this disorder.

We are also funding several clinical trials as well as studies of etiology and pathophysiology. If you have any questions about the portfolio, the representatives from each of the institutes are here and would be happy to talk to you about their individual grants. Dr. Battey?

Dr. Battey: Just along the lines of an opportunity that's emerging here at NIH, the -- we are entering a new era for gene discovery. It involves studies called whole genome association studies that are done on hundreds of cases and

controls. And we can now do these studies in a cost-effective manner, because of the advances in our understanding of the human genome, a relatively dense map of single nucleotide polymorphisms and a traumatically reduced cost to genotype, the single nucleotide polymorphisms.

So, Tom, I was going to ask, do you see anywhere on the near horizon the possibility of a whole genome association study for this disorder or the data from the twin studies that hereditary is compelling and yet it's clearly genetically complex?

Dr. Insel: So we currently fund one such study at Hopkins with Aravinda Chakravanti. There is another opportunity that has arisen with the GAIN Initiative, which is a public/private partnership initiative through the foundation for NIH, and those applications, I believe, are due today, in fact, and we're very hopeful that there will be at least one autism application in that pool.

Dr. Battey: The statistical data is compelling that this approach will be able to find genes that make up a relatively small fraction of the risk, which has been the problem in the past, I believe, or at least one of the problems in gene discovery

for this disorder. And I really think that this is an incredibly important issue, because only by understanding what these genes are will we know what sort of molecules to target for potential therapeutic interventions.

Dr. Insel: Right. Because to the FDA question of, you know, all of drug development will have to ultimately reside in having a molecular target for the development. One of the things that right now has become the rate limiting step for most complex genetic disorders, as you know, Jim, is having the DNA available from enough cases, enough controls. And here, we have the foresight of the AGRE Project that started collecting DNA in 1998 or something like that, so that we actually have a significant repository available.

To actually do one of these whole genome association studies, it takes a matter of a couple of weeks for 1,000 patients and 1,000 controls. So this could happen rather quickly.

Dr. Battey: That's what I wanted to make sure that autism was one of the diseases that's being considered for this first wave of genome association studies. I think we could potentially see a real breakthrough.

Dr. Swedo: Terrific. That's actually a perfect segue way to NDAR, the National Database for Autism Research, because it's much the same issue in terms of needing to build the infrastructure, have it in place, so that as new opportunities present themselves, you have that to work from. We have spent the last year, indeed, building that infrastructure.

I actually decided that it was a lot like building the Clinical Research Center. We watched it out of the windows of our clinic and it took them about a third of the time to get the foundation laid down and then once they did, the walls went up and everything happened very quickly. And I think we're at that stage of the walls going up and things happening very quickly now.

We have, in fact, the NDAR Team sitting behind us this morning, so if you have specific questions, I'm sure they would be happy to answer them for you. Just going through their key areas of activity, the technology architecture, that foundation that I spoke of has been acquired. It was modified from the Biomedical Informatics Research Network grid and has been housed now on the NIH campus over in Building 12 in a nice secure

well-fenced location.

The clinical assessment module was probably the most thorny of the things we have been dealing with, because, as you might imagine, this research has grown up by the individual investigators that have been doing it and we needed to make sure that we had a system that would meet all of their current needs and actually make their lives easier instead of more painful. And we are very pleased that the four month process of choosing a specific package has been completed.

We have the open clinic system now installed on the BIRN and have hired staff to begin to modify it specifically for autism, including the incorporation of ISAAC and some of the major tools that have been so integral to research to date. The imaging tools, there we're probably actually a little bit ahead, because the BIRN Network had been doing large scale neuroimaging projects from across the country, so we were able just to adopt that platform and move that directly.

Matt and his team are working on anonymization of images, so that you can actually have a true national database. You have to remove the face and make sure that there is no capacity to reconstruct

individual images from the MRI scans. The ontology is something that I have just come to appreciate in the last couple of months and that is actually probably the driving engine for NDAR.

The ontology is the dictionary that will allow a researcher in China to speak the same language and understand that they are using exactly the same characters as they look at the data as somebody in Indiana. So that ontology, fortunately for us, has been a science that is developed to deal with some of the cancer research through CABIG and we are entering into contract negotiations for an ontology system to be built.

As I mentioned, the staff is on board now. We have team leaders in each of the major areas. I would also like to introduce Ms. Louise Ritz, who we call Captain NDAR quite affectionately. Louise is taking over from the NIH side with CIT still, obviously, having the lead on building the technology.

And then there are two final pieces with that. One is the integration with the outside system. As you remember, NDAR is envisioned as the hub at the NIH, but the spokes out in the community, things like the Autism Tissue Bank, the NIMH Repository,

the AGRE database and now the Autism Speaks Registry, which, I believe, they are calling IAN, the Integrate of Autism Network. We are working very closely with Autism Speaks to make sure that the information they are going to be getting from the public will be seamlessly incorporated within this research database as well.

And the final thing is something that we would ask for your help with and that is the issue of data sharing policies. As you can imagine, this is a pretty sticky issue with the need for having the information publicly available as soon as possible, balanced by the need to make sure that that data is as clean and true as possible.

So the data sharing policy in general for the NIH has been established, but for NDAR, we are asking for specific input. And if you go to the NDAR website, ndar.nih.gov, it will take you to a link where we have a request for information and are actively seeking solicitation on opinions about when the data should be made public. That information is due back to us by May 15th, so there's not a lot of time.

Alright, any questions about NDAR before I move on?

Mr. Shestack: Yeah, a couple of questions. What do you have budgeted for it for the next three years, including this year?

Dr. Swedo: I just turned myself off, I apologize. This year's budget was $1.6 million. The mean is actually coming up with the budget figures for the next three years as we go after the -- getting that money, but $1.6 to get it on the ground. We will be refunding for -- in October of 2006 for 2007.

Mr. Shestack: And is that new money or is some of that coming from the money that has been set aside for data management for the CPEA and STAART Centers?

Dr. Swedo: No, this is all new money at this point in time.

Mr. Shestack: And is the DMSTAT data that, for instance CPEA and STAART Centers have been putting in for the last several years, is 100 percent of that exportable into the system or is it not, because it's a private, it was a privately designed data management system?

Dr. Swedo: Right. 100 percent of the data will be able to be incorporated into NDAR. The NDAR Team is working with DMSTAT to make sure that some of

the front load can be incorporated. So the proprietary nature of DMSTAT was actually in the software and sort of the forms development, etcetera. And that is an issue for NDAR in that everything from the ADOS and ADI-R to Vineland, all the rest of the instruments that the clinicians use are all copyrighted instruments. So getting those copyright protections as well as making sure that the system is in place to appropriately compensate the copyright holders is underway.

Mr. Shestack: Right. But ISAAC already had a system to do that.

Dr. Swedo: Absolutely. And we have been working with Clara and with you.

Mr. Shestack: That was public.

Dr. Swedo: Yes.

Mr. Shestack: That's great. Okay.

Dr. Swedo: They still had to pay for them though, Jon.

Mr. Shestack: Yes, we still have to pay.

Dr. Swedo: Yes.

Mr. Shestack: A royalty per unit.

Dr. Swedo: Exactly. And that's what we're working on.

Mr. Shestack: That's true.

Dr. Swedo: Right.

Mr. Shestack: And do you have a policy for your ACE Centers on -- is there in the guidelines a policy on ACE Centers on data sharing and putting data into NDAR?

Dr. Swedo: Yes. The expectation is that the ACE Centers will actually be using NDAR as their database. That's one of the pushes to make sure it's up and tested and fully functional by next spring. The data sharing policy that is out for public comment right now will be binding on the ACE as well.

Mr. Shestack: All right.

Dr. Insel: I should add that that's also true for the genetics there, particularly with the GAIN and the SHIFT coming forward, there is a very tight data sharing policy. It gives the principal investigator a short period of time for exclusivity for publication, but all of the data becomes publicly available, essentially with genotyping and the phenotyping data links up to that automatically.

Dr. Battey: But this is absolutely critical, because in data like this, there are many different ways that data can be analyzed. There's not just

one way to do it. And depending on how you stratify the cases, you can discover things that you won't find in studying the sample as in aggregate. This has been now shown countless times in other diseases and disorders. So it's absolutely critical that as many creative approaches to analyzing the data be pursued, once the genotype data is available.

Dr. Insel: This is really a change in the culture of science, this sort of discovery phase where we are increasingly aware that what you need to do is make the data available to as many people as possible, because you don't know where the next best idea will come from, whether it will be from Bangladesh or Boston. And once these things are on the web, everybody has an equal footing in being able to look at it.

So there are already examples, particularly from the Broad Institute at MIT where fundamental discoveries have been made by people who were not part of the collection of the data, but were able to have access electronically to the genotyping and some of the phenotyping. So this is -- we already know this works. Now, the question is getting it done and getting it out there.

Mr. Shestack: Apropos of that, there were, I think, 240 new families that were supposed to be collected by the STAART Centers and then put into the NIMH repository by the various sites, 8 to 10 sites. Do you know what the progress on that is? Because that's a large -- that's a big number.

Dr. Swedo: I don't actually know. We can absolutely get you that information where they are.

Mr. Shestack: Could we? Thank you.

Dr. Insel: That number sounds about right. I think what -- because I know the AGRE sample is only a fraction. I think it's about 60 or 70 percent of what's in the repository.

Mr. Shestack: Well, the rest of what's in the repository comes from other collections from Stanford or Iowa or Tufts previously, but it wasn't part of --

Dr. Insel: But some of it is to supplement it.

Mr. Shestack: -- the legislation and the policy that this 240 new families and then there was extra material on 435. And I don't mean to be an accountant, but, you know, it looks like your budget went down one year. So if you are supposed to get that stuff in the bank, it's a good idea to get it in the bank, rather than have someone have

to go collect it again.

Dr. Insel: Yes, we'll get you the numbers. I actually don't know whether the STAART Centers -- where they are in terms of the total number of families.

Mr. Shestack: And can you also talk about what the intramural activities are?

Dr. Swedo: You are so good, Jon. Thank you. That was actually next on my agenda.

Mr. Shestack: Great.

Dr. Swedo: So, yes. The Intramural Autism Research Program, for those of you don't know, I stepped down as the director of the Division of Pediatric Translational Research and Treatment Development for the NIMH, so that I could move to the Intramural Program about 80 percent time and head up a new effort there.

We are working a lot of protocols at the same time through the system. We have three that have full approval by both our Science Committee, which takes several months, and through the IRB, which takes a while. We are currently recruiting young children ages 12 months to 4 years for a screening protocol also for a large scale investigation of clinical and immunological factors at work in

regressive autism and we have a new trial of antiglutamatergic agent, Riluzole, for which older children will be eligible as soon as we complete the open trial in some children, typically developing children with OCD.

In addition, we have three protocols that are in various stages of review. In fact, I'll have to excuse myself later this morning to go over to the IRB for our Minacycline trial. That is the treatment of childhood regressive autism with Minacycline. You may know it as a tetracycline derivative, the old fashioned antibiotic, but it has some fascinating effects on NF kappa B and we're going to use it for its immunogenic properties.

We are also in collaboration with the Mind Institute, the second site for a pilot study of the Phenome Project. This gets into sort of larger scale NIH issues, which I'll just mention that the NIH Autism Coordinating Committee has been meeting very regularly with folks from the CDC as well to envision how we might undertake the Phenome Project. You might remember it's on the short-term goals of the research matrix to have that project planned and hopefully even launched by the fall.

What we have already determined is that it can't be just one project. It needs to be several different efforts. As you've heard, some of the epidemiologic efforts might be useful efforts based on the NIMH repository, the AGRE repository looking first at the genes and then at the phenotype and working the other way as well looking at behavioral characteristics and then coming back to the genome.

So we envision this as sort of making use of the retrospective data from the STAART, the CPEA Centers, from our other partners as well as prospective efforts either on some ongoing studies in Norway or Denmark or in new initiatives such as the Mind Institute pilot. So that's kind of the phenome.

And I think that's pretty much it for the Intramural Autism Research Program. I'm very excited that my two key staff members are here with me this morning, Audrey Thurm, you know very well. In addition, we have Dr. Sarah Spence coming to us by Steele from the UCLA. So we're very grateful for them.

Mr. Shestack: It's very sad.

Dr. Swedo: I know it's very sad for you, but very happy for us.

Mr. Shestack: We would like to say that we're very unhappy to have lost Sarah Spence, but it will be everyone else's gain.

Dr. Swedo: Absolutely. And we promise, promise; promise that we'll just strengthen our ties with CAN.

Mr. Shestack: Well, strengthen your activity in autism.

Dr. Swedo: Also true. Alright, let's move on to the Autism Centers of Excellence. We have already mentioned this. As many of you know, there is an RFA out. The applications are due August 11th. We will be reviewing them in late fall. They will go to council in January and we expect to have these centers and networks starting next spring.

One of the crucial things in the timing of that is that the STAART and CPEA Centers will be ending over the next 18 months to 2 year period with the CPEAs coming to closure about the same time as the ACEs are envisioned to be fully funded. So we hope that there is a seamless transition, but we're also actually hoping that we have sort of some new faces and I think that the networks component of the ACE will allow that to happen.

We have already heard of a number of very

exciting efforts in neuroimaging in clinical trials in genetics where institutions spread across the country are getting together to put together new networks that will be linked through NDAR. The RFAs are on the web if you have any specific questions about them, we should thank publicly Alice Kau and NICHD for taking the lead on getting these published and on the web and NICHD will also be primarily handling the review. So we appreciate that.

Alright, on to the NIEHS -- National Institute of Environmental Health Sciences just hosted a meeting with the CDC at Research Triangle Park on May 4th to look at the vaccine safety data link, a large link database maintained by several HMOs with over 2.3 million children registered there. It's thought that this might be a way to look at the potential association of Thimerosal from childhood vaccinations and the risk of autism.

They had panel members who had expertise in epidemiology, toxicology, biostatistics, risk assessment and clinical research, as well as a number of public advocacy groups. I actually attended the meeting and it was incredibly instructive how much is available, but also some of

the tremendous hurdles to overcome. And I think that the NIEHS and CDC will be working hard over the next few weeks to make a really rational determination about whether such an effort is useful.

And my final update is to just let you know that the annual CPEA and STAART meeting will be November 8th and 9th in Bethesda. Since this will be the last meeting of the CPEA Network, the focus of the meeting will be on each center's most significant findings from the past 10 years of CPEA funding and the STAART Centers will also be presenting a progress report. So we'll have that just before the November IACC meeting and I hope it will be a wonderful culmination of the 10 years of funding for the CPEAs.

Dr. Insel: Thank you, Sue. There is a lot there. Questions or comments before we move on?

Mr. Shestack: The gross amount of the ACE Centers as compared to the gross amount of the combined CPEA and STAART Centers is what?

Dr. Swedo: There is a public commitment to spend at least as much on the STAART -- on the ACEs as was spent on the STAART/CPEAs. Whether we will be able to spend more depends on (A) on what

applications come in and (B) what the budgets of the institutes are, but there is at least as much money going to be spent. And then if you throw NDAR on top of it, the overall investment will be greater.

Mr. Shestack: And with -- but the ACE Centers will come online in 2007, but the eight STAARTs will still be online until 2008. Can they overlap? Can they be similar investigators? How does it work?

Dr. Swedo: They can be the same investigator. If a STAART investigator put in a new proposal for a new center or was the PI on a new network, they would be funded for both at the same time. We also had envisioned staggering it, because the STAART Centers' money coming out of the 2007 budget, some of the centers will be coming online as early as possible in 2008.

Mr. Shestack: So stagger the start of them, but not the application process?

Dr. Swedo: Correct. We decided that we needed to have one review cycle to get started, so that we knew what we were going to have and not be trying to save money for something that might not end up coming.

Mr. Shestack: And then the renewal process, could you just tell me how that compares to renewal for say CPEA or STAART or other multi-year programs?

Dr. Swedo: I confess we haven't actually talked about that Jon.

Mr. Shestack: Okay.

Dr. Insel: Jon, the out years, after the first five years. Barry?

Dr. Gordon: To question the Thimerosal study being done through HMOs, that would also be an opportunity to look at other possible environmental influences. And I know you were summarizing very quickly, but are there thoughts to look at things such as fetal ultrasound or I don't know if that has come on the table or not?

Dr. Swedo: It didn't actually come up at this meeting. Cindy, do you want to comment on that at all?

Dr. Cordero: Let me just sort of comment that actually the information -- and this is what I raised in the medical record and fetal ultrasound may be there or not, but I don't think that there are any specific plans to add other environmental exposures on that, but we can find out more about

it.

Dr. Swedo: Well, actually, that's a great idea.

Dr. Gordon: I'm not trying to bring a Tom Cruise connection or anything into this, but I'm just -- the most collect typically pretty detailed data and, you know, in other situations the Thimerosal link has been an excuse to look for other things as well. I just wondered if that had come up?

Dr. Swedo: That was definitely the focus of the discussion at the table was that sort of spending the time and energy to go into this database just for one very small question would not be very fruitful.

Dr. Insel: Other comments or questions? Yes?

Dr. Zeph: One question. Is the Intramural Program that you were discussing, is that written up somewhere?

Dr. Swedo: We're just updating our web page to get it up on the web.

Dr. Zeph: Okay.

Dr. Swedo: As soon as we do, we can put it out to the link.

Dr. Zeph: Great. Thank you.

Dr. Cordero: I think in the past you reported that they were developing and starting inculcation therapies. Is that still ongoing?

Dr. Swedo: Yes, I don't know how I skipped that one. That is one of our studies that is under review. Lee is smiling at me because we've been talking about this over the past few days. The inculcation study was just approved by Science and will be going for IRB review very soon. I think one of the issues is the whole, always the question of, public health necessity versus individual subject risk. And we're just trying to balance and consider those.

Dr. Insel: Okay. Thank you, Sue. We're going to move on. Larke, it's great to have you here as part of the group and we'll have you talk about SAMHSA.

Dr. Huang: Thank you, Tom. I'm going to do the best I can. I have only been at SAMHSA for three weeks, so I'm going to try to give you what I could quickly glean.

