U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

INTERAGENCY AUTISM COORDINATING COMMITTEE

STRATEGIC PLANNING WORKGROUP MEETING

THURSDAY, FEBRUARY 21, 2008

The Strategic Planning Workgroup met in Conference Room 2172, Second Floor, 6001 Executive Boulevard, Bethesda, Maryland, from 9:15 a.m. to 2:51 p.m., Thomas Insel, M.D., Chair, Interagency Autism Coordinating Committee (IACC), presiding.

PRESENT:

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

DAVID AMARAL, Ph.D., University of California, Davis

PETER BELL, Autism Speaks

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

JOYCE CHUNG, M.D., NIMH

GERALDINE DAWSON, Ph.D., University of Washington

GERALD FISCHBACH, M.D., Simons Foundation and Columbia University

STEPHEN FOOTE, Ph.D., NIMH

DANIEL GESCHWIND, M.D., Ph.D., University of California, Los Angeles (UCLA)

MARGARET GIANNINI, M.D., Office on Disability, U.S. Department of Health and Human Services (HHS)

PRESENT (continued):

LEE GROSSMAN, Autism Society of America

GAIL HOULE, Ph.D., Office of Special Education Programs, U.S. Department of Education

ALICE KAU, Ph.D., Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) (representing Ann Wagner, Ph.D.) and National Institutes of Health (NIH) Autism Coordinating Committee

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

CATHERINE LORD, Ph.D., University of Michigan

CHRISTINE MCKEE, J.D., IACC

CRAIG NEWSCHAFFER, Ph.D., Drexel University

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

DENISE RESNIK, Southwest Autism Research & Resource Center

ALISON SINGER, M.B.A., Autism Speaks

EDWIN TREVATHAN, M.D., M.P.H., U.S. Centers for Disease Control and Prevention (CDC)

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PROCEEDINGS:

Dr. Thomas Insel: I've got a number of remarks to make at the beginning, but let's just start by doing some introductions around the table so everybody knows who is here. And I will mention the people who are on their way as well. So I'm Tom Insel from Chair of the IACC and Director of NIMH, most of which is upstairs in this building.

Dr. David Amaral: David Amaral from UC Davis.

Dr. Insel: We will need to, probably for the transcriber, we'll need to use the mic, sorry.

Dr. Amaral: David Amaral from UC Davis.

Dr. Edwin Travathan: Ed Trevathan from the CDC.

Ms. Christine McKee: Christine McKee from the IACC.

Ms. Allison Singer: Alison Singer from Autism Speaks and member of the IACC.

Ms. Ellen Blackwell: Ellen Blackwell from the Centers for Medicare & Medicaid Services.

Ms. Lyn Redwood: Lyn Redwood, SafeMinds and IACC.

Dr. Gerald Fischbach: Gerry Fischbach, Simons Foundation and Colombia University.

Mr. Peter Bell: Peter Bell from Autism Speaks.

Ms. Denise Resnik: Denise Resnik from the Southwest Autism Research & Resource Center.

Dr. Alice Kau: Alice Kau from NICHD, and I'm here – I'm here in Ann Wagner's place representing the NIH Autism Coordinating Committee.

Dr. Daniel Geschwind: Dan Geschwind from UCLA.

Dr. Geraldine Dawson: Geri Dawson, Autism Speaks.

Dr. Insel: And Craig?

Dr. Craig Newschaffer: Craig Newschaffer, late, from Drexel University.

Dr. Insel: And by my notes, the only person we're missing is Cathy Lord at this point, and she's on her way. So we'll get started. Lee Grossman might have been out of the room. So this meeting is officially called a workgroup meeting,

and it comes about a month after the four workshops that were held. And the four workshop chairs are here at the table. At least they will be when Cathy arrives so that we'll have a chance to hear in much more detail about what came out of the workshop.

We have also members of the IACC here because at the end of the day, they are the ones who are responsible for putting together a Strategic Plan. And they are the ones who will use whatever came out of the workshop or whatever comes from the discussion today to both figure out what will be in the Plan and to think about how best to develop the Plan from this point.

So what we're hoping for from today is really only a couple of things. One is we'd like to revisit the workshops with you to hear from each of the workshops here as much more detail about what came out, and what some of the -- it's interesting proposals for. And we have a list of the 41 proposals in your notebooks, and you should have received them as well. We've asked you to put scores next to them not because we're trying to

use these as sort of pay lines, or because these are priority scores or anything like that. The scores really were just to give us a sense of how much variance there would be and how much the group wants to deal with this cluster, because you can't really get your hands around 41 items very quickly.

We're going to have to figure out how to smush this down to something that's workable.

We were also interested because if in the way that people scored these, if there was a group that was just way, way, way down the list, that would be useful for us to know that they may be easier to deal with possibly. But also even those would deserve some discussion that we'd want to think very carefully about how to include what's on the list, as well as how to include what may not be on the list.

So the first piece of this is going to be a review to help us understand what came out of the workshops and to help us think about, for the first time, integrating across them. When you received these lists, they were not clustered by

workshop themes because, as it turned out, the proposals didn't cluster in almost any way by the themes that they were organized around. And that's just I think something very important anyway. But it does tell us that we'll have to -- there is an opportunity here, I think, -- to just bring a number of things which are clearly redundant across the different workshops into a new kind of cluster where instead of having 41, I think it's fairly easy as you look at them that you realize that's going to be far fewer than that.

So the first piece will be to do the integration. To look across, and to think about what -- a way as to a framework for now taking what we've got and putting it into some manageable format that the IACC could then use to begin to develop this Plan.

The second piece, which we'd love to get your input about, and we're going to really want the IACC members who are here to help us with this part as well, is to tell us from what you see in the list what we're missing. We have a chance, of

course, the IACC will have a lot more time to work on this. But probably not with all of the content experts and some of the funding groups that are at the table. So it would be really helpful as you look at this, then we will probably use some of the afternoon for this, to think about where the gaps still are, and if there are areas that weren't captured in any of the workshops or, if they were captured, weren't given enough of focus so that we can end up today with a framework for the whole set of initiatives and a whole set of approaches to a Plan that would include what we've heard already, what came from the RFI, and then anything else that we might want to include that wasn't in either of those two initiatives.

The next IACC meeting will be March 14. So we don't have a huge amount of time. The autism team is here as well as IACC members and others who get to help us out with getting this. We don't have a lot of time to get this wrapped up into something that the IACC can work with. But I think today we're at least able to come up with this framework and identify some areas that may

need some more attention. That would be for us, a very successful day.

I need to tell you just a couple of, sort of, housekeeping issues. One is that the Interagency Autism Coordinating Committee is by law a FACA committee, which means it abides by the Federal Advisory Committee Act. It means that all of the dealings of the IACC are in the public domain. They are open. This meeting is therefore, not an IACC meeting. And it's not -- it cannot provide advice to the IACC specifically. It can provide policy options, it can provide suggestions, it can provide recommendations for further exploration. But there is no way that a closed group like this can share or can come up with anything conclusive that would be for the IACC to either vote on or put into play. It really, at most, can help us to refine what we've heard already, and then to provide something. Again, I like the word "framework," for the IACC to work on in public session. And one of the reasons we wanted to have the IACC here is because we thought that, since

at the end of the day, they are the ones that are going to be using whatever it is in the conversation today.