SAMHSA doesn't have any autism-specific programs in their services portfolio, but there are two programs that I just wanted to mention to you today. We do have a program, that's the

Comprehensive Community Mental Health Services for Children and Their Families Program, which is a Congressionally-legislated program at about $105 million and it has served about 93 grantees in the past 10 years.

There are children, adolescents and transition-aged youths who are involved in this grant program, which is primarily given to states or other political subdivisions to develop comprehensive, coordinated systems of care for children with primarily serious emotional disorders as in the legislation, but we also do get children in there with co-occurring developmental disorders, developmental disabilities. There are children and adolescents and transition youth with autism and autism spectrum disorders in this grant program, although they are a very small percentage of the children and youth served.

Along with that program we do have a large-scale national evaluation across these sites and David Mandel, who was referenced earlier, has been one of the researchers who has done secondary analysis of this database, which is probably up to about 65,000 children now, and does have some work out on, I believe it was on, characteristics and

service referrals and utilization patterns of children with autism.

So it is a database that is open to other secondary analyses. I don't know what the number of children with autism is in the database, but it is a researchable, accessible database. The framework of that particular program aligns very much with this autism spectrum disorders road map that the Services Committee put together, so that is one thing, I think, that is relevant to this Committee.

The second piece I just want to mention is our National Registry of Effective Programs and Practices on the SAMHSA that will be returning to the SAMHSA website. It's undergoing a redesign and that will be an online searchable database of effective programs and practices that have an evidence-based support that have been reviewed by experts in the field around particular interventions.

Intervention developers are encouraged to submit to this and then it will be open to end users such as consumers, families, providers, payers for decision support in developing treatment plans. I think those are the two that I could come up with most readily.

Dr. Insel: Great.

Dr. Huang: Thank you.

Dr. Insel: Well, thank you very much and we're delighted to have you here. Ellen?

Ms. Blackwell: I have something to add. We're working with SAMHSA on provisions related to the Children's Health Act of 2000. We issued a rule and I'm going to get the year wrong, I want to say back around the time the Children's Health Act was passed, to protect children under the age of 21 from being improperly restrained and secluded, and I think that that often impacts the population affected by autism.

The Congress passed the Children's Health Act and SAMHSA has a piece of the regulation relating to restraint and seclusion in overall types of health care facilities. So we're working very closely with them to publish our final rule on restraint and seclusion in Psych Under 21 Facilities and on the final rule that impacts other health care facilities that might restrain and seclude children and adults with challenging behaviors.

Dr. Insel: Barry?

Dr. Gordon: I'm not sure if this is a question

for SAMHSA, but the children born to mothers who are addicts, who tracks them? In other words, there has been talk afoot that maybe there is a higher risk. I mean, there is certainly a higher risk of "neurodevelopmental disorders" in such children. I wonder if anybody would look at autistic-like features as a human model and who would track them?

Dr. Huang: One of our centers, the Center for Substance Abuse Treatment, there is a Pregnancy and Postpartum Women and Children Grant Program that has in the past -- actually it grew out of sort of the crack epidemic a couple of decades ago and they were trying to follow those children and those mothers. I can look into it and get more information on it. I don't know it real closely.

Dr. Gordon: Thanks.

Dr. Insel: Okay. The last, but certainly not least, on this list is the CDC which has been very busy recently. So, Jose, you can take us through the summary.

Dr. Cordero: Thank you. Well, yes, we have been busy lately. As you know, CDC has the CADRE Centers and they are completing their first five years and that has led to the development of the case control study, and in the next five year cycle

we expect to have the group funded as of September and we're looking forward to begin recruiting participants for the case cohort study in October 2006. The CADRE investigators have been busy publishing and I will talk a little bit more about some of the publications later.

The other network, which is the Surveillance Network, is actually working on a paper that we expect to have submitted for publication later and have it later this year comparing six sites where we would have data for regional sites. And, again, I think that publication will be early in 2007. We also have a publication under two points comparing '96 and 2000 from the Atlanta data.

We are also in the process of re-announcing the grant cycle and we expect to have 10 sites funded beginning of June 2006. In this cycle also we actually put out an RFA looking at new methodologies for looking at the prevalence of autism or ASD and especially we were interested in looking at targeting 4 year-olds, identifying a much earlier age. As you know, our surveillance is based on identifying children at age 8. So we expect that we're going to fund at least one sort of pilot study in that group.

In terms of publications, I just wanted to tell you about the report that just came in and you do have a copy of it in your folders. We published this May 5th, last week, and in essence it shows that based on parental reports, the rates of autism in the two surveys that we use, the National Health Interview Survey and the National Survey for Children's Health, the rates were 5.5 and 5.7. That, in essence, translates that for children 4 to 17 an estimate of about 300,000 cases of autism.

One of the things that is important is that this is a national representative sample and it's actually an example of using available data. Both the National Health Interview Survey is actually done every year by the National Center for Health Statistics and, as Sybil mentioned, the National Survey of Children's Health is funded by HRSA and it provides incredible data on the status of children's health in the nation and we have been able to use this data to look, now have sort of a representative sample to surveys.

One of the important things about these two surveys is that they have -- one includes the PEDS as sort of an internal, a set of questions, and then there are other series of questions about

behavior in the other. So that gave us at least some way of contrasting the question from parents, yes, my child has been diagnosed with autism, and compare that with responses and behaviors. And there is an internal consistency there that gave us some feeling that actually the data were pretty consistent.

The second thing is that the two surveys, basically, were pretty close in terms of the rates that were estimated from both and this data actually, 5.5, are within the range that had been seen before, between 2 to 6 per 1,000.

We also have another article that is actually being released today or later today that is based on Atlanta data and it's looking at the age of diagnosis. And the bottom line of this paper is that when we look at the first notation in any record that we found from the child about beginning an evaluation about autism versus a diagnosis, there is a pretty good lifetime. It goes from about 48 months to 60 months or 61 months. That is really very late.

Now, keep in mind that this is from 2000 a year for Atlanta data, so these are 8 year-olds in 2000. So these were children that were born,

basically, in 1992. We do have the hope that actually things are getting better. So those are two important papers.

And let me just add one point. You mentioned Hispanics and the issue of diagnosis. In this paper, if you look at the table you will see that parental reports of autism among Hispanics is significantly lower than it is in other groups, and our interpretation of this is that not necessarily means that the rates of autism are less among Hispanics, but that probably we have an under-diagnosis of autism in the Hispanic community.

We also have been busy with the Learn the Signs. Act Early Campaign. And you will be also seeing we have been working in great collaboration with Autism Speaks and Alison Singer will be speaking later on about that part. We continue to have our public health focus and from a previous report I think you may remember that we started with a broad parental community.

We have been focusing on pediatricians and the third phase is to go to child care providers. We are now at the stage where most of our emphasis is in the health care professionals, particularly pediatricians, and also the child care providers.

We also are focusing on the high risk populations and, again, for example, how do we reach out to Hispanics?

In terms of the specific activities that we particularly had in April during Autism Awareness Month, we had a four page insert in the AAP News, American Academy of Pediatrics. That is the most read pediatric newsletter and, basically, every member of the academy receive a copy of that. We also have had a number of activities in community outreach and using campaign champions.

We also have sent, I would say it's in the millions, the numbers of emails and all other electronic outreach to professional organizations from members of the organizations like AAP, AAFP and nursing organizations, etcetera. And you have seen this before. The message basically is a 4 year-old with autism, was a 3 year-old with autism, was a 2 year-old with autism, again reminding health care providers of the importance of early diagnosis.

We have had a lot of media outreach and in collaboration with Autism Speaks we have had a series of video teleconferences. I'm sure that Alison will talk more about that. Also in

collaboration with the Academy of Pediatrics, we have been working in developing an autism tool kit.

One of the things that we hear a lot is that pediatricians and actually all health care providers want more information about how to address the issue of autism, not as much in terms of the diagnosis, but how do you talk to parents? What do you tell parents and then what are the resources that we have in our community?

And last week during the American, the Pediatrics Society's meeting, we had a whole day meeting of the autism expert panel, and I think that we're going to have a very good tool kit and once it is completed, I do hope we would like to have that presented here.

The academy is also under -- with our auspices and also the Maternal and Child Health Bureau developing new guidelines on the management and diagnosis of autism, and that should be coming out in July. In terms of the child care, we are actually launching this in the fall and we are starting with the Head Start Conference. There is a great deal of interest among Head Start groups and we're really looking forward to that meeting and the launch for child care professionals.

We also are going to have a very specific evaluation of the Learn the Signs. Act Early. And it's going to be sort of a case controlled outreach study in two counties in Georgia. What we are going to do in these countries is going to do a very intense local campaign about the Learn the Signs. Act Early. And then work with the health care providers and actually determine what impact does it have in changing the age of referral. And that is going to be sort of important additional information.

And to finalize this, the campaign as a whole actually has been in a number -- have received a number of awards for several campaign components, and we are next week getting the award for HHS, a communications award, so we're very pleased with that.

Dr. Insel: Thank you, Jose -- questions, comments? Can I ask on the data that is in this, in the MMWR report, the lower prevalence in the Hispanic group --

Dr. Cordero: Right.

Dr. Insel: -- which you thought was due to just a difference in the way the diagnosis is made, is there any previous evidence that there may be an

ethnic difference in prevalence because we always look for that?

Dr. Cordero: Right.

Dr. Insel: In terms of going after mechanisms.

Dr. Cordero: Yes. For example, in California and New York and others, using other methods we haven't seen differences and so that is why I think that there is always a possibility that there is, but at least from population-based studies using other methods, a more consistent ascertainment approach, not having found those differences.

Dr. Insel: Okay. Gail?

Dr. Houle: Hi, Jose. I don't know if you were aware that we have been asked to participate with the American Academy and CDC in Dom Lollar and we had a conference call the other day on a component of the tool kit which would increase the referrals of infants and toddlers to the Part C Program for evaluation, because that is the primary program that is available throughout states and communities to provide services to infants and toddlers.

So we have some grantees who have been working with the academy for a while now on improving the rate of physician/pediatrician referral to the Part C Program. They have been testing out different

kinds of referral forms and different kinds of feedback mechanisms to see what strategies would increase the rate of referral.

And so some of their forms and work and strategies are going to be incorporated into that tool kit, so that is a nice collaboration of operationalizing some of the things that we have been doing in getting children referred to Part C for intensive evaluations and services.

Dr. Cordero: Yes, thank you, and thank you for mentioning that. And one of the interesting things of having the meeting and the tool kit and having the representative we had is that it was almost like a discovery that there were so many efforts and going on and potentials for collaboration that I think that we're going to have a very rich kind of tool kit with all kinds of very good information.

Dr. Insel: Well, that's really one of the reasons we're here, just to try to foster that as much as possible across agencies and it occurs to me that NICHD may be another useful partner in putting this together. So Jose would be the contact person as you think about what this might look like. Barry?

Dr. Gordon: Jose, you don't need me also telling you it's a very impressive study that you did and that the investigators and you at the CDC did. And you mentioned it was within the range of prevalence that others have reported but, in fact, it was at the high end of the range and I wondered how it, for example you think, compared to, say, the results of the so-called California Study where it seems to be comparable to that in terms of prevalence at least.

Dr. Cordero: Yes. It is in the range and it's in the high end of the range and I think it's sort of comparable to California, too. I think it's one of the interesting things. Something that I think is going to be very helpful, this study, the National Health Interview Survey, it is done on a yearly basis so we will be able to in the future sort of track what the prevalence is.

So I think that that actually would help with the questions you haven't asked. You know, what is happening to this rate? Is it going up or down? And this is just a snapshot, but with time I think we are going to have data that will give us some idea of the trend.

Dr. Insel: That is really key. I mean, that

has been the biggest deficit in this whole epi-picture. We have had prevalence data, but no incidence data and without that it's hard to know how things are changing over time. Other questions or comments?

Dr. Zeph: Just one. Jose, I want to make sure I understood what you said. Did you say that they found -- in the analysis related to onset with the 8 year-olds with the 1992, children born in 1992, that there was actually a four to five year lag between the initial mention and the diagnosis?

Dr. Cordero: The finding was that the very early first notice of something or evaluation of autism was about 48 months and then the point when the diagnosis was made in those children was 60. So, first, there was the first -- this is based on sort of first evaluation. It's possible that children may have had symptoms much earlier, but that is sort of the first notation in the record that there is a workup beginning on autism and then the second point is just when the diagnosis was actually made.

Dr. Zeph: Okay. Okay. I misunderstood then.

Dr. Cordero: Right.

Dr. Zeph: Thank you.

Dr. Cordero: Yes, it's about a year gap. Okay.

Dr. Insel: Other comments? Gail?

Dr. Houle: This is not a comment on the CDC, but if you're taking other comments, I just wanted to apologize, because I got here after introductions, and we have an IES representative here. Celia is here and so I didn't realize that.

I was late and I was looking for my notes and whatnot, but I'm glad to see that we now have two people representing us and I was remiss in not realizing that Celia was here and offering her the opportunity to make any comments about IES. So I wanted to know if that was all right with you.

Dr. Insel: Absolutely. We have got a couple of minutes before we break.

Dr. Rosenquist: Thank you, Gail. I wasn't really expecting to speak today, so I hadn't prepared anything. Just to let you know, the National Center for Special Education Research is the newest center within IES. We're less than a year-old. And in April, of interest to this audience, we just announced our Autism Spectrums Disorder Grant Program and it's up on the website and, essentially, it's for the identification, development and to establish the efficacy of

interventions with children identified with autism.

Dr. Insel: For those of us who are acronym challenged, IES stands for?

Dr. Rosenquist: Institute of Education Sciences.

Dr. Insel: And that is within the Department of Education. Okay.

Dr. Houle: That is something that came about in the last re-authorization of the idea where the research program or funding was split off from the services and training funding. And so Celia is working in the Institute of Educational Sciences where the research funding has gone with the new idea, the educational research funding, and I am in the Office of Special Education Programs which is the services and training, technical assistance components.

Dr. Insel: Any other comments before we break?

Mr. Shestack: Jose, maybe I misunderstood, but I thought that there actually was a slightly lower prevalence of autism in the higher age groups, in the kids above 14.

Dr. Cordero: That's correct.

Mr. Shestack: So doesn't that indicate some sort of a trend?

Dr. Cordero: Well, actually, certainly it shows a little bit of a trend, but the question is why. And one of the things is if you look at what we found, it's basically the same thing we found like in the Atlanta data for 1996 that sort of the rate by year, by age group, seems to go up to about age 8 and 9 and then declines.

We think that that has to do with first that the older children actually go unrecognized and especially these are children that would have been born in the much earlier years. And I think that the younger age groups having lower rates basically is under-ascertainment, not being diagnosed yet.

Mr. Shestack: So you don't think that there is actually just more autism in the ages of the children 4 to 17, but that the kids above that just didn't get that diagnosis at all?

Dr. Cordero: For some reason and I think that that's --

Mr. Shestack: I mean, is there a reason? I mean, it's quite possible.

Dr. Cordero: Yes.

Mr. Shestack: But is there a reason you think that? Is there any study that offers just a --

Dr. Cordero: That's about the time when there

was a change in the criteria for diagnosis and I think that many of these children probably were not diagnosed with autism, but with something else. That is sort of -- I'm giving you my personal opinion on that.

Dr. Swedo: Did you actually have surveillance data?

Dr. Cordero: No.

Dr. Gordon: Along those lines, the DSM-4 came out in '94, if I recall, and that helped codify criteria for autism.

Dr. Insel: Ellen?

Ms. Blackwell: I have a couple of things that popped into my mind that might impact children with autism, in particular that are being served in the school environment. Just to bring to your attention the fact that the President's 2007 budget proposes to eliminate Medicaid administrative claiming in the school environment, that's a lot of dollars, as well as school bus payment, Medicaid payment for school bus transportation.

For about the past 10 years Medicaid has paid for school bus transportation for children with disabilities. We have also covered the cost. We can cover the cost of aides that accompany children on

buses. Typically, that might be a child with autism that has behavioral challenges. The budget proposes to eliminate these, payment for both, so I expect that folks will be seeing some further instruction about that.

Also, we have a regulation that should be coming out fairly soon in an NPRM forum that talks about our policy on free care. Since the 1970s Medicaid has had a policy that it will not pay for services provided free to non-Medicaid individuals. The example this Administration uses most frequently is the school nurse example. In effect, a child who has Medicaid coverage should not be -- Medicaid should not be charged if the next child who comes in and has private health insurance coverage is not charged.

So following a couple of lawsuits where the State of Oklahoma prevailed about two years ago, the Administration proposed to codify our policy so that we could enforce it, and I think that that regulation should be coming out at some future date. So I just thought I would mention those since we were talking about education a few minutes ago, Gail.

Dr. Insel: It occurs to me there is so much

that is happening both in terms of what came out from last year, as you described, and what is expected from the President's budget in 2007, understanding that that may not be the final budget that comes out of appropriations, but it might be useful because you have gone through so many things to get a summary of many of these changes that we could distribute to Members of the Committee.

I think there are a lot of absolutely critical facts that you have gone through that will have a big impact for some people around the room, and many of them may be hearing about them for the first time. It would be useful to actually get this summarized in a way that we can all know what to expect.

Ms. Blackwell: Sure.

Dr. Insel: Barry?

Dr. Gordon: Just listening to you, advocacy groups want to fund more research, but maybe they should be funding more lawyers, too, because, I mean, we have already known it's difficult to figure out what's going on from the receiving end. It sounds like it's going to be even more difficult to determine a way through and it may vary by state, by locale, by this and that.

Ms. Blackwell: Well, some of these institutions CMS will issue through what we call State Medicaid Director Letters and, again, you can find those on our website. We issued about six of them six weeks ago. Most of them are related to the Deficit Reduction Act provisions.

There is one, and I feel bad using this word again, Secretary Leavitt issued a road map for Medicaid. In fact, I sent the link to Lee yesterday. Okay. So there is a road map to Medicaid to help that describes some of the efforts that we're engaging in to help people with disabilities.

Dr. Insel: Ellen, I think, you know, what we're struggling with is that some of these things, that because you're in the middle of it you can make sense of, are really impossible for people to decipher. Is there a way they could get sort of clear language about what this means?

Ms. Blackwell: I think that goes to my comment earlier about maybe at a future meeting I can come and talk about Medicaid and what we do and try to describe our agency. I mean, I think when people typically think of Medicaid, they might just think, well, the person has a Medicaid card and they get services, they get health insurance coverage. But

we do so much more than that and we fund so many services.

Somebody said to me the other day, the Medicaid director said the other day we pay for everything under waivers. So it's pretty amazing. I mean, when I sit here and say we have been paying for school buses, I would wager that few people understand that the Medicaid Program has been paying for school bus transportation for kids with disabilities, kids that have IEPs.

So in 1988, I have mentioned this before, the law changed. Medicaid was directed to pay before the Department of Education for services that are health-related services included in a child's IEP that are covered by a state's Medicaid Program. So Medicaid is an important finance aspect of the education system in this country for kids with special education.

I mean, again, I'm sure that, you know, most people don't think about that, but we do at Medicaid and we do all sorts of things. You know, mental health services, if you took a look at some of the North Carolina mental health reform stuff, I think you would be very surprised at what Medicaid is going to be covering.

I mean, that is actually a good thing. We have expanded a lot of services. So when we do things in one state, we typically try to do the same thing in the next state. But maybe it is a good idea for me to come in and talk about Medicaid in general because --

Dr. Insel: You're on. We're going to sign you up.

Ms. Blackwell: -- we have big money and it is very complicated.

Dr. Insel: But even before that, you know, if we could just take what you have described already this morning --

Ms. Blackwell: Today, right.

Dr. Insel: -- and get it as a set of bullets, especially the most recent comments about the President's 2007 budget, which I think many of us don't know about, because these are in the details of some very complicated budget language.

Ms. Blackwell: Well, and I can't stress enough the DRA development. I mean, all of us are running the trains, but we are writing these regulations now and we're getting ready to publish them. So, I mean, I think if folks are interested, take a look at the language that the Congress gave us to work

with and what would you like to see?

I mean, what do you think would benefit people with autism? How do you think we should implement these benefits because, as I said before, I mean, we are poised to issue regulations. We're still writing them. They are going to be, most of them, interim final regs, so there will be opportunities to modify them later.

But every day I think of something new. Yesterday I went, oh, wait, wait a minute, we defined that wrong. We need to do this. And so, as I said, we're really -- we can always use help. Send comments to me at ellen.blackwell@cms.hhs.gov and I will be happy to send you a list of the DRA provisions that I mentioned earlier. The benchmark coverage, we already issued a State Medicaid Director Letter and, as I said, two states have already implemented the coverage.

I haven't seen it. I just learned about this last night, so I'm very interested in looking at how these states implemented this benefit in their state plan. So, you know, we're in the middle. We're in the thick of it now.

Mr. Shestack: Is there a date interim regs will be issued by you?

Ms. Blackwell: Interim final regs, right. The Free Care Regulation is an NPRM.

Dr. Insel: Interim final means they are out for comment.

Ms. Blackwell: They are always out for comment. There is always an opportunity for public comment, whether they go for round one or round two. The NPRMs usually -- they circulate twice, but the interim finals, you know, we always have an opportunity to modify.

And I really can't stress enough I work with really nice people. We're trying to do the right thing. We're really trying to help people with disabilities and the elderly and try to figure out ways to make these laws work with the language we have been given and it is a challenge.

Dr. Insel: Well, that's great. We're really glad to have you here and I assume that your invitation for comments is not just for those around the table, but for everybody around the room.

Ms. Blackwell: Oh, absolutely, absolutely.

Dr. Insel: Great. Well, with that let's take a break. We're a little ahead of schedule. I want to reconvene here right at 11:00, so that we can stay

on schedule from then on. Thanks.

(Whereupon, at 10:40 a.m. a recess until 11:00 a.m.)

Dr. Insel: I would like to mention that if you are part of the Services Work Group, the group is going to meet at lunchtime. Find Gail and Lee and they will tell you where and when, but it's in the cafeteria, is that right, or why don't you gather here and you can meet as we break from this session and use the lunch break for an update.

Okay. Moving into the next part of the agenda, an update from the Early Screening Subcommittee and Deborah Hirtz will fill us in on the details.

Dr. Hirtz: Thank you, Tom. You have heard quite a bit already from Dr. Cordero about some of the very exciting things that are going on in terms of the Autism Early Awareness Campaigns, and so some of that was discussed at our subcommittee meeting yesterday. We really do feel very pleased that there has been some progress and that we have got things kind of underway and in a very good direction and started off with the Awareness Campaigns this past year.

We heard yesterday in detail, Jose mentioned the Academy of Pediatrics, but we heard in detail

from Paul Lipkin yesterday about the AAP Policy Revision Committee for Developmental Screening which is going to come out with a statement in July, and that also contains very specific recommendations for autism screening with a variety of possible instruments that could be used. And, also, they are developing with the help of CDC and others this tool kit that Jose mentioned.

In addition, we heard from Alison Singer, who I think is on the schedule after me, and it was a very interesting presentation about the wonderful things that are happening in the Public Awareness Campaign. So I will let her talk in detail about that.

We heard from the people in CADRE who -- some of the investigators who have ongoing research projects looking into what happens when they try to implement early screening in offices with particular emphasis on what are some of the obstacles, and I think the information that they are going to get from this will be very helpful in moving to the next step in what kind of things need to be addressed in the office setting.

We had an update from the Services Subcommittee, as well, and the final item that was

discussed is our latest version of our road map. We all have road maps. So this is the one that comes from the Early Screening Subcommittee that was put in your -- it's the one that has the colors on it that was put in your folder.

So where we are on this, I think, is that we -- this is the summary. There is a larger version that includes various projects, that either are underway or are planned; or that would address the specific elements, of the road map. So we have a number of next steps. One would be just filling in the gaps and the information on these various projects. We know about a lot of them. We need to know about all of them and what they are addressing and what the time table is and what more is needed.

As Jose said, CDC already has underway some programs to evaluate the impact of implementing these early screening campaigns and what kind of results are we getting from them and where are they leading in terms of referrals.

And, most importantly, we need to work and we will work and interdigitate with the Services Subcommittee, because the next steps in terms of the Early Awareness Campaign all relate to how can we better implement the referral and screening.

Once the screening process is done, how can we get up to speed on where we need to be in terms of referrals and people who are staffing to assess the children that are referred, and also then the next step which is treatment and programs for them.

So this means that we need to work very closely with the Services Subcommittee on these elements of the program and, of course, early awareness is not going to do us any good if we don't work on these other down-the-line pathways.

We would like you to take a look, the members of the IACC to take a look at our summary road map and give us any feedback on the general outline and plan. You can let me or Dr. Cordero know if you have any thoughts or comments, additions to this road map. We plan to update over the next six months and have even more to present on it at our next meeting.

Jose, do you have anything you would like to add?

Dr. Cordero: No.

Dr. Hirtz: Okay, any questions about it? Okay.

Dr. Insel: Okay. Thanks, Deb. We're going to move on to hear about the building national autism awareness. This is Autism Speaks' Ad Council

Initiative and Alison Singer will take us through this.

I think many of you already know Alison, but if you don't she is Senior Vice President for Communication and Strategy at Autism Speaks. She has been with the foundation since its launch in February of 2005 and is a member of the board of directors of the foundation. She served as acting CEO of the organization from March through July of 2005.

And those of you who don't know her personally probably know of some of her work. In particular, she was the producer before she came to Autism Speaks of the CNBC award-winning series that she did called Autism: Paying the Price. That was on now over, I guess, two years ago, is that right, a year and a half ago, something like that.

She has a BA in economics from Yale, an MBA from Harvard Business School and has both a daughter and an older brother with autism. Alison, we're just delighted to have you here and look forward to getting a peek at this Awareness Campaign.

Ms. Singer: Thank you. I am going to just talk briefly about how we developed the campaign. Then

I'm going to show some of the spots and then talk about distribution, because the best spots in the world are useless if no one sees them.

A little bit about the Ad Council. We applied for and were selected to be an Ad Council campaign last summer. The Ad Council was founded in 1942 basically as a vehicle to sell liberty bonds during the war. They have since reinvented themselves and are now an organization that is a consortium of advertising agencies and media groups that donate their time and media spots to run public service announcements.

They have 50 active campaigns. They select five new campaigns each year of which we are one. We have made a three year commitment to the Ad Council, but we expect our relationship to go far beyond three years. And just a few of the spots that the Ad Council is famous for, Smokey the Bear, Friends Don't Let Friends Drive Drunk and the crash test dummies. So these are some of the most widely recognized and impactful PSA campaigns that have been created by the Ad Council.

Our specific campaign is focused at the general public. We focus on the fact that autism is more common than people think, and what we're

stressing is the importance of parents recognizing the early signs of autism and seeking early intervention services if they think there is a problem.

Jose spoke a little earlier about our collaboration on this project. Collaboration with the CDC is crucial for us. One thing we did not want to do with this project is we did not want to empower parents to talk to their doctor to get more information and then have the doctors tell those parents wait and see, boys talk later than girls, this is what happens when you have a second baby. So the CDC is using its resources, as Jose said earlier, to target medical professionals, day care providers and we are using our resources to target the general public.

Secondly, the CDC is able to -- through our collaboration with the CDC we're able to drill down deeper into the Hispanic community. We're creating Spanish language ads. We're particularly targeting Spanish language media for distribution and we are utilizing the CDC hotline to answer any calls that result from the campaign in Spanish. We also have tried very hard to be collaborative in this project and we have sought input and counsel from a large

number of the advocacy groups, the science community and Government agencies.

We started this process by conducting focus groups. What we found initially will not come as a surprise to anyone in this room. We found a significant lack of awareness of autism and among those people who describe their awareness as high, what we found was that the quality of that awareness was very low. People said, oh, I know about autism, I saw Rain Man.

The second important thing we found was there was a disabling fear, disabling is the only word I can really use to describe it, among parents when we use the word autism. As soon as they heard the word autism in the focus group, people shut down. They were no longer receptive to any additional messaging. They said autism, that's not me. I don't have to know about this. This is not anything I have to worry about.

We also found that the most motivating piece of information we could provide to parents was prevalence. People were shocked when we used the statistic one in 166, so we wanted to make sure that we incorporated that data because awareness of that number made people open up, made them more

willing and more receptive to additional messaging.

So when we put together the creative brief for the campaign, we went with the message "Autism is More Common Than You Think." We had originally, as I said, felt we would go straight to market with a campaign that focused more on the early warning signs, what the milestones were, why the developmental milestones were as important as the physical milestones, but because we found that parents were not receptive to that messaging, we took a step back and we decided to do a campaign that was purely about autism awareness focused on the prevalence statistics.

So the supportive message in the brief is that one in 166 children is now diagnosed with autism. We wanted to take an urgent tone, but with everything we do we wanted to have a tenor of hopefulness. And the call to action in the campaign is to visit autismspeaks.org where we do have all of the developmental milestones laid out or to talk to your doctor for more information.

The name of the campaign is called "The Odds" and that is because the way we have developed the creative edge, you will see in a moment, is we juxtaposition the odds of activities that parents

are concerned or dream about that have a far less likelihood of occurring against the odds of a child being diagnosed with autism. And we are delivering the campaign across multiple media platforms, including TV, print, radio, web and some other nontraditional media that I will show you in a few minutes.

Now, I'm going to say a little prayer and try to play the spots.

[TV Car spot played]

Narrator: The odds of a child being in a fatal automobile accident are one in 23,000. The odds of a child being diagnosed with autism, one in 166. The odds say it's time to listen. To learn the signs of autism, visit autismspeaks.org.

[TV Broadway spot played]

[Child singing Twinkle, Twinkle Little Star]

Narrator: The odds of a child being in a Broadway show are one in 11,000. The odds of a child being diagnosed with autism, one in 166. The odds say it's time to listen. To learn the signs of autism, visit autismspeaks.org.

[TV Baseball spot played]

Narrator: The odds of a child becoming a professional athlete are one in 16,000. The odds of

a child being diagnosed with autism, one in 166. The odds say it's time to listen. To learn the signs of autism, visit autismspeaks.org.

[TV Spanish carseat spot played]

Narrator: [Speaks in Spanish]

Ms. Singer: I'm just going to play one radio spot.

[TV Radio piano spot played]

Narrator: The odds of a child performing at Carnegie Hall? One in 73,000. The odds of a child being diagnosed with autism, one in 166. Knowing what to look for and catching it early could make a world of difference to your child and you. To learn the signs, go to autismspeaks.org. Brought to you by Autism Speaks and the Ad Council.

Ms. Singer: I'm going to show you four of the treatments in print and then I have them available for anyone who wants to take them home, but this is our car seat ad for print and we have them in color and black and white. This is young Britney Spears. This is our soon-to-be concert pianist. That is our future Hall of Famer. We also have banners for the Internet. These animate when they are actually on the Internet. They go from the first, from the left to the right.

So what we did after we finished with the initial round of creative is we did a second round of focus groups. We found that the creative concepts were attention-getting. People paid attention to them. People felt that the everyday familiar situations that we portrayed made them more receptive than delivering the startling message of one in 166.

People liked the fact that we focused on the prevalence and, most importantly, the moms in the focus groups said that as a result of this ad, they would be likely to seek more information about autism and to talk to their doctor.

I'm going to take two minutes, I know I'm a little over, and talk about distribution because, again, the best spots are not worth anything if they are not distributed.

We have sent the TV spots to 1,600 stations across all 212 market groups. We have sent the radio to 8,000 stations, again both in English and Spanish. The print is going to 6,000 newspapers and 4,000 consumer magazines. The web banners go or have gone to the top 10 networks and they have already run on 200 websites, and we have created very special partnerships with Google, AOL, MSN and

Yahoo!

We have also looked at nontraditional distribution and this is new for the Ad Council. We will be running the television spots in the opening trailers at the Nantucket Film Festival and the Boston Film Festival. We're looking at outdoor space, benches, billboards, buses, sporting events. We have been pretty successful at getting them to run during half time at major league sporting events.

TiVo, we're going to announce probably next week that TiVo will be running the TV spots off the home page of its user interface. It's the first time they have used that space to run a PSA campaign. And we'll also be announcing in two weeks that we will be on the side of the Rice Krispies box.

The way we'll measure the successfulness of the campaign is, first and foremost, the easiest thing for us to measure is the number of pickups. That's when and where the spots run. But as important to me, if not more, is the shift in attitude or any change in behavior that results.

So we have already done a pre-campaign tracking study and we'll do a post-campaign

tracking study in six months. We look at awareness of the campaign itself. We look at awareness of autism and, most importantly, we look at any changes in attitude or behavior that is a result of the campaign.

We also look at the volume and subject of calls to the 800 number. We measure our web hits. We have already seen on our website a 700 percent increase on the Learn the Signs page. It's now our second most heavily trafficked page behind our home page. We look at the total number of donated media dollars. As a high profile Ad Council campaign, we're targeting $28 million in placement in the first year. It's aggressive, but I think we can do that, and we also measure our press coverage.

By way of press coverage, when we launched the campaign on April 7th, Suzanne Wright, our co-founder, appeared on The Today Show. That placement alone reached 5.5 million viewers. That same day Suzanne and Dr. Cordero did a marathon satellite media tour doing interviews with 22 of the network affiliates in one morning. It was quite an impressive showing and I thank Dr. Cordero for participating. That also hit 3.5 million viewers, and each one of those stations during the

interviews played at least one spot.

We have done 26 radio interviews across the country using members of our local volunteer walk staff and our board to try to get across the country, and we also were fortunate to receive from MSN a roadblock, which means our ad appeared on MSN on every page for one day.

The spots right now are running on ABC and NBC networks. We're focused on the daytime day part because that is highly attractive to young mothers, but we have been very successful in getting nice placements. On NBC this week we'll be running on Passions, on Days of our Lives, on The Tonight Show and on Law and Order: SVU. On ABC we'll be running on All My Children.

The spots have run on 54 stations across the country that we know of. Again, we won't get actual data for another couple of days, because we're only one month into the campaign. It's running on CNBC, MSNBC, a lot of the local cable stations. It's running on Noticias. It's going to start to run on Telemundo next week and we're distributed via CBS Newspath. That is the CBS service that distributes material to all of the CBS affiliates.

On radio we're running on CBS Radio, Sirius

Satellite Radio, XM. Print, we just distributed the print. The two commitments we have gotten so far from long lead magazines are Parenting and BabyTalk. Those may be the first two. Those are two of our most highly targeted because that gets right to our core demographic. And on the Internet we have been very successful with getting the banners placed and we also got the TV spots placed on the ABC News Now, which is the 24 hour news feed on the Internet.

As I said, this was a huge collaborative effort and I just want to specifically point out the members of our Advisory Committee. The work really reflects the input of a lot of people and I want to thank everyone who participated. I particularly want to thank Peter Bell whose commitment to collaboration is truly unmatched.

[Applause]

Dr. Insel: Jim?

Dr. Battey: Well, I thought that was very impressive and I think the NIH should hire you to try to improve our image and visibility. We would do well to have you deliver our message since we seem to do a pretty lousy job of it.

Dr. Insel: Jim, I don't think we can afford

Alison any longer.

Ms. Blackwell: I think we need Alison, too.

UNIDENTIFIED SPEAKER: I'm sure.

Ms. Blackwell: Yes.

Ms. Singer: Well, thank you.

Dr. Insel: Other questions or comments for Alison? Larke?

Dr. Huang: I have a question of how that connects with the tool kit that you're doing, because it seems to me that -- I mean, I thought they were very impressive. It seems to me that that quick, short message, putting it in like pediatricians' waiting rooms, because oftentimes we find that parents want pediatricians to bring up some of these harder issues for them. Pediatricians are unwilling to do that.

And if there was some kind of stimulus like your print material in the waiting room with that odds, The Odds Campaign, that that might actually trigger them bringing it up also. So is any of the print connected with the tool kit piece?

Ms. Singer: Not -- do you want to?

Dr. Cordero: Actually, we have a whole set of materials that we actually have for the pediatricians and, actually, it is for the waiting

room. And it's actually a set of questions about key points in development at different ages, so the parent can actually look at those and see is the child smiling or is the child having eye contact, etcetera. And it goes out and then that actually also has questions to ask the pediatrician to begin a dialogue, and that is something we have presented a couple of meetings ago.