If they could hear it directly, it might be even more useful to them. And they may have questions for clarification, questions for further exploration that would be harder to get at if we were just to share the transcript or try to show a summary. So I will be also asking the various members who are here from the IACC to really help us out to make sure that when you are making summaries or when you are trying to explain what's in this list, that they really understand what it is you are suggesting to us for these, what we'll call “policy options.”

Now, the last comment I'd like to make is just to remind the group of how we started with this Strategic Plan. We had our first IACC meeting, and I know, I guess almost none of the people who were here for the workgroup were in attendance, but we invited the Secretary of Health and Human Services, Mike Leavitt, and the Director of NIH, Elias Zerhouni to talk to the

group. And Elias made a really interesting, I thought, set of observations about how one should approach this planning process. And what he said was that if you have a whole bunch of boulders, rocks, and gravel in front of you and you have to get them into a vessel of some sort, what every group figures out soon enough is that you start with the boulders. That if you start with the rocks and the gravel, you'll never get the boulders inside.

So I think that's just good advice for us today, to think about starting with the boulders, and as you begin thinking about how to develop bins for the different items, or how to cluster them, that we think about the big items, the big issues first, some of which may be more process oriented, such as do we need a different way to approach the topic, or do we need a different way of approaching how we support research in this area? All those kinds of issues.

And so what I'm hoping we'll do after we hear from the workshop chairs is to step back a little bit and ask what are the boulders, and what are

sort of the big categories, the big bins that we want to be thinking about, and then we can work on the rocks and gravel as time permits.

Joyce, anything to add to that introduction?

Dr. Joyce Chung: Just that we're required to have people sign a competent interest form, which is on your packet. You may have seen these before and filled them out before, but you have to fill them out again for this meeting. And it's called a Strategic Planning Board Group Meeting on the title, and the date, and check one of the two options. And if you have any conflicts, please speak with me about that, and then we'll collect these in a little while. So thank you.

Dr. Insel: Okay, and we'll come to Cathy Lord who has just joined us.

Dr. Catherine Lord: Hi.

Dr. Insel: Thanks. We got started a little late, so you haven't really missed very much.

Dr. Lord: I'd just like to tell you all this is in Rockville, not in Bethesda. I've learned a lot about operating, what do you call those

things? The navigator things.

Dr. Insel: Oh.

Dr. Lord: Anyway.

Dr. Insel: Okay.

Dr. Lord: Not your fault. It is in Bethesda but that thing says in Rockville.

Dr. Insel: Right. Yes, it probably is right on the line. And for people who live in the area, the appropriate landmark is Toys R Us, which is behind us. And all parents know where this is for that reason. For about three decades, it was the only Toys R Us store in the county, I think so. Anything else, Steve or Diana, anything to add?

Dr. Chung: If there is a need, we can project anything, the initiatives or the scoring things up on the screen, if that helps.

Dr. Insel: Okay, we will project as needed, and I think we'll go in that direction pretty quickly. But I really wanted this to be much less formal. This is really meant to be very much a workgroup. Sorry we have to use the microphones, but I think you'll get used to that. I should also say that the restrooms are just outside as you

need them. There is a cafeteria downstairs where we can break for lunch.

Dr. Chung: We have lunch coming.

Dr. Insel: Oh, we have it coming. Okay, even better. And there is – let's try to keep this as informal and as much a conversation as possible so we get the best range of ideas. Unless there is anything else in terms of general issues, I thought we'd just get started by beginning a quick review, maybe 5 minutes or so per workshop. And anything else before we start? Anything else from IACC members?

All right. Let's go ahead and jump in. And we've got the floor chairs right here at this end of the table. I want to thank each of you for doing a great job on short notice with outstanding and diverse groups. And David, you want to start us off? You did the biology one, right?

Dr. Amaral: I did the biology one, right. Thank you, Tom. So the list of participants is in tab 3. You can see who is there. I think the biology group had a fair representation of

people at different levels of science. We had people on the cellular end. People like Kim McAllister. We had people at the imaging end like Tony Bailey and Eric Courchesne. And we had a mixture of neuroscientists. And we had some who had more of a neuroimmunological bent to their research. Then we had people who were clinical scientists like Sue Swedo.

So I think it was a very representative group. If anything, maybe we were lacking on the sort of cellular/molecular of developmental neurobiology, but it didn't seem to be a big lack in the meeting. So we –- the strategy we pursued was to start off by naming topic areas in the biology of autism that we thought needed to be addressed. I think we came up with something like 40 or -– what was it, Steve? -- 42 or something on that order. We had 42 topics and realized that would have been complete chaos if we tried to deal with all of them.

So on our first break, we took a few minutes and broke those down into themes. And then decided to tackle each theme. In our group,

rather than breaking into smaller subgroups, we were an ultimately small group to start with, decided to stay together and sort of struggle through each of the themes until the very last minute when we had to write the initiatives. So we took about a half an hour at the end and broke up into twos or threes and wrote the initiatives.

So our group went through -– I don't know, it may have been 8 or 10 themes, and then the end came up with 7 initiatives. And the initiatives that we came up with, I can point them out. If you look at the ranked initiative scores, which is in tab 5, there is -- the first two colored pages are yellow. But it's easier if you go to the ranked initiative scores. I'll just go briefly through these, because I'm sure we'll be talking more about these later.

So the first one was post mortem brain and tissue acquisition initiative. I remember Tom saying he thought that this had already been solved, but in fact, we're still struggling with the idea that there are tremendous techniques in order to analyze brain tissue. We can do

quantitative analysis of neuron number and use molecular probes, and there are all kinds of fascinating studies we can do on the post mortem brain; the problem is we don't have enough post mortem brains to really do the job.

And while the ATP, in particular, has done a very good job, I think, bringing this to the attention of the Nation, and even internationally, that there was a thought that there has to be even a better effort put into acquiring high-quality, post mortem brain material. So that is the post mortem brain and tissue acquisition initiative. Going down for developing biomarkers for autism, people were still saying that, you know, since we know that early treatment is the most effective treatment that can be done, yet we still are having a difficult time diagnosing children until they are 2 or 3 years of age.

And so to try and develop some diagnostic markers that are either prenatal or early postnatal, it should be a high priority. Then going down to the understanding mechanisms and

neuroplasticity in autism, there was a sense that, you know, based on work that's coming out from fragile X, that if we knew something more about what was the fundamental problem in autism, how could we institute a practice either pharmacologically or through behavior that could modify the brain to perhaps impose some treatment.

So I guess there was a sense that we need to know more about how plastic the brain is in general, and how neuroplasticity could be applied to autism, and how we could use things like functional imaging, perhaps, to assess whether you've had an effect, a treatment effect on brain plasticity.

Dr. Insel: So David, if I could just interrupt for a second. I think this is a good example for the kind of thing we'll need to come back to, because what we heard originally when we -– when the IACC -- talked about the Strategic Plan on the first meeting –- was they wanted initiatives that have clear metrics and clear outcomes with timeliness and some

accountability. And usually when you start one that says understanding something, you know, especially in science, you never get there.

Dr. Amaral: Yes.