Oh, and we also have for parents -- thank you, Kathryn. We are actually distributing to parents things like -- you all know about having the refrigerator that put -- just they had -- well, here what we have done is also joined that with developmental stages.

For example, for 18 months the simple pretend play like talks on a toy phone, and that is so parents can actually look at this and see the child is not doing that, then let's talk with the pediatrician. It is in that sort of way we have been trying to integrate.

Ms. Singer: We also have plans to --

Dr. Cordero: Let me pass this around.

Ms. Singer: We also have plans to produce the print as posters for doctors' waiting rooms, so I'm going to just pass around some of the print.

Dr. Insel: Are there questions or comments for Alison? Okay. Thank you. We're going to move on and we'll be hearing from Dr. Jane Pickett on the Autism Tissue Program, how brain donation advances autism research. Dr. Pickett combines a background of basic molecular biology and neuroscience research and clinical experience.

She has authored numerous publications in scientific journals as well as been a featured speaker at national and international research conferences. She has coordinated the development of the Autism Tissue Program, that's 1998, following a neuroscience research appointment at Princeton and I think she actually has been here before talking about this, but we're eager to hear the latest. So, Jane, welcome.

Dr. Pickett: Thank you. It's great to be here. The Autism Tissue Program, NAR's first scientific program, joined Autism Speaks with a recent merger. We're quite excited about that. I am very gratified by the continuing enthusiastic support for neuropathology research, and I do want to give an update on what has been going on with the Tissue Program in relation to the Autism Matrix, our various ATP operations, relationships with IACC

Members.

We interact with a number of them. Barry Gordon and Marshalyn Yeargin-Allsopp of the CDC are members on our Autism Speaks Scientific Affairs Committee. The Autism Tissue Program was started as a joint project with ASA and we continue to work on common goals. We have new projects, a couple of new projects with CAN. We're doing some international brain banking and look at the National Database for Autism Research as an opportunity to be able to share our data in a collaborative environment.

This is the Autism Matrix. The neuropathology goals are shown in blue. The ATP along with the NIH-funded brain banks constitutes the infrastructure for enhanced brain acquisition. I think we're there pretty well. This is a cumulative total chart of registrants through 2005. The current number is a little bit over 22,000 people who have signed up to donate brain tissue and our number of donors is 112.

The midterm goals for the neuropathology research on the matrix are to characterize, identify the brain structures that are involved and look at developmental time sequences and understand the neural circuitry and neural chemistry all with

the goal of understanding the common features, so we know what to do about treatment.

One of the ways we're approaching this is a Brain Atlas Project that started out with two collaborators and now it has been joined by many. It's a comprehensive stereology program where we have images and 3D representations of the entire hemisphere of about -- I think it's about 12 autism and control subjects. So what we do is we do slices of the brain and staining and counting cells.

And this is a representation of a 3D structure of a man with autism who was 23. It shows largely intact brain stem structures. Usually none of the pathology of autism has stood out as being a gross problem. They are fine problems, as I think we all understand now.

Mini-columns were publicized a couple of years ago as being changed in autism with an increase in number, packed more closely together, more regularly spaced. This research has been duplicated in a double-blind study by Casanova and is under investigation in several other labs.

We're very interested in this because these columns are units of function in the cortex and they are about 60 to 80 cells. They all come from a

founder cell and the founder population is put down. Their cells are born and they are in place by about embryonic day age 50. That is seven weeks of gestation, so it's very early. So these changes really to us mean that in the often larger brains with autism, we have a structural change that we want to understand how this impacts functioning.

Also in terms of development, this little chart here on the left is a listing of the ages of our donors. We have very young donors, a male aged 2, two males age 3, two age 4 and then on down the line. So we, of course, rely on a lot of animal studies for understanding the neurodevelopmental and then when we have brain donations of young children, we can look at the pathology of them.

This is just an example of relationships of structure and function and something called emotional body language. I just thought it was a good representation of the model we're trying to find and we're talking about trying to understand circuits and how all these cellular changes affect circuits in the brain. We're also, of course, looking at neurochemistry, a number of different receptors and genes and gene products.

The impact of neuropathology on research.

Well, we combine with other technologies. There will be a publication coming out soon about new pathways found in the brain by diffusion tensor tracking and these pathways are from the fusiform gyrus to the amygdala and to the hippocampus and they appear to be different in autism. And we are using the Brain Atlas slices to verify what is implied in diffusion tracking.

Mirror neurons have become very interesting lately. In animals these neurons are involved and fire both in doing a task and seeing someone do a task, and people are quite actively studying them in autism. But with imaging and the space in imaging is about a 3 millimeter cube with millions and millions of cells, if we can pin down the cube, go back to the cells and identify those mirror neurons, then we can maybe identify some of the changes that people are seeing in the subjects.

And neuropeptides and social behavior, there are a number of people now who are applying to or have applied and some are in application to look at oxytocin and other neuropeptides.

Basically, we started out doing outreach only about the importance of donation. This is our website. People can go online and register there.

We have an ASD-friendly donation process, an answering service 800 number that people can call and they will be put in touch directly with the Harvard Brain Bank. We provide family support. We have home visits after a donation. When we document donors and get all the information, as well as doing ADIR, we solicit tissue proposals and allocate tissue and track tissue and acquired data. We do that on the portal.

I just want to talk for a second about the difference between our functions and brain bank functions. Harvard is the designated autism bank supported by NIMH and NINDS and they are the ones that are responsible for obtaining the written consent. We always have consent for donation. We do want to follow-up with all of these families.

They arrange for the tissue recovery and they do elemental donor data mostly on the tissue, the postmortem interval. They handle the shipping, processing of the tissue, do a neuropathology exam, store the tissue and then send it out and they will do it according to our Tissue Advisory Board recommendations. So we're an umbrella to them.

We try to encourage people to donate to them, provide the answering service. We assist with

consent because it's so important to have that done. The Pathology Team to remove a brain is usually not mobilized until that happens, and then we have our review process. We keep our donor records after a home visit and our research data.

We have 11 members on our board. CAN has a standing member. It has from the inception. Tissue recovery protocols are on the McLean/Harvard website. We are having a meeting tomorrow; in fact, to review 15 more proposals and these are getting larger all the time, so we're excited about the interest in neuropathology.

Administratively, we have an Executive Committee and they are responsible for policy decisions and staffing and getting the Tissue Board members. Our portal handles our registrants and donor information. Our tissue proposals are put in online and they are reviewed online. We have information about ATP projects and our tissue distribution research data and the things that we can contribute.

To end, I will explain a little bit about the portal. This is a case data area and this page is a case list. People who are interested in applying for tissue will go on the portal and look at cases.

Those who have cases and are doing studies will go and find out more about the donor. There are a number of different pieces of information on these lists. This is about the tissue and tissue quality issues if there are any and the days in storage.

We also have perinatal condition reports. When they are available, we enter that data. Those are from our interviews and immunization reports. Then if we pick a specific case, in this case this is Harvard Case 6184 this was a female, 18, who has a very large brain, 2,100 grams. Autism is the diagnosis and she died of seizures. It talks about the tissue fixation and then it gives a list of similar donors. This was in response to a request for PIs for information when they are trying to match cases for their research.

The case summary going on, this person didn't have immunizations, was never immunized, negative for Fragile X. And then we show the different investigators that have the tissue. We have documents. That is our unstructured data. This is an example of the documents that would exist, the ADI, autopsy, neuropathology, etc. We can look at a specific case and then get a listing of all of the documents available.

This particular page is sorted on MRI. We have MRI available. For a number of cases we do postmortem MRI and this was started in David Amaral's lab in most of our cases. And we wanted a record of the brain structure prior to its being sectioned and distributed. Secondarily, we have these images for 3D reconstructions and research.

One of the things that we -- it was obviously a very rare resource and very important to control it as much as we could, but make it available to as many people as we could. So we started tissue libraries. We have a requirement for tissue sharing and data sharing we have people sign when they apply for tissue. So in the amygdala study that David Amaral and Cindy Schumann did, there are 50 and 100 micron sections of amygdala and limbic sections cryoprotected at their lab.

We have DNA now. This is a test. This is not coming out very well, but it's a check of the RNA quality. We put that information on the site and we have just started our first genetic library with 16 autism and 13 control donors at Tony Persico's lab in Rome, so people can get DNA there. Our Brain Atlas Project houses sections that have been retained for use by others. That is a picture of a

stained section on the upper left.

And, unfortunately, this isn't coming. Well, it comes out better there. Tissue array slides were made by Charles Eberhart at Johns Hopkins and you can put 99 small 2 millimeter plugs, the sections, on a slide and then section them. You can get about 100 or 150 replicate sections, so this is so that you can put a number of different cases on one slide and a number of different areas in any arrangement you want and do quick screening for antibodies and these are available.

We do tissue tracking of all of these distributions on the portal, too, because we want to also get the data from the use of the tissue. This is an example of some of the fine mapping that has been done. This isn't an autism case, but on dendrites in autism. So we're interested in neurodevelopment. Early growth dovetails with some of the studies, the head circumference and the Baby Sibs Program, so we're interested in seeing how that develops on our end and theirs.

We have our new genetic library. Now, we're getting more interested in it or not. We have always been interested and involved in proteins. I have to thank Tom Insel for bringing up the fact

with a brain research group here that anyone interested in autism pathology, contact me and David Jacobowitz did that. And it turns out that a parent has a new protein screening tool that he wanted to explore. So the two of them are getting together to talk about protein assessment and, of course, microRNA is another area of interest now.

International brain banking. We have started a collaboration with brain banks in England and are talking to other people in Europe. Two of the areas that are our challenges are the control pediatric tissue in some of our new projects. And let me just talk for a second about mortality.

We have to put this in the context of families. Ours have had a huge loss and it's sudden and unexpected. We have done now three mortality studies. We just did a current one in California, the first two we published, and we found a higher mortality rate especially in girls. We have a high mortality rate in boys, but a much higher one in girls and are very concerned about this.

Autism donors often have sudden and unexplained deaths called SUD and SUDEP and epilepsy, of course, is a disorder we're very interested in looking at and channelopathies seem

to be linked with autism. And then now there is a new childhood onset seizure disorder that was characterized recently, so we have some research interest in that area.

And on the 2001 study, that was a 15 year study from 1983 to 1997, there are thousands of codes of death. Autism is 299.0. Misadventures of surgical and medical treatment is 800. That is when someone leaves a clamp in your body. But they all can be condensed into 17 categories of death, at least in the ICD-9 old-fashioned system.

And what I did is very simply took our data and the bottom, the axis, is a percent. So the autism is in blue. So in injury and poisoning, the categories, the autism deaths when we looked at the deaths that year, 282 fell into 25 percent about of injury and poisoning. If you add all of the blue bars up, you will get 100. Symptoms and signs just means unknown. We have many unknown deaths.

Nervous system would be epilepsy or epilepsy-related disorders. Mental disorders is where autism would fit. Perinatal period, congenital disorders, all of these just appear in this unscientific chart to be higher and I think it just addresses an issue that we want to continue to look at this, and I'm

very happy that the CDC and Marshalyn has gotten behind trying to get information from places other than California. I think the California data was very interesting, but I think we need to get more.

The control pediatric tissue, putting this in the context of families. For an unaffected child that has died suddenly, of course the loss is immense and there is just little information about brain donation. Of course, I know who I'm going to go to for a campaign. One of the things that we are doing is tying into -- it's not just awareness. It's the system and the people that are also notified on a regular basis about deaths at the organ transplant industry. We're very interested in continuing to link up with them.

And HRSA has a Maternal Child and Health Bureau that we know quite a bit about from this Committee, but they also have a Health Care Systems Bureau where they have OPOs and tissue banks, and we are collaborating with the Division of Transplantation and we use Iowa Donor Network as a model. So the control pediatric tissue is something. What we need to do really is address probably a campaign, a national awareness campaign to let people know that research is going on and it

is important.

This is one of our ads that we put in autism magazines and we have information for donors. We have a parent DNA project. We're working with AGRE because investigators looking at brain tissue have come back and said, all right, I really need to know whether the genes we're looking at have come down from the mom or the dad. We entered our first family into that project last week.

And then there is also the Children's Hospital of Orange County where we are wanting to direct donations to the CHOC Hospital so that neuroprogenitor cells can be derived from the brain tissue. They already have neural cells and culture from rat and Fragile X brain donors so we're eager to get donations there.

We have many people coming to us to do study in autism from the geriatric disorders area and it's very important. I mean, there are these unique neuron populations that were dying and now they know that there's common protein accumulation among them. In terms of the grand plan and understanding common mechanisms, we would like to be able to have a chart like this to explain about autism.

Our personnel, I would like to thank everyone

who works. We have an hourly administrative assistant, some part-time workers, a full-time data person and we rely heavily on Alicia Holiday and Jenny Longmore of Autism Speaks.

So my goals and recommendations is that I would like to propose a two year plan of enhanced PR. This is something that we're going to do, but for this Committee I would like to see if we can engage more interest and visibility about the Autism Tissue Program and the idea of donation. It is a hard thing to talk about. And if it's disabling for people to hear the word autism, it's really disabling for them to hear brain donation.

We are also interested in new Tab members. People are getting busier by the minute, so it's hard to get their time, and we will continue to have meetings about brain acquisition, data meetings. We hope to be at the table with NDAR when they are talking about how to have a federated database and what we can do to join in, and we will be having a meeting with our PIs at IMFAR. So anyone who would want to join that, please, let me know. Thank you.

[Applause]

Dr. Insel: Questions for Jane? Jose?

Dr. Cordero: Jane, very nice, just tremendous progress. Can you go back to the slide on mortality? I'm not sure I -- I may have missed something, but what are the age groups that you have in that slide or did you look across or do you have some kind of --

Dr. Pickett: Ah, this one?

Dr. Cordero: Yes.

Dr. Pickett: Well, I think you have a good point there because the people that were identified with autism are probably younger. We're not catching a lot of the geriatric people because our group was from 1983 to '97, and those people identified with autism who died on the older end were probably in their '60s and then that would have been a very vague diagnosis. Obviously, back then they would have been born a number of years ago.

You know, this was a quick and dirty look at just the categories of death. Well, as we did this, we started, you know, wondering is this a health care issue? I mean, certainly, a lot of the children who have been in our donor population drowned and, you know, it's common for them to be infatuated with water and take off as fast as they

can when they get out.

But otherwise, there is asphyxia and then there are all these unknown causes that we do believe are associated with epilepsy even in those who haven't had, you know, true epilepsy diagnoses.

Dr. Cordero: Right. I was sort of curious because when I look at the profile you have for autism, very much it's the pattern that you see in younger kind of children, meaning younger but older than the first year of life. There is sort of a very interesting pattern like in the infant mortality, basically the first year of life.

Basically, about a third of all mortality, it's accounted for by birth defects, prematurity and SIDS. But once you go past the first year, injury basically is the leading cause and it goes until about age 25 or 29, and then the other conditions start to kick in. And it looks -- that is sort of -- sort of having an appropriate age comparison probably would give you something that is a little bit more similar.

Dr. Pickett: Right.

Dr. Cordero: In terms of the comparison.

Dr. Pickett: I agree and I'm hoping CDC does that.

Dr. Insel: Jane, what can you tell us about medications? How many of the children in the bank were on medication?

Dr. Pickett: Probably 75 percent of them and we document that, too.

Dr. Insel: And is that a confound for much of the anatomy or is it thought to be irrelevant?

Dr. Pickett: Well, I think that's a problem. We have talked about what is a control, you know, for this population and, you know, I think people with epilepsy is probably a better control than the so-called unaffected person.

All we can do right now is track that and I know for a while Fred Volkmar was on our board and he asked if our neuropathology could somehow measure the effects of medication over time. And I said, well, that's not really an aim and I don't know how that would be done, but it certainly is a provocative question to look at.

Dr. Insel: Just one other comment. One of the places where we have had the most traction recently in schizophrenia is by not only identifying DNA variations that look like they are associated, but then going into the brains in the postmortem collection and finding that many of those were

associated with splice variants or very different patterns of RNA expression for that particular genomic region. And I think it's really helpful that you are now partnering to get both the DNA, as well as having the neuroanatomy.

Dr. Pickett: Right.

Dr. Insel: Because there is a whole opportunity there that hasn't yet been explored.

Dr. Pickett: Oh, exactly. I think we're at the threshold. We're really at the midterm of the matrix.

Dr. Insel: Any other comments or questions? Okay. We will break here. Let's reconvene at 1:00 for the scientific updates.

[Whereupon, the meeting was recessed at 11:54 a.m. to reconvene at 1:00 p.m. this same day]

Dr. Insel: We've got about an hour to do the science updates and we're going to begin with a presentation on early indicators and developmental trajectories in autism by Dr. Rebecca Landa, who is the Director of the Kennedy Krieger Institute Center for Autism and Related Disorders. She is an Associate Professor of Psychiatry at the Johns Hopkins School of Medicine. She completed her post-doctoral training in psychiatric genetics,

consulted and presented internationally on both clinical and research topics.

Currently, she is funded by the NIH and the CDC to conduct studies of the early detection of autism spectrum disorders, early intervention for ASD, neurobiological basis and the prevalence of autism. Rebecca, welcome.

Dr. Landa: Thank you. Okay. Thank you so much. I'm really honored to be able to speak before you today. The work that I'm going to be sharing with you comes from our NIMH funded study of infants at risk for autism, because they have an older sibling with autism. And our first paper is now online on General Child Psychology and Psychiatry.

This study has yielded a lot of practical applications as well as theoretical and scientifically relevant applications, including understanding infant learning mechanisms, being able to teach people what to look for in infant development, to look for signs of autism spectrum disorders, developing efficacious treatments and informing neuroscience about where to look in the brain process. So these are the people who have funded us.

I'm going to move quickly through some of

these slides, so I can show you some of the babies. As we have heard so far today, there is an urgent need to identify autism as early in life as possible. We know that autism, we believe that autism has its neurobiological onset during pregnancy. Parents see something is wrong with their child by the time the child is 24 months of age. We have some retrospective studies of autism indicating decreased social orienting, babbling and imitation.