Dr. Insel: So we'll want to come back and refine. We'll have some time today, but on some of these issues, if this is one, for instance, and I just use this as an example because of the others --

Dr. Amaral: Sure.

Dr. Insel: -- that we think is really a great idea, then the question would be, how would you know when you've done it, and how would you put milestones around it, and those kinds of things. And it's quite different than saying we need 372 brains by 2012, you know, which is kind of -- it is much more of the quality of what we're looking for.

Dr. Amaral: And I should say, I'm sort of paraphrasing the initiatives, but there is a lot more detail even in the written versions of the initiatives and some of these issues. I should also say, too, that when Steve sent them back out

to us, we did circulate them within the members of the biology group. And so we did get some feedback, and they vetted it. So the current versions of the initiative are ones that everybody has had a chance to at least look at and provide some feedback. And the biology team was actually good about providing some feedback.

Dr. Insel: And those are all -- so the actual text is under tab 4?

Dr. Amaral: Right.

Dr. Insel: Okay.

Dr. Amaral: Let's see, we had Jackie Crawley and others who were very cogent in their plea for more effort being put into animal and cellular systems for understanding, again, the basic biology of autism, but for developing realistic animal models of autism that could be used for developing treatments and testing putative treatments. And that's both looking at when there is known genetic variance that has been associated with autism trying to look at what the outcome is in animal models, but also we'll get to looking at things like immune etiologies of

autism and using animal models or cellular models to – as assays.

Let's see. We had -– it's interesting -- there were two people on the panel, Carlos Pardo and Judy Van de Water, who were more immunologists than neurologists or neuroscientists. And there was a very strong feeling that the time had come for seriously looking at a potential immune basis for at least some forms of autism. And so that's looking at both the children and perhaps the parents of the children with autism. Looking at whether their immune systems may be dysregulated. But also, again, coming up with animal models of immune etiologies.

The last two, going down the page, multidisciplinary longitudinal studies of infants with autism before age 3. There was a strong sense that from the imaging studies, we know that a lot of what's going to be most -– instead of major changes that are perhaps going on in the brain are either going to be prenatal or immediately postnatal. Work by Eric

Courchesne and others showing that there is precocious brain growth during the 2nd or 3rd year of life, for example. Pointing to the fact that we need to do more in terms of understanding early brain development. So typical brain development, first and foremost, but understand how it goes awry in autism. And the problem is that it's going to need the development of new strategies, special imaging. For example, the youngest child that's in the literature is only 18 months old. So it is with autism, obviously earlier than that at this point, although there are some initiatives on the way through one of the ACE networks that might cover that field. Nonetheless, the whole idea that we've been looking at autism in much older individuals when brain development has pretty much come to a standstill, and there is more bang for the buck if we could look at the point in time and that would be somewhere between 1 and 3 years of age.

So that -- not only structural imaging, but people are talking about using MEG and other kinds of techniques as well for those kinds of

studies. The last one is the gender differences and biological features of autism. And I guess from the biology group felt, and I heard this in other groups as well, that we've put a lot of attention on males with autism but don't know whether even things like the brain changes that have been now so well documented, whether they are characteristic of girls with autism as well.

And we know that there are a lot of sexually dimorphic aspects with the development of the brain. We don't know whether that confers some risk to boys and some protection in girls. We just don't know anything about what's going on in the female brain as a child develops autism. So there has to be much more emphasis put on that as well. That was more than 5 minutes, I'm sorry.

Dr. Insel: That was great. Any clarification issues? Okay.

Cathy, we're just looking at kind of a quick review of what came in.

Dr. Lord: Yes. I prepared a really quick review. But I think our group and Craig, I'll say a little bit about epidemiology, but maybe you

can chime in. Our group was charged with looking at epidemiology screening, diagnosis, and behavioral aspects of the phenotype. So we, like the other groups, really are covering a pretty broad base. And I think our group worked really well and tried to cover all those things. So we were really, I think, making a real effort to try to be equitable in terms of covering issues from, you know, how do you know how many children have autism spectrum disorders, to how do we know that quickly and efficiently, to how do we screen for clinical populations, and how do we know that our screenings work, to how do we actually make diagnoses, and what does that diagnosis mean to families and kids. And then also how do we better define the phenotype so we better understand what it is that we're studying and what the disorder is that goes along with the neurobiological links. And I think we realized that, you know, we've come up with things that are reliable and valid, but we still probably are not describing what autism spectrum disorders really are, at least in terms of the biology.

So I think that, you know, just looking at the list that David was walking you through, we –- one of the issues I think we've faced was that there really are poles in two quite different directions. One is a practical issue of how do we do things quickly and efficiently so that we can get large samples from, you know, populations without a lot of time and without of training and that can go, say, across cultures. How do we do that? And that's one issue.

And then the other side is how do we use the information we have to know more about the children and adults that have autism spectrum disorders so that we can better understand what it is that's going awry and what's still going well and how can that lead into treatments. And those are actually quite different questions. And I think many of the instruments we have are sort of solidly in the middle but not doing a great job of either being quick and easy or telling us more than -– or telling us enough to lead us into better understanding of what this disorder is.

So I think that was one pull that we really –- you can see that we have kind of schizophrenic recommendations. We have real recommendations like number 18, which is, you know, you can see just by how long it is, that's the fourth one down, you know, that we're trying to accomplish a huge amount of things, and there we're going for depth. And then we also have recommendations like number 33, which is the third one, which is "let's go for efficiency," because we do know that in this field there are many things where we've got to have large samples because there is so much heterogeneity. The kids and adults are not the same. So if we study 20 kids, we're going to have subsets of two, and we don't know what those mean.

So I think another dilemma we face, which is also apparent in these, our recommendations, is the question of how specific should we make recommendations. Like I think we also felt like there needed to be some attention to females and girls. And also underrepresented populations, low-income families, minority families, so

there are sometimes very specific things that we felt like get lost when somebody is doing a big study and just doesn't have enough of these special populations.

On the other hand, those aren't the big questions necessarily in terms of science, or they are relevant, but the reason they've gotten lost is people have been trying to answer other questions that need bigger populations. So again we've sort of vacillated between, you know, these very broad recommendations, and then say, "Wait a minute, we're worried that this is going to get lost." And I think there is also a lot of overlap, I think, between the kinds of things that we've talked about, for example, toddlers and very young children, which I think almost all the groups mentioned. Girls, links between genetics and phenotypic analyses. Links between neuroimaging and phenotypic analyses, and then trying to decide what is, you know, are these really subsets of kids and adults with ASD, or are these dimensions, and how do we measure those dimensions? So I think I won't go through the

ones on the list just because I think they are probably pretty self-evident. But you'll see that we had, I think, 11 initiatives that our group suggested trying to cover the range all the way from risk factors and counting how many kids with ASD -– how many kids there are with AHD – ASD, and things like the State of the States. What are the differences across the States. So very practical things to much more really what it ends up being sort of basic science because we're trying to identify what are the aspects of the phenotype that will relate to the biomarkers that in the end, should tell us perhaps what's going on with these disorders. Yes?

Ms. Resnik: Cathy, it would helpful if you wouldn't mind going through those a little bit, just so that we can mark them.

Dr. Lord: Oh, sure, sure. The number 33, which is the third one, which has to do with trying to speed things up, basically. Having quicker, easier ways.