We don't have any medical tests for autism and we don't have any really diagnostic criteria for children under autism -- with autism under 3 years of age. But yet, we know that there is something called experienced-dependent neuroplasticity and that we have windows of opportunity. And the more that we learn about infant brain development, the more urgency, I feel, for developing infant interventions for autism.

So how early can we really detect autism? Well, we don't really know when the symptoms begin to express and we don't even know what symptoms we should be looking for. I thought I knew when I started this study, but now I know I didn't. We need to know are these symptoms the same over time

or how do they change. Can we really come to a point where we agree on the age at which we can diagnose autism and how would we predict autism from infancy?

So we have selected this prospective longitudinal research design by studying infant siblings of children with autism, because the literature said that 4 to 10 percent of the children who have an older sibling with autism would themselves have autism. It appears that that number is an underestimate, although none of the people in the baby/sibs research consortium have the proper designs to be able to really look at recurrence risk, because there is sampling bias.

And I have found this out just yesterday when I looked at the data. We have parents complete a form when they enter the study. Do they have concerns about their baby? And about 46 percent of the parents who entered with their babies at 6 months had concerns. But 85 percent of parents who entered with 14 month-olds had concerns. So we have a sampling bias.

Okay. Then we also have something that's known in the field as broader autism phenotype, which the field has said involves language and social

developmental disruptions. So we're going to talk today a little bit about the progression of autism. And the data I am presenting to you today represent 128 infants who have reached their 30 or 36 month outcome point. We try to get them to 36 months. I had a few kids who hadn't made it quite to 36 months, but I didn't want to leave them out of the analyses.

So the data I'm presenting to you today involved 30 children with autism spectrum disorders, 22 with broader autism phenotype and 66 who were essentially unaffected. We tested these babies about every six months from 6 to 36 months of age looking at social, language, motor, cognitive, temperament and adaptive functioning.

Today I'm only going to be reporting results on the Mullen Scales of Early Learning, the communication and symbolic behavior skills and the ADOS, Autism Diagnostic Observation Schedule. I'm going way fast, aren't I? But hang tight with me, so I can -- this is the piece I really wanted to spend time on.

So at 6 months of age what we thought we would see was really social disruption and disruption in synchrony with care givers. And we're still in

process of coding those data, but the big hit is really in passivity and motor disruptions. And the motor disruptions involve somewhat late onset of milestones, but also some issues with hypotonicities, some atypical movements and problems with motor coordination.

And so the reason I have these pictures down here is that, you know, do babies go from this kind of compelling social connectedness at birth and get to this point? And can we interrupt that process somewhere in between?

So if we get to the 14 month data, there is just a lot to tell, but I'm going to boil it down to just a few things. And that is that the two biggest predictors of an autism spectrum disorder at 14 months of age involves an aspect of joint attention called -- well, involving -- monitoring the attention of others. And we call this a three-point gaze shift. And you will get to see it. I'll show it to you in a video tape. But it's basically an infant being able to monitor the attention of a social partner.

This is really the platform people believe for the acquisition of later theory of mind being able to understand other people's intentions and beliefs

and perspectives. The other thing that joined up with that at 14 months to predict autism later is the number of -- the variety of consonants produced during communicative bids.

And so if you put these two things together, you correctly classify whether a child will have autism or not autism at 36 months with 82 percent accuracy. That was kind of interesting, because we force ourselves to make decisions about whether we believe a child should be classified as having an autism spectrum disorder at every visit and then we have confidence ratings.

At 14 months of age, of the children that we classified that we believed had an autism spectrum disorder, 72 percent of them remained stable at 36 months of age. And what's interesting is that number is the same for the 24 month-olds. And unfortunately, I can't show you my growth curves, some of my growth curves that could explain that a little bit better.

But with regard to this business of who did we pick out at 14 months of age who would have an autism spectrum disorder at 36 months of age? That's these kids. This is the ADOS Communication Algorithm Score and on the communication algorithm

a score of 2 indicates autism spectrum disorder and a 4 indicates autism. And remember, Dr. Lord, who developed this instrument, always cautions us that your score on this instrument does not equal a diagnosis. Clinical judgment has to be combined with this.

So for the kids that we diagnosed or classified as having an autism spectrum disorder at 14 months of age, those -- that's these kids. And you can see that their ADOS communication score remains rather stable between 14 and 36 months of age. These are the kids that we did not consider to have an autism spectrum disorder at 14 months, but they had it at the 36 month visit and look what happens to their social -- their communication score. The higher the score, the more you would look like an autism spectrum disorder classification.

These are the kids -- this is a combination of broader autism phenotype and unaffected and this is what happens. They fall clearly into the very normal range by 36 months. So with regard to the social domain of the ADOS, this is what happens with the early onset cases and this is what happens with the later onset cases. We miss them at 14

months, possibly because they really didn't have an autism spectrum disorder yet or their symptoms weren't magnified enough for us to detect them, because they were still in the same place with kids who didn't end up with autism, who are reflected here dropping into the normal range whereas these kids escalate into a more autism picture.

Dr. Insel: Becky, could you just, on those, give us a sense of the proportion?

Dr. Landa: Yes.

Dr. Insel: So the top line?

Dr. Landa: So it's about half of the kids with ASD are here and about half the kids with ASD are here. It falls right on -- almost right down the middle, interestingly. And I'm not going to be speaking specifically about regression today, but equal numbers of children in those two onset patterns are equally vulnerable to regression. Regression being defined as a worsening in social symptoms, an increase in autism symptomatology, ala, echolalia and so forth, an actual loss of raw score points on language measures and receptive or expressive language.

Dr. Insel: Did you see the converse that children at 14 months were up in this very high

range, who then by 36 months looked fine?

Dr. Landa: That's the bad news. If a child really looks flagrantly autistic at 14 months, it can happen that by 14 months they don't fall into the spectrum, but they haven't gotten a clean bill of developmental presentation yet.

Unidentified speaker: I'm sorry, I don't understand.

Dr. Landa: What I'm saying is -- okay. So if a child shows that they have -- if they are fully autistic at 14 months, by 36 months they don't develop normalcy. Most of them remain in th spectrum.

So what I'm going to show you in the next five slides are typical development and autism. So this is a 4 month-old with an -- who ended up with typical development. This is a baby sib of a child with autism, whose development quotient was 100, which is like, you know, baby IQ.

And so what you are going to see in this video is that this baby is continually socially engaged. Is either looking at the care giver, the mother, who is bending down doing a very unusual form of peek-a-boo or glances over to the examiner. This baby's vocalizations are coordinated with the care

giver. This baby has rhythmic limb movements and better -- paired with vocalizations and the baby is showing a lot of smiling.

How do I make this play? Oh, I see. Thank you.

[Video played]

Narrator: Peek-a-boo, peek-a-boo, I see you. You're not going to want to be in that seat, are you? No, no, no, no, no. No, no, no, no. Can you sit up real big? Can you sit up real big?

Baby: Squealing.

Dr. Landa: Looking at her standing with the back to his mom. Okay. So that's a 4 month-old who is very engaged, did not have autism. This is the worst 6 month-old that we have in our study. He looks autistic already. He doesn't look at his mom during peek-a-boo and she could not get him to look at her through covering her face and so she decided to cover his face, hoping that he would look at her hands.

And when she removed her hands, his eyes would be pointed in the direction of her face. And he does track the movement of her hands to her face, which you will see in a minute. He has no social engagement, no directed smiles, no babbling, continual raspberries and he is motorically very

still.

Narrator: Where's Stephen? Peek-a-boo. You're not going to peek-a-boo today.

Dr. Landa: And she keeps saying you're not even looking. Then she decides to play this little piggy and he likes it. You see him smile.

Narrator: This little piggy had roast beef. This little piggy had none.

Dr. Landa: He really likes it, but he doesn't look at her.

Narrator: Wee, wee, wee, wee, wee all the way home. Hi. You look at my face. Ready? Are you looking? You're looking at your feet. Are you looking? Where's mommy.

Dr. Landa: You just see him track the movement of her hands to the face. He will look at the hands, but not to the face.

Okay. So now the little guy that you saw at 4 months, this is him at 14 months. And so you're going to see this is the communication is symbolic behavior skills developmental profile. So the examiner blew up a balloon, let the air out and then laid the balloon in front of the child. The child picks it up and he is going to make a request for her to blow it up again.

So you see him integrating across developmental domain. You see eye contact, positive affect and communication happening simultaneously. He has socially engaged behavior regulatory bid and he has purposeful object exploration. See how the balloon flaps and he flaps it in a very meaningful exploratory way. And that was a very hard to see three-point gaze shift there, but so the gesture of giving, looking at the examiner and smiling all at the same time, that little three part integration across developmental systems is one of the greatest vulnerabilities in 14 month-olds with autism.

So here is the little guy you saw at 6 months with autism. And so what you're going to see here is also the communication and symbolic behavior scales, but this is a wind-up toy. He doesn't engage. He doesn't share affect. He doesn't show eye contact. He doesn't have any babbling. There is no initiation of social communication. You can see his motor problems. You can see what looks like hypotonicity. He doesn't cross midline. He has difficulty isolating his fingers when he tries to pick up the toy and so let's have a peak.

But he is interested in the object and he does try to get it.

Narrator: Can I wind it again?

Dr. Landa: Okay. And so this is him again. Now, what happens, this is immediately subsequent footage, is that he spots the Cheerios over on the table to his right and he makes a request for them, but the form of the request is quite idiosyncratic. The clinician, who is the blonde haired gal, thinks that he wants help with the wind-up toy, but his mom is able to read his signal. He doesn't integrate it with gaze or affect.

Narrator: You need help?

Dr. Landa: So what he really wanted was Cheerio and I just show that to illustrate the idiosyncratic nature of his communicative bid and the failure to integrate across his other systems.

Now, I mentioned a little bit about regression and so this is a baby who did regress. And so his early learning composite was 126. The mean of the instrument is 100 with a standard deviation of 15 just like regular IQ. And so he was sort of super performing at this age. I'm showing you this clip, because this just precedes the peek-a-boo and the mom calls his name and when she touches him, he has an unusual reaction.

Narrator: Joseph, pat-a-cake, pat-a-cake.

Dr. Landa: A kind of thing that's so easy to miss and I'll just show it to you again.

Narrator: Roll it. Joseph.

Dr. Landa: But, you know, he looks at her and he --

Narrator: Pat-a-cake, baker's man, bake me a cake as fast as you can.

Dr. Landa: He's not really looking at her, positive valence in his face and then she continues to have a peek-a-boo again.

Narrator: Peek-a-boo.

Dr. Landa: He is moving. He is active, engaged. This is very typical there in that clip. This is him at 14 months and you can see he looks a little socially anxious sitting on his mom's lap, but looking -- doing a lot of three-point gaze shifts between the toys and the examiner and wants to put the candles in the cake, but just isn't quite sure if it's really okay, kind of looking for permission. At this age, his development quotient was 101. A lot of real nice gaze to the face. Nice share positive affect, really high quality attention.

By 24 months of age, he is not responding to me calling his name or trying to get his attention.

I'm trying to do this joint attention task. I'll show you what it looks like in a typically developing 14 month-old first. So here's the examiner. Here is the object over here that he is supposed to look at and she will call his name and look over at the object. He is socially responsive. He looks where she is looking without a pointing gesture. Then he initiates joint attention looks at his mom, integrates to his mom, gaze gesture and a word. Tries to get her to look at the toy.

Narrator: Thomas, Thomas, look.

Dr. Landa: So lots of checking in with people around events, objects and so this is a 24 month-old with autism. The same little guy you have been seeing.

Narrator: Joseph, Joseph, Joseph.

Dr. Landa: He points. He wants that thing back.

Narrator: Hey, sweetie pie.

Dr. Landa: But now he wants to get down and look at the wheels on the car.

Narrator: Hey, Joseph.

Dr. Landa: But I'm trying to take it.

Narrator: Joseph, look, look. Joseph, Joseph, look.

Baby: Cries.

Dr. Landa: So it kind of looks like he might glance over there, but he doesn't really get it. There's really no social engagement. He has real autism now and his IQ has dropped to something like 75. And so this is just another little way for me to show you what's happening socially between 14 and 24 months.

[End video]

Dr. Landa: This black line is the early onset group and the pink line is the late onset autism group and the blue line is the combination of children with the broader phenotype and typical development. And this is initiation of joint attention to get other people to look at what you're looking at from 14 to 24 months. And the children who we diagnosed or classified as having an autism spectrum disorder at 14 months, they don't have any initiations of joint attention. And at 24 months, they still don't have any.

So my point is if we don't treat this, you're at stagnation point. And for the later onset kids, they don't have very many, but they have some and by 24 months, they are at the same places where they were. And then you see this is the trajectory

of kids who don't have an autism spectrum disorder.

This slide shows the stereotype behaviors of repetitive interests and so I've broken this slide into three groups. This is a group of kids right here who never met criteria for autism, either clinically or on the ADOS. This group here are the kids who met criteria on the ADOS for autism spectrum disorder, but did not receive a clinical judgment of an autism spectrum disorder. And these are the kids who met on the ADOS and had a diagnosis of an autism spectrum disorder.

And so this is the ADOS algorithm item for repetitive and stereotyped behaviors. And I just arbitrarily picked the fact that they would have two or more points on that, and so you can see that about 5 percent of kids who never meet for autism have -- meet this criterion at 14 months; they never really develop any over time. Kids who met on the ADOS have -- about 20 percent of them show these things at 14 months, but it dwindles down to about 10 percent by 36 months. But kids with ASD, 60 percent of them have these things at 14 months and almost 90 percent have them at 24 and 36 months.

So I just wanted to show you what that looks

like in a 14 month-old. This is going to be really fast. But this is a little guy who is in a room with lots of interesting toys and he fixates on these locks and his mom can't divert his attention.

[Video played]

Dr. Landa: She rolls a ball into his space. He has been doing this for a while. So he situates them and then he flicks them around a little bit. Then he resituates them and reflicks them around a little bit. And then he carries them around the room and comes back and sits them back on the ground and reflicks them around a little bit.

[End video]

Dr. Landa: So what about diagnosing autism at 14 months? Well, this is very tricky territory and it's tricky for two reasons. One reason that it's tricky is because not all children who end up with an autism spectrum disorder manifest clearly enough for somebody like me who does this seven days a week to pick it up.

And in the kids who do manifest at 14 months, when I first started this work, I missed kids, because I was taught and believed that at 14 months the things that you wouldn't do if you had autism is you wouldn't imitate, you wouldn't have three-

point gaze shifts, you wouldn't point, you wouldn't have a beautiful affective smile in a peek-a-boo and I realized that at 14 months, autism is more a matter of degree.

And so you can't expect an absence of skill. So if you're doing a screening where you say does not point, that you're -- you know, that's just not characteristic of autism at 14 months. They do point still. They might be following a pointing gesture. I didn't show you a video tape of this, but this is something I call empty joint attention and we also have empty imitation. And that is where the kids might sort of mindlessly imitate, but it's not social engagement.

It almost looks like it was just they were happening to be passing by, it's almost like they pick up, you know, a peanut off the floor and pop it in their mouth. It's that unlinked to anything really meaningful. So we can't just rely on the fact that they do or they don't respond to a joint attention bid. Pointing happens, like I said, sometimes for social purposes, but usually it's like Joseph did in that video tape to get back the cause-affect toy that I took away from him.

Three-point gaze shifts are happening, but

they are quite infrequent. This is a matter of degree. You can get a gorgeous peek-a-boo, so it looks like if you really excite and arouse these kids, you can get a social engaged interaction, but we have to look at shared positive affect in a more -- in a bit of a more complicated task than just a peek-a-boo.

You can get good responses to favorite songs. You can get good smiles and they may communicate and they may have eye contact, but they don't integrate smiles, eye contact and communication. That's sort of the big take home message. We do have the challenge of normal variation, so that's why we can't look at just one thing. We have to look across systems and if we're not sure, we have to follow these kids carefully.

Okay. So in conclusion, we can diagnose autism at 14 months. I should also tell you that all of the children who had an autism spectrum disorder by 36 months were not typically developing at 14 months. So if we pick up more kids than we should at 14 months, it's probably okay, because they probably needed to be in intervention anyway, even though it wasn't autism per se.

Some children continually to progress in the

manifestation of the symptoms, even past 24 months. So we do see repetitive and stereotyped behaviors early. Sometimes they look normal, but they are too long, too intense and to the exclusion of doing other things. Regression is a real phenomenon. I'm thinking of it really as a progression of the disorder, rather than thinking of it as regression specifically.

In my sample it was quite insidious. Many times parents didn't notice it, but by the time they came back, it was a different child than who had been there before. So early detection is essential. Social gains are minimal if we don't treat. Our intervention study indicates that we can alter that, at least in 24 month-olds. So, you know, this is the story that I have as of today. So if you have any questions, I'll be happy to answer them.

[Applause]

Dr. Insel: Questions? Jose?

Dr. Cordero: Very nice, Becky. One of the things that I'm struck -- when you show the data, especially the graph showing 14 months and 24 months, the sort of like benefit of the longitudinal follow-up and can you sort of comment

a little bit more on how do you see sort of instead of just having sort of cross cut observations, just sort of linking them over time and how would that be more robust or less robust in terms of recognition?

Dr. Landa: Right. Because especially in infant siblings of children with autism, there is a lot of havoc going on in the developmental system, such that there is -- sometimes the kids will come in for a visit and, like I was telling Jon a little earlier, there are some kids who come in who look very developmentally delayed at 14 months, but by 24 or 36 months they are showing a lot of improvement.

I think unless we have this kind of research, we aren't going to understand prognosis, we're not going to understand the possible transitions in this disorder. What ages are these brain changes happening that are causing behavioral alterations? What are the actual mechanisms of learning in these children?

And the other thing that I haven't talked about is developmental psychopathology. I mean, some of these children at 14 months look like they're going to have ADHD or anxiety disorders and

certainly by 36 months it even looks more intense. So following these kids until they are into their school aged years is going to be essential.

Dr. Insel: Becky, could you give us a sense of how good this will get? I mean, if you put all these measures together, what -- given that there is a lot of normal variation, you mentioned that, and it shows up in some of the data as well, how refined do you think it will be ultimately in -- at 14 months?

Dr. Landa: I think we will be able to pick kids up. And the kids that we pick up who don't end up with autism, they -- some of these kids were in treatment. So in other words, we're probably pretty right if we pick it up. And we don't actually have to call it autism, if we're uncomfortable with that, but we have to get these kids in treatment, that's the bottom line.

So I think, Tom, to answer your question is can we come up with a diagnostic algorithm for autism at 14 months? I'm quite sure that we can. The point is that we have to understand that there are going to be kids who might not meet it yet who need to be followed. And all baby sibs of children with autism need to be followed developmentally, I

think, from at least the first birthday. And the other thing is that some children may get better, but these kids need treatment.

Dr. Alexander: Rebecca, when you make your presumptive diagnosis or tentative diagnosis at 14 months and initiate some sort of an intervention program, two questions. First, is there any way you can differentiate between what we might call the false positive at 14 months, who might have gone on and done fine anyway, versus the one who is a therapeutic success, thanks to the intervention that you did?

And second, what kind of impact do you see on the parents when you make this kind of presumptive or tentative diagnosis at 14 months?

Dr. Landa: Okay. So the first question is we are -- our treatment studies actually not these children, so we're tracking their treatment, but we are not treating them. So your question about can we -- who are the false positives. As I say, none of those children go all the way to normalcy by 36 months, even if they get a lot better and merge out of the diagnosis and that is quite infrequent.

We are actually trying to figure that out right now. So is it IQ? Is it a number of words? Is

it, you know, the fact that they are at least making more non-verbal social bids? Is it something about the way they are interacting with toys? We're going to look at that.

The second one is about care giver parent. I mean, this is an issue that's very near to my heart and what we have begun to do with parents is, you know, we ask them to tell us if they are concerned when they come in. So we try to get some sort of a measure of what are their insights. And we see these kids over two sessions, so we have the luxury of working -- having a little time. Because on that first day, parents get a lot of insight into their child and they sort of narrate to us what they are seeing.

And at the end, we have come to having sort of a little list of developmental qualities and milestones that we go over with parents so we can check in on various things. Are we seeing things the same way? And by the end, the parents pretty much are the ones telling us. It's a real joining.

Dr. Battey: Just sort of a variant on Duane's really good question, I think, and that's as with most intervention strategies, I'm guessing that some of the kids benefit a lot from treatment and

some don't appear to benefit very much. If that's true, do you have any way to predict who is going to benefit from the intervention that's offered? And if you don't, are you looking for predictors of good outcomes or better outcomes?

Dr. Landa: Yes, we are. Unfortunately, from this sample it's hard to tell if children are going to be treatment responders or how much treatment impacts, because most of these kids don't get into intervention before their 24 month birthday. And if they get into intervention at 24 months, it's an hour a month or an hour a week, general special ed services. So it's pretty sparse.

From the Early Intervention Study, what we are learning about, and those are kids who entered treatment between 24 and 30 months of age, and we treat them for 10 hours a week with parent training for six months, and the kids who are not showing robust changes to that intervention are kids who have significant attention difficulties, such that they are completely self-absorbed, their IQs are very low, like 30. So those are the kids that we would expect.

But I have to say that there are some of those kids that look like that, who are tremendous

treatment responders. So we just need to look at it more carefully.

Dr. Insel: Yes?

Dr. Zeph: I was wondering about this particular group of kids or siblings and this family has already been through this before and maybe living with a child with autism in the family constellation. You said you were following the treatment, but you weren't -- or the intervention, but you weren't providing it. Is there any way to kind of sort that out in terms of the different types of -- my guess is that if the older sibling is in some kind of treatment, that the family might begin to generalize that or --

Dr. Landa: Right. That would be our anticipation and we do see that sometimes, especially if children are in discrete trial intervention. Parents will use that kind of interactive style with the younger children. What's interesting is if the child with autism, through whom the baby was ascertained, the proband, if the proband is severely affected and the baby is verbal, even if they have autism, the parents have a harder time seeing autism in the child, because to them this child is the wonder child. So that's

where we get into a little bit more of a conundrum.

Dr. Insel: Lucille, go ahead.

Dr. Zeph: Just in terms of how it affects the data that you're getting and if you are able to analyze any kind of, I'm thinking regression analysis, but, you know, in terms of what's happening with this particular group of kids and the various types of intervention and whether or not that is having some kind of confounding effect on your data in general in terms of the trajectory of the development?

Dr. Landa: Right. So we are at that phase now where all of these wonderful questions are we're just doing those analyses. So we will be looking at that. Unfortunately, there's going to be so much variation in the age of onset intervention and the intensity of intervention and the type of intervention in this small sample that's going to be hard for us to tease out.

Dr. Insel: Well, thank you very much, Becky. We're going to need to move on, but we really appreciate you joining us to get us up to date.

[Applause]

Dr. Insel: The final scientific update is from Helen Tager-Flusberg, who is going to talk to us

about behavioral and neuroimaging investigations of social and communication impairments in autism. Helen is well-known to this group, I think. This is, I think, your second time presenting. She has received her undergraduate degree from University College London and her doctorate in psychology from Harvard University. She is currently a Professor in the Department of Anatomy and Neurobiology and Pediatrics at BU, as well as a Professor of Psychology at BU as well.

She has been involved with autism research for over 25 years and is currently principal investigator of one of the CPEA Centers as well as the Director of a STAART Autism Center at BU. Thanks, Helen.

Dr. Tager-flusberg: Thank you very much, Tom, and thank you all so much for inviting me back. The room seems a lot fuller this time around. I actually did change the title of my talk when I realized the last time I spoke primarily about my own research program and the work that I have done expanding it out on language and communication.

And today what I wanted to do was to talk about the twin side of the social communicative impairments by focusing primarily on the social

effect of impairments. And what I'm really doing here today is representing a large group of investigators, both in the Boston area of my colleagues as well as my colleagues in the Wisconsin area that are all part of our STAART Center as well as the CPEA.

And I'm really excited about presenting to you. It will be very different from Becky's in depth analysis of a particular research question. What I really wanted to get across today was the full range of the multidisciplinary research that we are doing, all the way from the cell up to, the single cell, the family and to try to convey how these multidisciplinary centers are so important and how exciting it has been for us to be able to have two sites where we're essentially playing our ideas that generate from one site into the work in the other area.

Okay. So if we think about social affect processes, these are at the core of the social communicative problems. And what I want to talk about, first of all, is the question of what are the underlying mechanisms. And I'll be talking about behavioral studies, actually multi-method behavioral studies on social information

processing, taking that into the brain in vivo brain imaging studies, looking at the social network and face processing in the brain, taking it down to the cellular level in our neuropathological studies, thanks to the wonderful work of the ATP. And finally to bring that back full circle to ask the question, a really important question, I think, and our data, I think, speaks to this, on how social affective impairments, in particular, affect family functioning and parent well-being.

Okay. So we begin with faces. Faces really are probably for humans the key social stimulus. They are the core of our social relationships. They are critical for communication and so that's, of course, how I have become interested in faces with my interest in language and communication. We respond to and with our faces to express emotions and they really are the counterpoint to voices and language. So they are absolutely crucial.

And I think by studying faces, we, and of course several other, many other research groups around the country, believe that by studying faces, that will provide us to some of the clues to the mechanisms that underlay the social impairment in autism.

Now, we know that going back a long time that there is atypical processing of faces in autism and the question that we began with is where is the breakdown? So this is the work of my colleague, Dr. Joseph, that's part of our CPEA, started out looking at recognizing faces. They are shown one face and now they are asked which of these two faces did you see and you can see they are almost similar. This is when they are asked to choose which face they have seen earlier when they are given the whole face which differ by the eyes or when they are given with the parts, just the part of the eye that's actually changed.

And the finding from this important study was that the only atypical processing, they don't process faces differently altogether. It's simply in the eyes. It's the fact that they are not recognizing the eyes better in the whole presentation as do the control children. So then we asked well, what if you cued children to look at the eyes would that make a difference? And the answer is that performance goes up, but they are still not processing it in the same holistic way that typically developing controls would do. So there is clearly something different with the eyes.

So following on from Ami Klin's marvelous work on eye tracking, which he did with dynamic stimuli, I'm sure you have all had a chance to see the Virginia Woolf movies; we used the same kind of methodology to look at eye tracking in these face recognition paradigms. And here what you can see is time spent looking at the mouths is the same but, indeed, they are looking less at the eyes in this paradigm as well.

So why do children with autism look less at the eyes? We went on to look at whether it has to do with arousal and some of the ideas for looking at arousal came from our colleague, Richie Davidson, over in Wisconsin, and we implemented this in behavioral studies. We show the children faces like this, some of which have direct -- the gaze is looking directly at you, some their gaze is directly against.

We measure skin conductants and our main finding is that the difference is that the children with autism are showing increased skin conductants or arousal. There is something too arousing about that when the eyes are directed at them. Okay. And here we see that, in fact, skin conductants response is related to face recognition. Those kids

who show less arousal are doing better in their face recognition.

So there is a story here then that is linking arousal, eye tracking, whether they are going to look at the eyes, and then their performance on face processing tasks.

We have also taken this into brain imaging studies and I will begin with the brain imaging studies that we have done in Boston, and this is primarily the work of my colleague, Nouchine Hadjikhani, in collaboration with our group. We know from several studies in the literature that have found that there is a lack of activation. The brain does not seem to light up or be processing in this particular area, the fusiform gyrus, which is the specialized face processing area, and there are several studies which found that people with autism don't activate this area.

Well, we used a different kind of paradigm. We just showed them the faces passively and we placed a cross on the screen directly in the middle between the eyes, and we told our participants, please, look at the cross, look in that area all the time. They were very compliant. They were looking at the eyes, at the center of the face. And

so in our study, which we published a couple of years ago, we actually didn't find differences then in fusiform activation. Our participants with autism did activate the fusiform area, but there are these methodological differences.

On the other hand, they did not activate other areas of the social brain, that whole social network. There is not just one area of the brain that processes social information. So we certainly found significantly less activation in other cortical areas that are related to face processing.

And, moreover, in a recent study which I think is available now online, we found cortical thinning in those particular regions of the cortex that are particularly crucial for social information processing, and we found that cortical thinning was related to social symptoms in our sample.

And this has now been replicated by our colleagues in Wisconsin using a different method for analyzing cortical thickness in the brain, Moo Chung and his group, and he found cortical thinning in similar regions of the brain, including the STS and the superior temporal sulcus and the orbital frontal cortical regions, and in his study it was related to emotion, face emotion recognition. That

was the paradigm that they had.

Let me move on then now and talk about some of the face processing neuroimaging studies that our colleagues in Wisconsin have been doing. And I think they have really been pioneers in the study that was published last year in combining in the face processing, in the neuroimaging studies, looking at behavioral performance, reaction time, functional activation, as well as eye tracking all in the same participants, in the same experimental procedure to look at individual variation then in face and emotion processing.

So these were their faces and what you see is that the participants with autism have performed. They are not as good at recognizing whether a face is showing an emotional expression and their reaction time is slower. And then they also then looked at eye tracking in these participants and, again, this parallels both our own work on eye tracking, as well as the work from Ami Klin's group.

And here you see typical controls who were eye tracking primarily in the eye region of the face, and here are some of the examples from the participants with autism. So there is certainly

less fixation and, again, it's specifically to the eye region of the face.

And then when they looked at the brain activation patterns, they found somewhat less fusiform activation. They found more activation in the amygdala and the orbital frontal cortex in their participants with autism. More importantly, this was a focus remember on individual variation, that brain activation correlated directly with looking time because they were able to track looking time in these participants.

And so this really tells a very nice story with our original face processing experiment where we didn't have eye tracking, but we were essentially forcing all our participants to look directly at the eyes, so we found no differences. Where you let that vary, but measure how much they are looking at the eyes, you see the difference. So I think what is important about this, it tells you that the brain is not broken in terms of face processing, but it's a more complicated story than that.

Now, in the Wisconsin data set we also found increased activation to the amygdala, and they have been looking quite extensively in now a rather

large sample at the size of the amygdala in individuals with autism, and they have divided the participants into sort of the pre-puberty and post-puberty group.

We know that the amygdala continues to grow during pre and post-adolescence. And what they found in their participants was a decreased size in the amygdala, the red are the autism, and basically they didn't show the age-related increase in the size of the amygdala post-adolescence. More importantly, the size of the amygdala predicted both slower judgment in judging the faces. The reaction time was slower in those participants, as well as avoiding the gaze, looking directly at the eyes from the eye tracking data.

Also then, we brought it back around to the symptoms, not wanting to keep everything just within our experimental measures, and in their samples the amygdala volume predicted, both, social reciprocity as well as nonverbal communication, but, importantly, not repetitive behaviors and interests and not verbal communication. These are different components of the autism phenotype in this group of participants after correcting for both age and brain volume.

More recently, we have followed up a group of siblings. Again, this is in the Wisconsin group, and this is very interesting. It touches back to looking at risk in siblings. We know Becky talked to us about the broader phenotype, looking at the broader phenotype in these kinds of experimental and neuroimaging studies.

And the essential story, it's a sort of complicated slide that is summarizing a lot; the siblings also show the reduced size in the amygdala. They also show the same relationship between face area activation in the brain and eye tracking in the siblings, which we did not find in control participants.

However, what we did not find in the siblings and these are unaffected siblings, they do not have autism, they did not show the same relationship between amygdala activation and fixation time in siblings. So they are not showing that atypical arousal pattern, the relationship then with the amygdala. So they are showing some components of what we're seeing in terms of the neurocognitive phenotype for the social impairments, but not all of it.

So then let me turn to looking at the cellular

level and this comes from the work of my wonderful colleagues at BU, originated by Tom Kemper and Margaret Bauman and followed up now the work of Gene Blatt together with Bauman and Kemper looking at postmortem tissue. And, of course, we do work very closely with the ATP in this research.

The study I'm going to present to you looked at the anterior cingulate cortex, which until recently was the only area in the cortex that had shown these kinds of histological abnormalities that were reported quite a long time ago by Bauman and Kemper, decreased cell size and increased packing density. And what we have been looking at then is the serotonin system at the level of receptor and uptake sites in this particular area of the brain.

Now, we know from lots of other research that serotonin seems to be one of the important neurotransmitter systems that has been implicated in Boston -- in autism. I know, one can't equate the two, although I seem to sometimes. So using certain kinds of standard techniques to look at what are the receptors, what do some of the receptor sites look like and what do the uptake sites look like.

And, basically, what we found was that there were no differences in the 5HT uptake sites in any of the areas of Broadman's 24. That's part of the anterior cingulate cortex. There were no differences between the cases and the controls.

However, we did find a significant reduction in both the 5HT 1a and the 5HT 2a receptor density in all layers, but most particularly in the deep layers of the anterior cingulate. And this is one of the autism cases and you can see the differences. It's very hard to look at here. Now, there is some overlap across the populations, but you certainly see the differences between the two groups there.

So to summarize so far, faces I think are the key social stimulus along with voices, but key, and we know that there is impaired processing of the eye region of the face. We have seen that people with autism look less at the eyes because looking directly, I shouldn't put the "because" there directly, but certainly we know that looking directly at the eyes is correlated with increases in arousal.

Now, activation of the brain area that is important for face processing is directly related

to both the time spent looking at the eyes and also to performance on these kinds of face processing tasks and we saw that also in our unaffected siblings. In autism, and uniquely in autism and not in the unaffected siblings, we found activation in the amygdala which was also related to looking time.

And from our other studies there are certainly failures to activate other parts of the social brain when looking at faces in a variety of different tasks, and that I think perhaps speaks to the kind of local versus sort of more long-time kind of connectivity in the brain perhaps. We're now following that up with diffusion tensor imaging studies, but I don't have anything to report on that.

And, finally, we found a reduction in the neurotransmitter system that is crucial to social processing. We looked at that in the anterior cingulate and are now extending that out to other regions in the social brain. Okay.

So, now, let me bring it back finally to what are the impacts, what kinds of impacts can we see of these sorts of social affective impairments on families and children in general. As part of our

staff center, we have a large scale longitudinal study of toddlers and this is my colleague, Dr. Carter, in Boston, and we're looking not just at the longitudinal development of the children, but also of their families and the impact of one on the other.

And I'm just really giving you here a tiny slice of our data. We looked at stress and depression in the mothers and fathers and it's not surprising to say that both mothers and fathers, the fathers are in yellow here, have increased levels of stress over a clinical cutoff. This is the depression and this is the stress level. I'm not showing it very well here. There are no differences in the stress levels between mothers and fathers statistically. However, the mothers are at more increased risk for depression compared to the fathers. Okay.

But then the question is -- what are the child characteristics that are related to stress in both mothers and fathers? And we looked at all sorts of predictors. Is it the child's IQ level? Is it the child's level of language? Is it autism symptom severity? Is it emotional dysregulation, externalizing behavior? These are some of the kinds

of predictors we put in.

And, interestingly, it is absolutely not the child's measured level of IQ, their adaptive behavior skills or their language. That is not what predicts stress in the mothers and fathers of these families. For both mothers and fathers, what comes out is social impairment. So the degree to which the children are not relating to others, are not making eye contact, are not sharing affect, are not engaging in joint attention, are not truly socially engaged with their parents, that is related to the stress level. Okay?

And for the mothers it's also dysregulation, that is sort of affective issues, as well as eating problems, sleep problems. You will not be surprised to hear that for the parents in the room. And for fathers it was also externalizing behavior, the child being highly aggressive or self-injurious.

And I think these are important data to begin to think about in terms of not just thinking about what is it that families need, but also what kinds of treatment programs do we need to be thinking about and intervention, how can we provide support not just for the child, but also for the families all together.

We need to focus on parent well-being. We need to focus on what is contributing to stress and we need to focus on how to reduce this in the families because, again, one of the things that we know from other research is that reductions in parent stress and depression do themselves have an impact on how efficacious our treatments of the children are going to be. So I think we're just beginning to take a look at this kind of story, and I think that there is a lot that we need to still be following in these children.