Dr. Geschwind: It actually turns out that one's from the risk factors.

Dr. Lord: Yes, okay. But, sorry.

Dr. Geschwind: Is this the same one, I mean --

Dr. Lord: Yes, I think --

Ms. Resnik: It's been clear as you go through awareness.

Dr. Lord: Sorry.

Dr. Geschwind: Yes, no. I mean, we actually wrote --

Dr. Lord: Okay, so you wrote it but we --

Dr. Geschwind: So it's actually -– you have one, and it's the same one that we have.

Dr. Lord: Yes. And we just murdered –- I'm sorry.

Dr. Geschwind: That's actually great.

Dr. Lord: Yes.

Dr. Insel: It just wasn't outstanding.

Dr. Lord: There is quite a lot of that. 18, which is also, I think I'm the person who kept saying when we were going through all the other initiatives, this overlaps at 18. So I think this actually overlapped with initiatives from other places, too. And has to deal with trying to both

reassure that what we're diagnosing, to move beyond what the diagnosis apparently is, and then I think this other emphasis is really on dimensional measures. Can we really come up with a good measure of social deficits or breaking social deficits into subparts that is relevant, both for children and adults with ASD, but also the broader phenotype?

Risk factors, this is from the risk factor group, I think --

Dr. Geschwind: It's number 23.

Dr. Lord: Numbers, yes, 23. Which has to do with –- and this might be -– Dan, I don't know whether this came up in our group or your group?

Dr. Amaral: Yes, it's --

Dr. Lord: The prenatal issues. The next one is 32, which is making sure that screening and diagnostic instruments actually work with minority or disadvantaged populations, down to 19, I think that we have a lot of studies showing that screenings, at least, of very young kids have not very good sensitivity. And perhaps pretty good specificity. But we actually don't

really know how they work in the real world. And we really need to deal with the sensitivity issue if we're going to use these to be telling people your child doesn't have ASD.

I think 24 is from us, which is comorbidity. Oh, that's treatment. So it probably isn't. We had one on comorbidity, too, which is just the fact that we think that, you know, many of the factors in the outcome for individuals with autism have as much to do with other things, especially by the time people get to be adolescents and adults as they deal with the core features of autism.

Prevalence, number 7, is basically continuing to trap prevalence so if we can see if things really are going up, what's going on there and what's different in different places. 16 also overlaps. I don't think that's ours, but we also had something about very young kids. That may be --

Dr. Amaral: That was ours.

Dr. Lord: That's yours. Okay, see I'm just claiming. And I think 6 also overlaps with ours.

And I don't know -– see, we added genetics into everything we've said, Dan. So I think this is probably yours, number 6.

Dr. Geschwind: Yes, thank you.

Dr. Lord: The State of the States is, I think, ours. And that's the idea that things are really not fair across the U.S. And if we -– that this –- we need to better understand. I mean, when I was head of the NRC Committee, we couldn't even get information from the States. We weren't allowed to discuss it because it was so awful in terms of how radically different things are from different -– across different States. But that seems important. And the last one on the front page is gender differences, which is the biology, but we also felt like that's a really important issue. Shall I go through all of --

Dr. Geschwind: Maybe just calling them out.

Dr. Lord: Yes. Let me think. Now I can't –- actually, I can't remember if 25 was ours or overlap. But I think again, it's phenotypes. Here we were thinking of phenotypes that may not actually be classic ASD but might overlap. It

would tell us something where we know more about the biology of the disorder, and 37 has to do with using existing data to try to look at -- to try to pull more information again about the epidemiology of autism.

38 has to do again with, sort of, changes across time. So it fits with the toddlers. And we had an initiative about adults. And then 4 really overlaps, I think, with 18, which is -- 4 is devaluating diagnostic criterion approaches. And cost outcome studies, that intervention models. We also had something on cost. And then the last -- I think 11 was administrative databases, which overlaps a lot with 29 in terms of -- again, there are people who thought there is a lot of information, perhaps, in State registries that might be useful. And the last thing is just looking at what is, what -- you know, we know a lot -- well, we have standardized ways of making diagnosis. But what does that actually accomplish in a clinic or in an educational setting? What are the consequences in terms of communities and also

families who are going through this process? Because we primarily looked at it in terms of categorizing or describing more than what does this -– what does this actually do for the child that they have this kind of diagnosis?

Dr. Insel: That's great. Craig, anything you want to add to this?

Dr. Newschaffer: No, I mean, I think Cathy covered that fine. There were three or four initiatives. I guess you only can mention three or four overtly epidemiological in terms of either risk factor initiatives or descriptive studies, but what's interesting is you look across the initiatives, there are opportunities to, you know, embed epidemiological approaches and a lot of the initiatives that have emerged from the other groups as well.

Dr. Insel: I think one thing that's really interesting in hearing you describe this is that there are such clear, sometimes divisions between, you know, needing both this rapid diagnosis, as well as a much more indepth, more informative, much longer -– and we do need both.

And it's clear that when the group comes up with something, ultimately for a Strategic Plan, we're going to have to find a way to straddle that, and maybe you'd have to say that we'd want to see an approach that would be staggered, whether it would be very rapid kind of high throughways of tagging who's at risk, and then something that would come in later that would be far more informative.

But it's interesting to see how this played out. And I think what gets lost is when you try to do these kinds of lists and the scoring is that you need everything, at some point, and you have to -– you know, the real challenge is to how do you integrate it all so that you have something that looks systematic. That's why I said at the beginning, don't think about this as a priority score list, because it's really not that. This is just a way of trying to array all of the options and then thinking about what we need to do now, which is how to integrate them.

Dr. Chung: Can I just say that we made a decision to not label them by workshop? Because

all of the chairs have discussed the fact that lots of things overlapped and fell between, and we thought if we had kind of reapplied those, it wouldn't work. So if there is a little bit of confusion about that, it's great because I mean there is -– you know, you're actually working at the march. And so you know, I want to explain that some people wanted them done differently, but we did that on purpose. So I hope that --

Dr. Lord: Well, it's working. I didn't mean it --

Dr. Geschwind: No, David and I were -– yes, because David was there. He is reminding me. Yes, no. It's great. Actually, it's exactly -– yes, yes.

Dr. Insel: I'm not sure who comes next, or Geri?

Dr. Dawson: Yes, yes. We also had a very diverse group. And I think one of the functions for us, like Cathy, was that it was such a broad scope. And so we had a very diverse group in terms of the people on the Committee. Just to mention a few kinds of people -- we had clinical

neurologists. We had folks that are more on the frontline of the Department of Health and Human Services. We had parents, physicians, psychologists, psychiatrists, early-intervention specialists. People who were really more involved in service research and also folks that represent the more biomedical interventions. And so it was a very diverse group. And so I think the challenges were twofold.

One is that, because we didn't want the group to be too big, we kind of had one person that represented each of these facets, which meant that in your own facet you didn't have someone to really bounce ideas off of in a deep way, right. You were just representing that area. And the other thing was just trying to organize, you know, how would we prioritize and think about core domains that had to be addressed.