What I have shown you today is really the cross-sectional data from our first year of the study. As we follow these families, we'll be able to look at this, again not just looking at you were asking the question of what predicts success in treatment. We'll be able to look at that in terms of the children, what are the child factors, but we are also most especially interested in what are the parent factors, the family factors, that might also be important predictors of response to treatment.

So, finally, I would like to thank especially the support for our research programs, both from the NIH as well as the foundations, and most especially to the children and families who have

really been our partners in advancing knowledge about autism spectrum disorders, and we have been following some of our families in the CPA who are still coming back.

We're thinking about how we can write our next grant to keep a hold of them. They have been with us for nine years and, of course, we started our partnership with our STAART families about three years ago. So thank you all very much. I think the work of this Committee is so crucial to keep up with the pace of what we're learning every day about this mysterious disorder we call autism. Thank you.

[Applause]

Dr. Insel: Thank you, Helen. We have about five minutes for questions. Maybe I will lead off with -- I guess the obvious one is how do you understand that fundamental problem with looking at the eyes? Why is that in children with autism either stressful or arousing or aversive when it isn't in other children?

Dr. Tager-Flusberg: When it isn't in other children. Well, I mean, I think what I have sort of shown you today is a picture. If you sort of try to imagine it, we have our puzzle piece, our nice

Autism Speaks puzzle piece and there are several puzzle pieces.

We have looked at the social one. I think what we have done is to draw within that a lot of dots. Okay? There's a lot of dots that are giving us clues. We're not yet at the point where we can completely connect all the dots together and there are probably different ways in which one could connect the dots.

But I think the clue here has to do with amygdala, amygdala growth and it's not just the amygdala itself, but it's probably how it functions in concert with other brain areas that are all part of this social network. I'm sure you know from out of your own intramural program the incredible work that has been done on a different neurodevelopmental disorder, Williams Syndrome, which is another disorder that is extremely close to my heart and everyday life.

And there I think we have a very different picture of social impairments. There are differences, but this wonderful work from Karen Berman's lab which shows that it's not amygdala activation, per se, although that is reduced, but it seems to be downstream influenced by the lack of

activation in the orbital frontal regions, which is another important part of the social network, that is contributing to the atypical response of the brain, and from our own work we know on the behavioral and cognitive, as well as skin conductants and we're now moving into eye tracking with them as well.

The picture will be different, but I think it has to do with how these networks, these networks that are critical for social information processing, get set up. The amygdala seems to be at the core here. We know so much now about differences in size and developmental change. Although this has not been done longitudinally, the cross-sectional data I think are quite compelling.

And so I think it's how these networks get set up very early in life and then how might we influence that downstream, as Becky was talking about, in terms of intervention. So I think it has to do with the social network, the amygdala. Here what we're seeing is atypical sort of increase in arousal, that looking directly at the eyes seems to lead to over-arousal. And so in order to reduce that, they don't look at the eyes.

They are missing a great deal of critical

information and, thereby, that affects their formation of the social relationships and that, in turn, it's the lack of eye contact and joint attention then that leads to really increased stress in the family. So I think it's a very complicated picture. The increased stress is probably not helpful in trying to figure out ways of maybe introducing face processing in a way that would reduce the arousal in the children. We need to think about that as we develop treatment programs.

Dr. Insel: So, Helen, just to clarify then, your picture of this is that you have an abnormal pattern of development in brain circuitry that leads to the looking at the eyes becoming in some way aversive.

It's not the other way around, that your sense is that the reason you're seeing this amygdala activation is just like with any other aversive stimulus. In these kids that's going to light up because looking at eyes is aversive and it's just like the skin conductants. It's just another measure of --

Dr. Tager-Flusberg: Right.

Dr. Insel: -- activation or arousal.

Dr. Tager-Flusberg: Yes. I mean, that is the story we tell now, but absolutely we can't tell that for sure because we're not doing longitudinal studies with these children at this point from an early enough time point. I think doing the imaging side will be more of a challenge, but we are planning to do some of these eye tracking studies and I think at Yale they are doing that already, and so are the group at the Mind Institute, the High Risk Infant Group there who are looking at that.

I'm not sure if they are looking at other measures of arousal, but it's fitting all these pieces together and looking at it long-term in the same children, being able to build up that picture that I think will be most informative.

Dr. Insel: Okay. Thank you, other questions? Sue?

Dr. Swedo: Helen, that was absolutely lovely, just a wonderful way to just see such a complex and beautiful program pull together. I want to follow on what Tom was just asking and ask if you or you know of studies being done on habituation. If this is excessive arousal from this area, are there studies of habituation to try and extinguish it?

Dr. Tager-Flusberg: To try and extinguish this behavior?

Dr. Swedo: Yes.

Dr. Tager-Flusberg: I don't know of any studies that have been looking at that. Okay. I do know that it's actually very hard to habituate some of these babies, to get them to habituate, so we have tried to avoid thinking about using habituation methods. But as a way of reducing this, I don't know. Maybe other people here do.

Dr. Battey: If, in fact, you're correct in your model and it's looking at the eyes that is at the core of eliciting this aversive phenomenon which causes them to not want to look at faces, have you tried essentially creating faces that have no eyes and seeing what happens?

Dr. Tager-Flusberg: No, we haven't done that.

Dr. Insel: I think Richie Davidson has done this. I believe there is a study in which -- and I think this was the lead-up to the Kim Dalton study that you showed where you cover the eyes and there is less anxiety.

Dr. Battey: Less of the skin reactivity and more time spent looking face?

Dr. Insel: Well, Helen, I thought that was

part of their --

Dr. Tager-Flusberg: No, I don't actually -- I'm not sure. I'm not sure they did that with kids with autism. That may be from something else. I don't remember that.

Dr. Battey: Thank you.

Dr. Insel: A couple of questions here and then we're going to move to public comment. Go ahead.

Unidentified speaker: I'm thinking about simpler animal systems to look at this issue and there are some closely related species pairs that do and do not make eye contact within the same species, different strains do or do not. So have you looked at amygdala volume there to see about that causality?

Dr. Tager-Flusberg: I don't know about that. I certainly know about the difference between wolves and dogs, but I don't know what the neuroanatomical studies of those species look like. Yes?

Ms. Chafeman: [Speaking off mike]

Dr. Tager-Flusberg: No, those were simply examples. There is nothing particularly specific. I mean, we thought they would be sort of looking more at the mouth because they are being asked to judge are these faces emotional or not and they looked

everywhere. They were looking all around.

Dr. Insel: Sophia, you get the last question.

Sophia: Sorry. Beautiful talk, Helen. Just a quick question that is sort of following up on what Tom said. I'm just trying to think about sort of the underlying cellular mechanisms and the issue of timing. So I'm curious if you can remind me and comment a little bit on Cindy Schumann and David Amaral's study on the amygdala volume because, if I remember correctly, I mean, it was actually they saw quite an increase in size, although I think it was -- no, actually, that was both. It was a bilateral increase.

Dr. Tager-Flusberg: Um-hum.

Sophia: So it was only one side. And, secondly, I know that there is a temporal difference, right, I mean, depending on the cross-sectional age at which you look. And here you didn't see a difference when you looked at the younger ages, which is when these behaviors are presumably, from your's and Becky's talk, sort of starting develop. You only see it during adolescence. So I'm trying to pull it all together.

Dr. Tager-Flusberg: Okay. Well, in David Amaral's data on amygdala size, the early growth

and so the enlargement of the amygdala relative to controls was in a kind of pre-7, okay, much younger ages. Okay? And then in typically developing children you see continued development in the size of the amygdala and this was exclusively in males.

There are important sex differences here which I have not really addressed in this talk, although our imaging studies -- well, there are a few girls, but it's mostly boys. But then they leveled off so that there were no differences between autism and control, because the autism children, there is a slowing growth of the amygdala at the time when the controls are now catching up.

The picture I showed you was pre-12.5 and our data essentially map onto -- that group maps onto the older age group of Dave Amaral's studies where there is no differences by case and control. And so then in the older children, those were post-adolescents, these were, or adolescents, post-puberty. In typically developing children we saw an increase in size. We didn't see that, still stagnated growth in the size of the amygdala.

But these are cross-sectional data and we really have to be cautious how to interpret all cross-sectional data. Based on, you know, the

marvelous work of the -- of J. Gates work here, longitudinal does not -- it's not the same. You can't just map them on the point-to-point. If I take a group of 3 year-olds, 6 year-olds and 9 year-olds and look at the same time that's cross-sectional data, it's not the same as taking the same group of children and measuring them at 3 and at 6 and at 9.

And so far, that is part of what I say about we're beginning to place the dots in the pattern. I think part of what is involved in connecting the dots is really moving towards longitudinal studies not just the behavioral studies, but also these neuroimaging studies. So I think that is going to be crucial to fill out the picture.

But I will tell you what is really exciting, and I do want to end with this, I feel -- I think one of the last times I was in this room was a long time ago, 1995 for the State of the Science Conference, and at that time there was no unanimity. There was no replication in this field. Okay?

And I think what is really exciting is as our methodology has become so much more rigorous and so much more integrated, in part I think because of

the networks that you have created here, now we're really being able to see replication and how studies that Dave Amaral does with younger kids overlaps and meshes nicely with the kind of work that we're doing with a somewhat different age group.

And I think that is really an exciting time for autism research, to see this kind of replication, to see how the picture is really fitting together, and it's not that we're all just sitting there in our own labs finding something different from everybody else, and that is what is really going to advance this field. So thank you all again very much.

[Applause]

Dr. Insel: So I hope you will be willing to forego the break, so we can move right into public comment and we have got about half an hour for that. I would ask those of you who want to make public comments that you use the microphone and you identify yourself, and we hope you'll keep your comments relatively short. That's really short. We didn't --

Ms. Debold: Is this on? No. Let's see. I don't know how to work this.

Unidentified speaker: It's on.

Ms. Debold: Is it on? Sorry. I have a written statement and I would like to make another comment, if that's okay, based on some of the presentations today.

My name is Vickie Debold and I speak here today as a representative for the Coalition for Safe Minds, Sensible Action for Ending Mercury-Induced Neurological Disorders and also the National Autism Association, and my comments here today were provided in advance in writing to the Committee, but I wanted to update the Committee Members regarding our ongoing research and analysis activities and to mention that presentation of this work has been accepted as an agenda item for the November IACC meeting and we want to thank you very much for that opportunity.

In case the Committee Members don't know, on August the 25th and 26th of 2005 a symposium entitled Environmental Factors and Neurodevelopmental Disorders was sponsored by Safe Minds and NAA with a very generous contribution provided by the National Institute for Environmental Health Sciences. And at the symposium 16 scientists from 13 of the nation's leading

research universities and eight scholars from within the National Institutes of Health presented papers that summarizes current knowledge as it relates to autism and environmental factors.

Additionally, representatives attended the symposium from 11 autism advocacy organizations. Work is currently underway to prepare recommendations that summarizes the conference proceedings and identifies recommendations for future research. Safe Minds and NAA believe our report will be of great interest to those serving on IACC since the proposed research documents the latest environmental research on autism, identifies unanswered questions and suggests next steps needed in environmental research, and we hope that our preliminary road map will be included.

So I also wanted just to ask a question and actually sort of raise a concern again about the report that was in Mortality and Morbidity Weekly Report that Dr. Cordero spoke to, and recognizing the limits that we have with cross-sectional snapshot in time data, we have a couple of concerns with the prevalence data.

I would say the major concern is that we suspect that the overall prevalence may be too low

and we base that on two things. One, if I'm not mistaken, the question that was asked of the parents in the survey was "Has your child ever been diagnosed with autism by a health care professional?"

And if I'm not mistaken, when I read your report it suggested that you believe that parents are responding for full-blown autism as opposed to also including PDD/NOS or Asperger's diagnosis. So, I mean, if that is the case, if we fold those numbers in, then the prevalence is actually quite a bit -- I think much higher.

The second issue deals with a difference in prevalence that you reported across the age groups, and for the older groups if that -- and those prevalence numbers for the older groups were between 4.1 and 4.3, as compared to the younger groups of 6.8 to 7.6, and this is in the National Health Interview Survey data.

So if the data for the older groups does represent under-ascertainment, as you suggested that it might because parents may have forgotten that their child had previously been diagnosed, then again there is another reason to think that the prevalence is actually much higher than what

you came up with.

So the numbers that we have been using of one out of every 166, or now it looks like it has been amended to one out of every 177 or one out of every 180, that may actually not be true even though we're very fortunate now to have national data, as opposed to localized data.

Now, if for example -- if, however, that, the prevalence data for the older age groups, is actually true, which I sort of think -- as a parent of an affected child, I think it probably is true. I don't think I would have forgotten and answered that question wrong.

Then if you look at the two big chunks of age groups, you're looking at prevalence rates for the older groups and the 12 to 17 year-old groups plots out to something along the lines of one out of every 230 or 240 compared to the two younger groups, the 6 to 8 and the 9 to 11 groups. That plots out to about one out of every 140. So we're comparing one to 140 to one to 240.

And I did run the statistics on these age groups and I know you reported in the paper that the chi squares weren't statistically significant, but whether I ran it according to the various age

stratifications or I chunked it out using the two big groups and omitted the younger groups, I still got chi square statistics of over 20 with p values of .000.

So I am really interested to find out exactly how the statistics were run and how that you came to the conclusion that there are no differences. And I realize this is a snapshot in time and we really need to look at this over time and look at different age groups, but I think that the data do present some very interesting challenges for us and, obviously, if that, in fact, that the older age groups do have a lower prevalence than do the younger age groups, I think that would help us to begin to perhaps look at environmental mechanisms that, you know, deserve more attention.

Dr. Insel: Thank you. Jose, do you want to take just a minute to reply?

Dr. Cordero: Yes. Thank you for your comments. I think that in the first part on the prevalence, I think that actually what we said in the paper is that we believe that actually parents, when we were asking the question about autism, they are not only responding about autism, but actually the spectrum, and that some parents that actually had children

with either Asperger's or PDD/NOS are actually saying yes to the question. So that is sort of answering your first part.

In terms of the statistics, perhaps Cathy, who is one of the authors, can explain what statistics were used to look at the age distribution. What this data are is about parental reporting, and for that to happen there is sort of a series of things that have to first happen. First, there has to be some recognition and that there is something different about the child and, second, that the diagnosis, the suspicion is made and that actually the doctor says the diagnosis, comes up with the diagnosis.

So in the 4 to 5 being younger, actually I think that that probably represents children yet to be diagnosed. In terms of what happens with the 12 to 14 and why that is lower, we think that that has to do -- if you look at those 12 to 14 and 15 to 17 wherein the times that that actually -- if you sort of look at the numbers, I think I was just looking, that would be like 1986 or 1990 time that the major change happened in the times of diagnosis of autism in terms of the DMS. And so I think that that may be also what is happening there. But, Cathy, would

you like to comment on what -- the tests that were used?

Dr. Rice: Certainly. It's good to know that people are reading it so carefully, as we expected, and I think that's important also to recognize that no one study can certainly answer every question. And I think in a lot of ways this study raises more questions, which is important to moving the process along.

I just want to caution you about taking these data as indicating trends too significantly without further, because it is a parent report of a diagnosis and so we understand that certainly parents know when their child was diagnosed with autism. And unfortunately, I think the translation of parents forgetting was not actually what the researcher who had responded to that question said.

I think what she had indicated was there may be children who had an earlier diagnosis who after treatment no longer were showing those symptoms and so, therefore, the diagnosis may not have been current, so they may not have been reporting current diagnosis versus past. It's hard to know, because it was a survey and all of those different ways that people could answer the question was not

evaluated.

In terms of the -- again, remembering that it is a parent report of a diagnosis, certainly, we also recognize it was a nationally representative sample, but it was a sample. And so the statistics that we ran were weighted based on the sampling strategy and I, myself, didn't personally run them, but we can certainly connect you with the person that did.

But using the sampling -- so using the straight chi squares wouldn't work with the sampling strategy that was used to say okay, we have this small sample from different racial and ethnic groups, we're going to extrapolate to the overall sample. So the statistics we ran took that into account and, certainly, we would be glad to follow-up with you about more details on that.

Other information just also to keep in mind in terms of prevalence. This is one piece of information that CDC is using to try and understand prevalence and it, certainly, does confirm our ideas about the prevalence in the snapshot being in the upper range of the 2 to 6 per thousand estimate that we have, but we are trying to collect more detailed population-based information too, that

doesn't only look at a previous diagnosis, but looks at symptoms within the population to say both diagnosed and undiagnosed autism as well.

So we're preparing those reports and hopeful to have those data out as soon as we possibly can this year also.

Dr. Insel: Thank you. I think if you can say around, Cathy, after the meeting, I'm sure there may be other questions as well from people who want the details. Other comments?

Ms. Chafeman: Hi, I'm Cheri Chafeman.

Dr. Insel: Cheri, before you start, I just want to make one correction from the previous comment. For the next meeting in November it's correct that there will be a discussion about environmental factors. David Schwartz is coming to do that. He is the Director of the National Institute of Environmental Health Sciences and we have asked him to make a comment about the meeting from last August as well as to give us a much fuller explanation of how that institute is working on several aspects of environmental factors. So that's for the November meeting. Sorry.

Ms. Chafeman: No, that's okay. Thank you. Hi, I'm Cheri Chafeman. I'm a representative of UA and

I'm a mom of a young man, 9 years-old, who has autism. And I had a question for Dr. Pickett. I just wanted to know if there is any mechanism to measure heavy metal in brain tissue and if that's being followed.

Dr. Pickett: Well, I think the mechanism, we have had two proposals.

Dr. Insel: Can you come to the mike?

Dr. Pickett: Oh, sorry.

Ms. Chafeman: Thank you.

Dr. Pickett: Well, let me just say that we invite proposals to study brain tissue and we have had two proposals. They were returned or where there were more questions about how they were actually going to measure mercury, and we didn't get responses, so we had nothing to approve. So that's where we're at. Whether they can be, I've talked a little bit with Cindy Lawler and I have said that if someone comes to us with a new proposal and there are issues regarding technology, we can put them in touch with people Cindy knows for that group, because they do know how to measure them. It just hasn't happened. We haven't gotten the proposal that has been, you know, complete enough to approve or disapprove.