So we started with a top-down approach. So rather than generating 41 ideas, and I remember we came in hearing about these 41 ideas, we

immediately felt very intimidated, like, you know, why aren't we as creative or something. But instead, we started top down and identified basic themes and then broke into subgroups, and then generated ideas from those. And our three subgroups ended up being treatment with a focus somewhat more on the psychosocial behavioral, and then treatment focused more on the biological animal models, and biomedical end.

And then a third subgroup that was really looking at the interface. And most groups actually did involve some interface, but the third group, specifically, was looking at the interface between those two. And so let me just, rather than going through each of the initiatives, which I'm happy to do, but let me just outline briefly what some of the ideas are that came forward.

The first one was this issue of neuroplasticity came up. And I think it came up in two ways. One is in looking at human development. So there was an interest in the concept of prevention, that we might be able to

intervene in autism before the full-blown syndrome is present, and therefore alter the developmental trajectory. And then a related theme with that is the idea that there is this tremendous variation in outcome that we have very little understanding of and that probably defines different autisms from a biological or genetic point of view, and we need to get a handle on that.

So I think one thing was studies that really do have a model of prevention that examine that and build into that some hypothesis with respect to why is it that we do see very much plasticity in one case and other children not showing as much plasticity. Related to that was developing infant/toddler interventions. If you're going to start this early, then what do you do with a baby that's at risk, and how do you think about defining at risk, and how do you handle that clinically? Now we do have some of those studies there at the beginning right now. But it's still a very early field.

And then I think if we're going to be

studying plasticity, it does raise the question of developing methods for infant neuroimaging, and you brought that up. And I think an area functional in imaging, this is very important. So we might be interested in technologies that, whether it's electrophysiology or could be optical imaging is another, I think, area of great promise. So there is a whole area of kind of scientific development there that needs to go on.

Neuroplasticity also came up with respect to animal models. So there it's very important that we be able to develop relevant animal models. What are the behaviors that we would think are important for defining one? But it is one of the areas where we are seeing a lot of excitement. So, for example, you know, the MECP2 gene and then looking at those knockout myacin, how we can restore function? Those are such exciting developments. There is a feeling that's an area that we should invest in, and that, of course, raises this question of neuroplasticity again.

Okay, a second theme was the need to address novel or/and commonly used treatments that are not very empirically supported. So there is recognition that there are a lot of treatments being used by parents, and parents are claiming, you know, these are effective. Some are even saying that kids have recovered, and yet we have very little research on some of these techniques. So this is the, you know, biomedical intervention approach. And so we really need to just get out there and study these and understand them, and we're likely to learn some very important things.

Next is the role of comorbidity. So it's recognized that comorbidity is a huge issue in terms of prognosis and the outcome. And I think it shows up in two regards: one is psychiatric comorbidity, which is a very important issue as you move into school age and adolescence, and probably will allow us to understand the genetics of autism, in terms of thinking about, kind of overlap between autism and some of these highly comorbid disorders.

But also comorbidity in terms of medical conditions. So whether we're talking about GI or sleep or seizures, these end up having a huge impact on individuals. And so one of the interesting ideas that came up was what is the impact of addressing these comorbidities on children's ability to respond to behavioral interventions or issues around plasticity and outcome? Because it may be partly these comorbid conditions that are blocking progress.

And then the next issue was biomarkers and how they need to be brought into treatment. Now what I have is it's required for every treatment study is that they at least have one hypothesis on some sort of, you know, biological subgroup. In other words, that even if it's just adding something to try to increase our knowledge, because I think we just recognized there is such a tremendous heterogeneity, and unless we force people to start thinking about biomarkers that would identify specific subgroups that might respond to specific interventions, I think we're going to now make a lot of progress.

Let's see. Next was the need for better outcome measures. And this is huge. You know, no matter how good we are at developing these interventions, whether it's pharmacological or behavioral, or otherwise, we don't have very good outcome measures that are sensitive to change, and so it's not a very sexy topic, but it's kind of one of those tools that we've just got to have if we're going to make progress.

And then next was the need to develop and test interventions for adolescents and adults. And I would say this is going to be hitting us right in the –- square in the head pretty soon, right, that we have this population of aging individuals that we don't have almost no interventions except for maybe a pharmacological intervention instead of an empirically tested.

And then finally, a related set of proposals that have to do with that we do now understand, at least to some extent or we believe, and I think we will show with almost certainty, soon, that early intervention, behavioral intervention has

a positive effect. What we don't -– haven't done is to look at effectiveness studies out in the community. So these interventions are very much localized to small groups or small agencies, and the issues and distributing them widely had not been addressed. And that leads us into service research. And I know in other areas of mental health, this is an active area of how do you disseminate well-known interventions out into the community.

And then that leads to the need to do cost-benefit analysis, which could, I think, be very helpful in advocacy. So I think that covers it, yes.

Dr. Insel: Questions, comments? We'll come back to all of this in greater detail, but we just wanted to get through the quick summary. Dan?

Dr. Geschwind: Yes?

Dr. Insel: You did risk factors?

Dr. Geschwind: Yes, risk factors. And we were the last group, and we benefited from the previous groups in terms of having some process and Steve's guidance, you know, in helping us get

through. We had a relatively diverse group at one level, and then it was, you know, essentially two major groups. A bunch of either clinical-based folks who do, kind of medical research, or more basic genetic folks, and then a bunch of people who work on, kind of, risk factors, epidemiology, kind of policy outcomes work.

So we have those two, in a way, fields represented. And that posed a challenge because the language and the kind of knowledge base in those two fields are really quite different. And so in, kind of, 8 hours to communicate with each other and come up with things was a, you know, real challenge. And I think the way that we did that was essentially by starting with a plenary session where everything was on the table bouncing around. So people got to hear what everybody, you know, everybody was interested in. And then broke up into these really essentially two major groups, a kind of environment/epidemiology group and then genetics group. And the reason for that was not to separate them. As you'll see in some of the

initiatives, many are combined initiatives. But to kind of get -– to not to worry about the technical detail so that the people that are working on it could actually move through these things rapidly.

So we ended up coming up with a total of 14 initiatives, some of which can be kind of collapsed into other, many of which overlap with things we've heard already. So I'll just go through them really quickly.

The first is this one that Cathy mentioned, collaborative development of streamlined diagnostic screening approaches. It's not just for genetic studies. It says “genetic” here, but if you read the initiative, you know, that title erred in a way. It's for any large-scale study where you need more than a few hundred people. So that would be environmental screening as well as genetic studies, outcome studies. And Cathy already alluded to why that's so important. Tom mentioned this as well.

You need large populations. You can't do 2-day evaluations. On the other hand, a

screening approach misses a lot of information. So but the idea is that you need a screening, kind of, diagnostic and assessment approach to do any large-scale studies. And I have a sense of what autism is in the population and get large enough samples have power to do any research.

So I'm going to jump to another initiative, which really gets to Tom's question, I think, which is called gene-based phenotyping. So the way that we dealt with this issue of how do you do kind of just to phenotyping “light” versus phenotyping “heavy,” was essentially this issue. You need population, you use a screening device. But we need -– once you have identified homogeneous groups with a kind of relatively singular etiology, patients with 15q duplications, fragile X, other abnormalities that would be found with them.