Ms. Chafeman: I was actually thinking not just -- my son was poisoned by arsenic and our Dr. Layton, who is quite well respected in the field, feels -- has tested his patients for mercury and they are coming up with actually higher levels of arsenic and in some cases lead. But arsenic then mercury. And anyway, I thought that would be just food for thought, brain thought, brain food.

Dr. Pickett: Well --

Ms. Chafeman: And then --

Dr. Pickett: -- if you have researchers that are interested, send them to me and I'll give them the path to make a proposal.

Ms. Chafeman: Okay. Thank you. And then I just wanted to reemphasize something I had said six months ago. I think Lee actually had brought this out and Jon that there just needs to be a guidance for parents of where to go, what to do. Not just the organizations that we go to, but maybe a map of different types of procedures and interventions that can be followed.

I thank God, you know, I feel that I have many resources I could go to as a parent and often I am just in a tizzy not knowing which steps to take next. So I would ask if there is anyone -- any way

to find a public information slot that could be offered to parents, I think that would be very helpful.

And last, but not least, I just want to thank you as a parent. I'm sure there is so many autistic children that wish they could verbalize this, but thank you from the bottom of mine and their hearts for dedicating yourself to make each child and adult with autism have a better life. So thank you.

Dr. Insel: Thank you. Jose?

Dr. Cordero: Just I wanted to comment. I think that in terms of metals sort of like mercury and arsenic and others, I think that in the collection phase there needs to be some special steps to follow, because there is so much of these compounds that are just in the environment that it -- you even do a good job in terms of how you collect them, in terms of being metal-free objects. So you actually are going to get some contamination.

Dr. Insel: And, Cheri, on your other point about resources, besides the autism source book, which many people have used as kind of a guide to where they can find the next best intervention or best advice, you may want to look at the group that we had at one of the previous meetings, the Autism

Treatment Network, which is not here today, which has a website with a lot of information about medical aspects.

One of the things that we keep hearing over and over again is that when parents take their child to the pediatrician, when the pediatrician hears autism, they don't hear anything else and the difficulty in getting good medical care for a child with this disorder. So the Autism Treatment Network, ATN, has taken that on as a focus for helping families to get the best medical care they can and they have a number of contacts of physicians who they recommend for that purpose.

Ms. Chafeman: [Speaking off mike]

Dr. Insel: So the question is how do parents find out about these things? And there are lots of information on various websites, including from the people who are around the table, most of the agencies and certainly the advocacy groups have a huge amount of information. We haven't talked about the Autism Speaks website, which has become a really major player as a source of information for all kinds of resources. We have tried to provide as much of that as we can as well from our own website, although we don't have links for that

purpose. Yes?

Ms. Trapanier: Hi, my name is Cheryl Trapanier. I'm a mom of a gentleman of 30 and I work in autism research and my comment has nothing to do with either of those. I was impressed with the awareness campaign. I mean, the ads are dazzling and I think it is going to make a lot more people take a look at their child and evaluate their child's behavior and come forward.

There is lots of information out there about what to do, but there isn't -- the resources to provide adequate treatment aren't there. And, you know, there are going to be -- I'm not sure what's going to happen. I think, eventually, there's going to be a pressure to create more resources and that's a good thing. But these shock troop parents who are going to be turning to their school system -- and, you know, I come from Montgomery County.

I live in Montgomery County and they have a reasonably good response, but most of the regions around here don't. And I'm sure that most regions around the country, you know, other than a few that we know of really don't provide adequate, you know, response. And, you know, the huge amount of information about medical treatment, I mean,

currently the best supported treatment for autism is ABA, you know, and possibly other things.

But ABA is the one for which there is evidence. And lots of school systems claim to give that, but they give it maybe, you know, three hours a day for three days a week or they call it ABA, but, you know, there are a lot of things called ABA. So I'm just seeing a big social problem on the horizon and it's a problem all newly diagnosed families have. They really don't know where to go and, in fact, there is nowhere for them to go.

Dr. Insel: One of the ways that we sometimes formulate this is that there is a communication or an awareness gap, which is what we have talked about mostly today. There is an access gap, which is something that we have talked about through the services plan here, the services research or services road map or matrix.

But there is a third gap, which is the quality gap and we haven't really spoken much about that here and whether the kinds of services, when you get them, that are available really are either evidence-based or are of the quality that have really a promise or not is still a question that Larke Huang talked before about putting on the

SAMHSA website a list of those kinds of resources that would be available, not just for autism, but across a range of disorders.

And that's one of the approaches to at least make sure that the information is there. But you still have this quality gap, because not everybody who puts out a shingle that says ABA is doing the same thing. Jim?

Dr. Battey: Yes, I mean, I agree completely with the comment that was just articulated, but I would only point out that it's a problem that goes way beyond treatment for autism. For example, for children that are born unable to hear, we have a cochlear implant. It's a spectacular intervention. Most kids end up on grade level who get cochlear implants, if the implant is put in early enough. The problem is it costs $55,000 and the Federal Government is not reimbursing and the third-party payers are spotty in their reimbursements.

We can document that it is cost-effective to put implants in these kids in terms of the taxes that will come in, not having to educate them in schools for the deaf. So this is a huge problem, a huge national problem that goes way beyond. I mean, it's a problem for parents with autism, but it's a

problem for lots of parents.

Dr. Insel: Jose?

Dr. Cordero: I just wanted to take a couple of minutes to reflect, I think, in what we have done in the last three years. I think that we have done quite a bit in terms of increasing awareness and I think that you saw today in terms of the awareness campaign. It's quite significant progress. And I think similarly, looking back at the presentations we had today on research, I think that we are moving in terms of understanding better the issues of what underlying mechanisms lead to autism.

At the same time, listening to comments, but also seeing some of the -- having some of the experience, I think that we are way behind in terms of addressing the issues of services and the issues of treatment. And I really wonder if we need to sort of think in terms of the future in the upcoming meetings of this Committee to how can we sort of devote perhaps more time and effort of understanding the issues as you were saying.

It's not only services, it's really sort of the efficacy of treatment, but also access and the quality of those services. And somehow I think that's an area that in the last three years we

haven't done as much progress as we have done in the areas of research and the areas of awareness.

Dr. Insel: So why don't we put that on the November agenda along with looking at this matrix and where we are so far. This could be part of the mid-course correction.

Mr. Shestack: I have to say that I actually don't remember now how many years I have been coming to this meeting and sometimes there is a little self-castigation and sometimes there is a lot of self-congratulation, but really, the federal response is so completely out of proportion to the size and cost of the problem in terms of emotional pain, in terms of financial pain, in terms of people who need help from the age of 2 to 70.

This group doesn't actually, in its recommendation when it writes its reports to Congress, write a recommendation or an admonishment or a suggestion on how legislation should be shaped or what the administration policy should be. It is, I have to say, stunningly ineffective and I take complete responsibility as one of many at the table that it's nice to have these show meetings, but really at the end of these meetings, I leave so depressed that I just don't know what to do.

And the bare minimum, rather than talking about it here, would be when this group writes its report to Congress to say -- not to say we have been doing a great job, but say whatever job we are doing is completely out of proportion to the problem, and the problem, that is going to just get bigger. And if there are 300,000 people with autism between 4 and 17, how many are there under 4? How many are there over 17? How many of them will be off their parents payroll soon when their parents are dead, demented or bankrupt or suffering from Alzheimer's?

There is nothing back from this Committee to the President of the United States or the leaders of Congress or Senate that says wake up, this is a tidal wave that is going to hit you and you're going to be paying for it forever. That would just be the minimum thing to just put a billboard out and say that this is a big problem and that all of our work it isn't enough yet and put it on the National Agenda in a way that it just isn't. Thanks.

Dr. Insel: Did I hear a suggestion about the best way to do that, Jon? What would be the platform to make that comment?

Mr. Shestack: You're the Director of the National Institute of Mental Health. You're the Director of an institute. You're the Director of an institute. Why don't you just like make a phone call to the President of the United States? They probably would take your call.

Dr. Insel: No.

Dr. Battey: No, he wouldn't, Jon.

Dr. Insel: Let's be realistic here.

Dr. Battey: No, he would not.

Mr. Shestack: Well, we'll have to see what we can do to help that.

Dr. Insel: It's more likely the phone call would go the other direction as Dr. Battey can attest, but it's not --

Mr. Shestack: Well, that happens, too.

Dr. Insel: That's the price --

Dr. Battey: Along with the dismissal slip.

Mr. Shestack: Okay.

Ms. Blackwell: Tom, I have a comment. We, at Medicaid, serve -- have incredible opportunities in our waiver programs to serve children and adults with autism. We have really two or three waivers that are targeted at kids with autism. States come to us with these proposals. We don't go to them. So

advocates should approach their State Medicaid Directors and start crafting these waiver proposals. We process them pretty rapidly.

We approve just an immense array of services that can benefit people with autism. We can waive certain income requirements, so that people with higher incomes and kids with higher incomes can receive services. So I would have to say that there are many services available and I, myself, find it puzzling why more states have not approached us to provide services, specifically targeted to children and adults with autism, because we do have that opportunity.

Out of 300 waivers, three are targeted at people with autism, possibly four. I mean, think about it. So there are many opportunities, advocacy, get together and approach their State Medicaid Directors and make these proposals. We approve most waiver applications. So there are many opportunities.

Dr. Insel: Yes, go ahead.

Ms. Chafeman: Pardon me. I have a question for you. When I discussed with the pediatricians who I have had relationships with as well as various insurance companies why they don't pay for initial

developmental pediatric assessments, they say because Medicare does not pay for it. Pardon me if I'm saying Medicare. Maybe steps versus Dr. Insel making a suggestion or the Committee making a suggestion if the Government approves that in Medicare and suddenly the insurance companies, if they are using the excuse the reason that they don't pay for it is because our Government's medical services do not consider that an important or paid for service, possibly if it's approached in a different way as to say listen, if you cover it ahead of time and you do these developmental checkups, we could catch these disabilities early and it will eventually save our Government incredible amounts of money.

And then a question I had and pardon my ignorance if this was done already, but, you know, people go out and lobby for all different types of things. And your suggestion for different states coming to Medicare and saying that we want to have a waiver and it's a matter of just getting it out of the box and asking, why can't efforts by our organizations or autism organizations by -- or the different entities that are interested in supporting autism research go and, caring for the

children and the adults with autism, try to get the Government to have tax credits to pharmacies -- excuse me, insurance companies that will pay for these developmental checkups?

You know, I think that that would be an incredible incentive for insurance companies and it could work from a very clear and easy financial view. If you look at one child who has autism, they could follow one person that's 30 years-old that because it was caught early, look at all the expense it has cost the insurance companies, the Government when it ends up becoming a Government's problem to fund all their expenses and to say listen, if you cut this off in the beginning, then it will save everyone money. It will give a person a better life.

So I'm lost when it comes down to how to go about doing this, but I'm just proposing this possibly to be a way to handle it.

Dr. Insel: All right. Celia? Stuart?

Mr. Spielman: Ellen, I do have a question for you. You spoke earlier about the difficulty of mining autism data from the Medicaid roles. I'm wondering if the mining of such data is entirely unprecedented. If whether CMS has ever looked at

the population it served and provided information that would allow advocates to understand whether they are fully utilizing available benefits under Medicaid plans, under waivers?

I know from our Maryland experience was it took a long time for us to get the waiver through. And as you well know, state budgets are subject to fluctuations that the Federal Government is not subject to as states go from boom periods to bust periods, it seems like almost overnight. And the Federal Government, having the luxury of printing money, has a little bit more insulation from that process.

But I, as an advocate, would really value some data on how CMS is serving the autism population, so that the population has some way of gauging what is the proper role for the Federal Government in the financing. What is the role for the private sector? The data on this is just so extraordinarily hard to get and again I understand going to your agency and saying look in a different way than you have ever looked before.

I know that's difficult. I'm wondering if that's just impossible or merely difficult.

Ms. Blackwell: Stuart, remember we count data.

We count our budget by services and not by diagnosis. I think I mentioned that before and that's part of the problem. We have instituted a new electronic waiver application. We spent over a year and a half rewriting the 1915-c application and it does include quality and measurement managers that were -- measures that we are really proud of.

So now when states apply for a new waiver or a renewal, they have to tell us how they are doing. I mean, so in the past, these waiver applications were pretty difficult to -- I mean, we didn't really know how our waivers are doing, so we're hoping in the next few years as we, you know, put some focus on quality and Medicaid, we actually have a pertinent individual in my division and that's her job to be our quality person within the waiver.

So we are really planning major efforts in the new waivers and in the current waivers to take a look at how things are doing. Again, you know, we can look at a particular waiver and, for example, your autism waiver or a DD waiver and, you know, it's very difficult to parse out people with autism, unless we do it by service type.

And that's what I mentioned earlier with this new state plan option. How do you target when you're not able to say this benefit is going to be delivered to people with autism? I think that you have to do it by benefits that might apply to a particular population. So again, we can look at how much we're spending on particular benefits that might be delivered to people with autism. That we can do. But, you know, again, you would have to identify for us what services you think those are.

I can tell you in the waivers how many states are using what particular service. I think at the last count we had over 350 services that we currently offer in the waiver program and these are not for the most part 1905-a services. They are enhanced services, enhanced personal care, and enhanced behavior management services. So we have some data, but it's not great.

Dr. Insel: Go ahead.

Ms. Trapanier: Do you do outreach to the states? I mean, it sounds like you have money to give away.

Ms. Blackwell: We do outreach in terms of our grant programs. For example, the Systems Change Grants. If you go on our website, you'll see that

we do post, you know, every year an invitation for states to submit these applications to us. But again, advocates have to work with their State Medicaid Agency to submit the applications. I mean, we don't generally -- I mean, we are partners with our states. States come to us. We don't go to them. So we generally tend to react to proposals that states put before us.

But, yes, we do invite people. We have forums about once a month. We had one this week on the new home and community-based services option in Medicaid. You know, we have -- there are opportunities for the public to call in and interface with us, certainly, during this comment period, but your real -- I mean, I can't stress enough that advocates need to work with the State Medicaid Agency to make these proposals to us. We pay for half or more, but the state has to make the application to CMS.

Ms. Trapanier: I didn't realize before today that some services are paid for by CMS to children in school. And I'm pretty sure most people don't know that. I don't know that most advocacy organizations know in what ways trying to get a waiver in their state would benefit their

population.

Ms. Blackwell: Well, most Medicaid services in the state plan, OT, PT, speech, audiology, mental health services, the school bus transportation, personal care, which would be in the form of an attendant who frequently might come with a child who has autism to school to help manage challenging behaviors.

Ms. Trapanier: But --

Ms. Blackwell: Medicaid is paying for all of those services.

Ms. Trapanier: Yes, my point is there needs to be a more effective way to get that information out to people.

Ms. Blackwell: I think school systems are -- I mean, this benefit has been in place since 1988. Most school systems are billing Medicaid.

Dr. Houle: Ellen, I wanted to say that most school systems do bill Medicaid.

Ms. Blackwell: Yes.

Dr. Houle: For low income qualified students.

Ms. Blackwell: Yes.

Dr. Houle: For their speech therapy. You as a parent may not know that the school is billing Medicaid.

Ms. Trapanier: That's what I'm talking about to get out parent advocates to push for an autism waiver in their state. For the states that don't have an autism waiver, they need to --

Dr. Houle: They don't need a waiver though to bill Medicaid for the --

Ms. Trapanier: For school services.

Ms. Blackwell: Right. Gail is --

Ms. Trapanier: Okay.

Ms. Blackwell: That's correct.

Dr. Houle: It's a good share of the revenue that they have to pay for these related services and health-related services.

Ms. Trapanier: Yes, so that's what related services are. But they don't know that you have money to provide. Well, I guess, it's a partial matching grant?

Ms. Blackwell: Yes, yes, under the waivers. I mean, the school services -- if the state has opted to provide them in a state plan, you know, as you said, Gail, the parent probably wouldn't even be aware, might not even be aware that Medicaid is footing the bill for many of those services.

Dr. Insel: I think we need a short course here really to find out how this --

Ms. Blackwell: But under the waiver option, as I said, only three or four states. I mean, there's one that might be coming into the table, but advocates should be, you know, looking at the operational waivers in the states that have them, Maryland, Wisconsin, Indiana and, I believe, Maine is the fourth one. The Wisconsin waiver is sort of -- it talks -- it mentions autism, but it's primarily targeted at people with developmental disabilities. Look at those waivers, see what services the states are offering, look at the state budget, see if the state will put up half the match.

I mean, we have waivers that serve 100 people, 200 people, very small waivers. We have waivers that serve 3,000 people, 4,000 people. So often times it isn't a big pot of money. A state could propose to serve a couple hundred people and Medicaid would pay for half. So certainly those sorts of things are great for us to look at for future reference and for other states to talk to each other and figure out what is the best approach.

Dr. Insel: Okay.

Ms. Trapanier: And parent advocates need more

information.

Dr. Insel: We have to wind up, because of the hour. I want to sort of respond. Unfortunately, Jon left, but I think that the point he raised is the frustration that he feels is something that a lot of us around the table felt as well. And as hard as people have worked here, the fact is we still don't have a cochlear implant for autism. And there is a real need to think more about how we deliver the services and the interventions that exist, but we don't really have the kinds of interventions that we would like to have for this disorder.

They certainly don't measure up to interventions that we have in most of the rest of medicine. And so there is a huge need on both ends of this, both to improve the service delivery, but also to make sure we have something that is far more effective to deliver. And I think everyone around the table has got a role here in trying to make sure that in three years Jon is less frustrated with what we can do.

It does take more than three years to make things happen and we know that in the case of deafness as well, where it was decades before we had that.

Dr. Battey: About 40 years.

Dr. Insel: Right.

Dr. Battey: To develop the modern cochlear implant.

Dr. Insel: So there is hope, but not exactly just around the corner. It's going to take a lot more work from everyone and as Jon says, perhaps a lot more investment, so that we have an investment that matches the magnitude of the problem.

With that, I want to thank all of you for your attendance and your participation. We will meet again on November 17th and we're available between now and then, as always, by email. Thanks.

(Whereupon, the meeting of the IACC adjourned at 2:55 p.m.)