It's in those populations that now you need to go very, very deep with what we call phenotyping, which basically means just measuring with imaging, cognitive neuroscience, et cetera. You know, GI, whatever, you know,

immune function. Measuring everything you can in those populations because there, even though they're small groups, you'll have power to actually get somewhere and kind of define what the syndrome, that part of the autism is. That was one kind of idea of how to stratify those things.

So another -– so this second, you know, we talked about biomarkers a little bit, but didn't have an initiative because the biology folks had already done that. But we really were strongly in favor of that, of course. The second would be 23, risk factor studies. Focusing on preconception, prenatal, and perinatal. That had a lot of discussion, and that was something that across both -– all of the groups, you know, all of the people from all the different disciplines -- really was very, very clear.

Focusing on preconception, prenatal, we just don't even have a database of that at an epidemiologic-scale level, and that really needs to be done. That's going to be very informative to anything we do. Okay, 21,

analysis of mechanisms underlying the interplay of genetic and environmental factors. That was interesting because, you know, again it was the genetic environment. And one idea of the genetic is that if you have environmental perturbations, things that are, you know, that can cause bad outcomes, it's not going to act equally in everybody. Certain people may be susceptible. So it's much more powerful that homogeneous groups, again, defined by something. It could be clinically defined, but we're -- but you know -- but genetic really gets to causality. So if they have the same cause, then looking at the environmental interplay would be kind of another powerful way to get at that. And one of the difficulties, and Tom was there, and he'll attest to it, is, and that he brought up, which I think is a very important point is the methods for doing this, and the kind of approaches of fairly, you know, they are not fully worked out so that this is a whole area of study that needs a lot of thought and investment.

In forming the genetics and neurobiology,

number 5, of autism spectrum disorders, and related disorders based on new heritable phenotypes. And again, this overlaps with something Cathy mentioned. We need a deeper more detailed understanding of the trajectory imaging, electrophysiology, sleep, et cetera, enhanced tracking of ASD prevalence in children and adolescents. So not just at the birth cohort but later and looking at trajectory.

I mentioned gene-based phenotyping and cognitive neuroscience, which is number 6. Toward the bottom, they're all ready. Risk factor studies and special populations, number -- is that 34? I don't know. The idea was there, you know, kind of Chernobyl. You know, there is a special population that had been exposed to radiation, a huge environmental catastrophe. So one can take advantage of natural disasters, et cetera, you know, in special populations, and they should be studies to actually assess what the outcomes are. That was from the epidemiologic side. That gives you a lot of power.

13, a large-scale resource of genomic data on ASD. The idea here was, again, phenotype "light," in a way, starting light with a screening device, just get a very large population, 10,000 to 20,000 kids, and 10,000 to 20,000 controls. Something in that range and do extensive, you know, basically create a database of all the genetic polymorphisms, abnormalities, et cetera, that you find, and then that could be a huge research tool for looking at everything from environment to, you know, and going back into that group.

So I set up this large database. New paradigm for clinical genetic evaluation and subsequent diagnosis, you know, 10 to 20 percent of the people who walk in the clinic now can get a genetic diagnosis, to find you know, essentially a causal abnormality or likely to be causal. So how do we deal with that, how does that change the evaluation of children with autism, the need for genetic counselors? And so at some level, a kind of one has to -– it's going to be very, very helpful for that to be top down in a

way, for that to be, in a way, agreed upon, and then disseminated. Or else, what you're going to have is people in rural areas, they won't get any of that. People in certain States will get some of it. So you know, it falls in the State of the States thing, I think. And just all the variations.

The resource, and then 37, develop resources to coordinate large population-based ASD initiatives. And this again has to do with trying to link everything together at a bioinformatic level. There are a lot of environmental, epidemiologic, a lot of different databases, CDC, IAN, NDAR, State registries. How do we link those? And that would be very, very important.

I think the rest of the things have really been discussed except for 11, merging and analyzing administrative databases relevant to diagnosis course interventions and long-term outcomes. Again, this is an epidemiologic approach, and there is a lot of data out there, especially at the State level. It just hasn't

even been tapped.

So I think most of the others, you know, some of our others actually overlap with other people more touched on. I think that's about -– that's really about it.

Dr. Insel: Anybody else at the risk factor meeting, anybody had anything?

Dr. Newschaffer: Just a couple of things about a couple of the initiatives. Not going into too much detail, but just on the enhancement of the tracking of prevalence. I think “enhance” is another one of those verbs like “understand,” and it doesn't give you a good flavor. There were a number of ways where the group felt there could be really informative and valuable enhancements. If you have prevalent systems, whether they're registries, whether they're prevalent assessment systems like we're starting in the United –- in the U.S. -- adding data elements onto those large-scale prevalence systems is one quick way of getting some of the large samples that are being talked about in some of the other initiatives. So there is an obvious

connection there.

The other thing to think about with prevalence assessment is, you know, one of the things that we've been very concerned about for a number of years is understanding time trends, and in addition to having the best information available on prevalence over time, additional information might be needed to link prevalence studies to understand, to really understand, what's going on with time trends.

So that's just examples of just flushing out a little bit of the bones on the word “enhance” to give you a little flame. And the other interesting thing, quickly, I want to comment on is on the initiative. I talked about risk factor studies in special populations. Natural disasters is a good example but serve an extreme, no pun intended, extreme example. There are other ways that the epidemiological approach we felt could be very effective if you focused on groups that either had high levels of exposure, low, or no levels of exposure. Groups with certain phenotypic or risk factor profiles that

were known.

So it's using epidemiology to drill down in special populations to maybe have better yield than we can have in larger studies of a broad group.

Dr. Trevathan: Yes, just to add one thing. Of course when we're dealing with large-scale epidemiologic studies that impact children in the population, we are dependent upon what's being identified in the population. And so even with our fairly sophisticated techniques for going in and finding children who meet diagnostic criteria for an autism spectrum disorder, even if the word “autism” or “autism spectrum disorder” is not in the record, which is really what we're doing, which is very labor intensive. In the absence of really terrific screening and early diagnostic tools in communities, we're limited as to how young, how far down we can go, you know, the age range to identify children.

So for example, number 33 here, we're looking at number 3 on this list down from the

top. One of the reasons they were interested in trying to understand trends or what are the trends in the population of children with autism at the age of 3 instead of at the age of 8. In order to really do that, we need to streamline the community ability to do effective screening, get these kids into rapid evaluations, and identify them in the community.

So these things do dovetail and do connect. So I would say the early diagnosis is really very important for us to be able to enhance our population-based epidemiology.

Dr. Insel: Yes, so that will be our next step here is to think about how to integrate these so you'll have initiatives. But we will want to, as Craig was saying, we'll want to build action terms into these that are, you know, really going to be very accountable and measurable. Can I, before we get to the next stage, one thing would be helpful for us would be to hear something about the process by which each of these workshops happened. Did you feel, for instance, that -– several of you mentioned that the groups

at the table were diverse, then you mentioned that sometimes that posed a set of problems as well, because they came with very different world views, and even different language sometimes -- did that become a problem or was that an opportunity, is one question. And the second question is one of the things we always worry about at NIH when we bring people together, especially scientists, and we ask them what would be the most important things for us to be doing going forward, they generally say fund whatever I'm doing and do it a lot more. And I want to know, to what extent, you felt that was in play in the discussions you had, and how much that was affecting what we we're saying, and how much of it was an impediment.

Dr. Geschwind: Yes, and I think you raised the issue that, you know, scientists and people in the biomedical enterprise are stakeholders in a way, as well. And so, you know, it's hard to really figure that out. You know, my overall impression was that having these groups, it was the split that we did to work, you know, because

we had 8 hours, essentially, to write these things, was really to facilitate the kind of mechanics. What was fascinating is that as people talked and communicated, it was clear that there were very, very shared visions, different ways of stating it or slightly different needs. Again, we just discussed the screening and streamlined diagnosis. I mean, that's something that really was at the top of everybody's list, whether it's an epidemiologic study or a genetic or a gene-environment study. It doesn't really, really matter.

And so and I think -– so I think that actually, and all of these, kind of, initiatives were agreed upon. In other words, so a group would go and kind of write it, then we'd come back to the table and discuss it and bat it around a little bit. And so there was discussion around it. So you know, so I think it was actually that way, you know, we actually met as a group, broke up, had a discussion, came back, discussed it more, wrote, and then at the end, came back.

So you know, this kind of entered a process,

I think, worked to some extent. I think as well as it can within a day. And so, you know, that's the caution is that now looking -– now I think it's really important that we kind of look back and reflect and ask, kind of, what did we miss in our fervor, in a way, you know, to finish everything. And you know, in that day, to see if there is something that we actually might have missed.

So I actually thought -– I don't know -- we should ask some of the -– obviously, I'm a stakeholder, too, because I was, you know, running the meeting. But I'd like to hear from some of the other folks who were there, you know, what they thought about it.

Dr. Insel: And also from other chairs.

Dr. Geschwind: Yes.

Dr. Insel: I think this is kind of an important issue for us. We need to know that what we've got is free of any implicit conflict of interest. Let me just add one more thing to this question, and that is as I was hearing you describe these initiatives, I found myself

sometimes saying with the brain bank, "Oh, yes, we've done that already," kind of thing. So that's not a problem. Actually, I think if people, when they were talking about what might go into this Plan, we're talking about things that are already underway. I think for us -- I don't think we would see that as necessarily a difficulty. So I don't -– I don't think we've talked about it at any of the workshops. But was there an assumption that if it's something that we're currently doing, that it shouldn't be in the list, or shouldn't be on the Plan? Were those things intentionally left off, or people were willing to say, you know, even though you're doing this, we need to do a lot more? I don't know.

Dr. Geschwind: Yes.

Dr. Insel: Okay. I wasn't sure whether there was an assumption that we should only have things on the list that were not currently being pursued in some place. Other questions or other thoughts in terms of the process of these workshops and whether you think people gave us the best science

and free of any personal investments or self-interest?

Dr. Dawson: Well, I'll just comment on my group, and I'd love to hear from others that, who were there. I felt very good about the fact that even though people came in with a lot of different perspectives, and there is even a perception, maybe in the field of treatment, that there is a lot of divisiveness or difference of opinion or service.

What I actually saw happen in the Committee was that people were very interested in each other's points of view and very open to them. And people treated each other, I thought, with a lot of respect and, you know, even though they might have had a different orientation in terms of how they might think about treatment. So I guess my feeling was that people were passionate about what they were talking about because they kind of believed in the science, rather than they thought it would end up feeding funding back into something that they were doing. I just -- I didn't get that sense.

I thought people did have self-interest, but the self-interest had to do with maybe just a belief that this is an area that really needs to be invested in. So I think it was -– I'd like to hear from others that were there, what you thought. I don't –- Lyn or anyone?

Dr. Insel: Or Lee?

Dr. Dawson: Yes, Lee.

Ms. Blackwell: I'll have a few words. Say Geri, thanks. Yes, I agree with you. I think that we had a really dynamic group, and at the end of the day we all kind of got to the same place. But a couple of your comments about what we talked about, I felt like we're maybe a little bit off. I think one thing that came out of our group was that I heard you say that there is an oncoming interest in adults and issues across the lifespan. And I can certainly say that from a Federal perspective, we are here now, okay. We don't have kids growing up. We have millions of people we're trying to serve at CMS that we don't know how to serve.

I mean, every day I talk to State officials,

and most of our States are starting to put together workgroups and duplicate what others offer because they don't know what services to provide to adults. And I would also question, do we really have solid evidence that a lot of these early-intervention services work? And you know, Gail isn't here, and I can tell you that there are people with their big checkbooks, the Department of Education and CMS were very interested in looking at evidence about, you know, what is a good model, what works. And you know, I'd just like to put that focus back on across the lifespan.

Dr. Dawson: I think those are really very good points.

Ms. Blackwell: I agree.

Dr. Insel: Lee and --

Mr. Lee Grossman: Well, I've been involved in a lot of strategic planning -- probably too much over the years. And I think in the process that we have here, I never got the sense, and I never got a feeling from anybody that we were getting feedback on this, that there was any

conflict of interest, or other like underhanded types of things that anybody should be concerned about.

All the groups were well represented by the authoritative experts in the field. And for that regard, I think whoever put these groups together needs to be applauded. The problem was or is that the people that were also invited were somewhat what I call the “usual suspects,” albeit very, very excellent at what they were doing, but the work product to me is what you would expect to come out of this type of process with the people that are in there. And that's how most strategic planning processes develop.

It's determined and directed by those that are in the room and putting this together based on their perspective. I guess what I had hoped and what many people are getting in touch with our organization about is the fact that they were hoping that there weren't going to be the usual suspects or that there would be a greater diversity of people outside of the research science anti-age community involved in the

process to bring much more relevance to the output here.

There is much in the way here of very excellent and much-needed research that has to be done. But it, for most of us, has extremely little relevance to what's happening on a day-to-day basis in the community. And it seems like there is not this balance in this strategic planning process that many of us had hoped would be there.

Dr. Insel: Other comments?

Me. Redwood: And I would like to echo what Lee just said. You know, the parents and the children, we're the consumers of your science, and living with this disorder day in and day out, we have a lot of information we can bring to the table. And that's one of the things I felt lacking, Tom, is that there really weren't as many parents there as I would have like to have seen. And I think by having that, it would increase some of the relevance. You know, we want treatment for our children now and you know, I understand that mechanisms and etiology, and

APPY type investigations are hugely important, but at the same time, there are abnormalities in our children, there are comorbid disorders where our kids are really sick, and if you were to look at those and actually treat them, and take some of the science you have now and rapidly translate that into treatments, you could really help improve the health of our children.

You may not be able to recover all of them, but they certainly would feel better. And I don't see much emphasis on those types of initiatives. You know, I think you have to ask yourself the question, do you agree that children with autism have say, oxidative stress? If so, are you testing for it, and are you treating it? Just really simple things like that. Immune dysfunction, we all know it's a huge problem, but that type of information doesn't get rapidly translated into treatment, and that's where I think the advocacy community and the parent community feel so frustrated because they're doing a lot of these treatments on their own, and they're shooting in a black box, and they really

need the help of NIH to know if these therapies are safe and effective and whether or not they really result in benefit for our children.

Dr. Dawson: I just want to ask a question. So on the treatment group, I think about 50 percent of the participants were parents, and about 50 percent were not traditional NIH researchers. So you know, if you actually go through the list, you'd be surprised.

Ms. Blackwell: The other thing I think it's important to point out is if you hearken back to the RFI that NIH issued, over half the responses -- and NIH just categorized these responses, I mean, I counted each one -- are on treatment. So I think when we debate what are our priorities, I mean, it's important to sort of think that treatment is -– not that these other ones are not important as well, but that's where the focus of the response is, and so I think we do need to sort of calculate that in when we talk.

Dr. Insel: David.

Dr. Amaral: I just wanted to get back to your process question, but also address this as well.

I think even during the biology group there was an awareness that our ultimate goal is for treatment, and prevention, if possible. The problem is trying to define the targets. Everybody is sympathetic with the goal that we're going to get to a treatment as fast as possible. But, for example, we've spent a lot of time, you know, talking about the immune issues in biology grew. The problem is exactly where to intervene at this point. It's not all that clear, and so you know, I think where some of the projects and initiatives that were defined were to get as quickly as possible to the point where we can think up some reasonable processes and strategies for intervening. But I don't know, I think we're just not there at the moment. I'd love to be there at the moment, but I think we're not there at the moment.

In terms of the more general process, I think actually it turned out amazingly well. I was not all that optimistic that in 8 hours you could get a group of people together. And you know, I do think that there was a very –- so I

was able to sit in on all of the groups that week because I'm still learning. And it was enormously beneficial for me to hear the discussions. I thought all of the groups were actually very generative, and you know, sort of unbiased in large part in terms of coming up. In our group in biology, we had Patrick Bolton and Tony Bailey from Great Britain. So they may benefit from NIH. But you know, not necessarily as much as probably citizens here. But yet they were fully engaged in the process of trying to figure out what's the best possible science that we need to do over the next, you know, 5 years or so.

I do think, having said that, that I think it was very productive, and we've come up with a lot of interesting initiatives. I do wonder if the complexion of each of the groups had been slightly different, whether some of things -- you know, some things would have come up that have been missed. So I'm not all entirely confident that we've come up with all of the best initiatives at this point in time. That's going

to be part and parcel of who was at the group. Some things were going to be avoided.

And the other thing that I came away with thinking is that I'm not sure I would agree with the, sort of, critiques that a lot of what we've recommended here are, you know, really good science, solid science stuff that needs to be done. I'm not all that sure it's visionary science at this point in time.

I was a little disappointed in the process in that regard. I mean, I -– you know, so I was very impressed in the risk factors group, for example, where they were talking about this new paradigm for doing genetic phenotyping using things like array CGH, and you know, so I thought -– I went home thinking well, "Boy, every child diagnosed with autism in the United States should have array CGH," you know and that should have been one of the initiatives. You know, that's got to be done. Or something like that.

Yet, that, you know, that hasn't come out in the initiatives. And I think, you know, there could have been --

Dr. Geschwind: It actually is. So that's the new paradigm for clinical genetic evaluation.

Dr. Amaral: Okay.

Dr. Geschwind: If one looks at it in detail, it has to do with the testing. And you know, so for that particular one, it actually did get in there. But I agree with the spirit of what you're saying in that we just have to be, you know, we can step back a little bit and see, you know, did we get everything? But I'm glad that you think we should get that. You know, the -- you know, I think it's a really, you know -- as a kind of clinician and a scientist, I'm struck by what you said because it really reflects, in my mind, kind of a difference of where people are coming from in terms of the folks who are trying to -- everybody is trying to develop an understanding so we can develop kind of this idea of molecular, you know, targeted therapy to something that we can actually say this is for sure in this group of kids.

And yet at the same time, this translational idea, and I think many of us believe, and

actually it was Geri a few years ago, who said something that made me realize that there is a lot of room to take what we know now, maybe not at the molecular level, but at the kind of behavioral cognitive therapy level, and actually implement that. You know, the question is how. So there is a lot of -– you know, I think there is a lot of room to translate current knowledge into therapies. You know, there are all kinds of questions from how do we do it, how do we get enough people trained out there that, you know, are highly enough trained to do this, you know, et cetera, to, you know, who is going to pay for it?

You know, but I do really agree that there is a lot that we could translate and as a medical community in general, one has, you know, one has to figure out how to do that. I think that's a big issue that kind of transcends everything that each individual group was talking about rather than these focal initiatives.

I would say something though, that is very translatable. You know, this thing that David

mentioned that he came out of the meeting saying, "Oh, we should do that." We can find a genetic cause now, which blew me away. Eighteen months ago you would ask me would I have predicted these findings, I would not have predicted it. So it's something totally surprising to me as a somebody who comes at this from a neuroscience and genetics perspective, that 10 to 20 percent of people who walk into clinic now using some of these modern techniques, we can give them a genetic diagnosis, in other words, we can identify potentially what the cause might be from that perspective.

Of course, that leaves another 80 or 90 percent that were not. But for those kids -- that has implications for risk, for counseling in terms of children and other stuff. So you know, so I wanted --

Dr. Insel: So what about therapy? What about therapy?

Dr. Geschwind: So you know, the therapy is the next, you know, we don't even know what the phenotype of these kids is. Like so the idea of

the gene-based phenotyping would begin to get there. It's, you know, that doesn't necessarily translate rapidly to therapy without an understanding of mechanism.

Dr. Dawson: I guess just following up on that though, I guess I would say that is an important step to therapy. Right, because for one thing, this whole heterogeneity has really got us bogged down. And I think understanding, if we can start to understand subgroups at a more molecular level and how they may respond to different treatments, then we can begin to personalize, you know, the medical approaches. Whether we're talking about currently existing pharmacology, or you know, the animal models that come from some of these findings.

So it's not an immediate translation, but I think it's a critical step in actually getting to where we want to be.

Dr. Insel: So the good news is you don't actually have to do the Strategic Plan for us if that's going to be our chunk. The people at that side of the table who have to eventually make

this work. But I thought it would be helpful for you to hear some of their concerns.

I'm reminded of years ago when I was giving a talk to a group of family members in, what was it, Oregon, and one of them said, "You don't get it. You're talking," the line was that, "Our house is on fire, and you're talking to us about the chemistry of the paint." And I do think we have to be really focused, even now as we think about, you know, how to shape these. Because we'll be now refining these, some of these initiatives, to think about some of the potentials for short-term payoffs, and what it is that will give people in the community a sense of possibility and hope, as well as real changes. Some of the things that Ellen's been mentioning about being able to understand what the State of the States kind of issue, you know, giving people a sense of what the landscape is.

I wonder if we ought to take a break at this point for 10 minutes after Peter and, okay, there are other comments. Okay, let's do that, and then we'll take a break, and then we'll come back and

actually start the work of this meeting, which is to kind of do the integration. Peter?

Mr. Bell: I just want to, I guess, acknowledge the fact that I clearly got the sense from all four of you that there is a little trepidation and uneasiness about the diversity of these groups going into it. But that your coming out conclusion was, "This was great." It was actually a good process, and I think what we're also hearing here at the table is a little bit of a sense of maybe it wasn't diverse enough. Or maybe some of the certain perspectives weren't given enough opportunity to be a part of the process, and so forth.

So I think that there is probably a good happy medium. And the difference between this process 5 years ago where there were, I think, eight people sitting around the table coming up with a matrix, we've made some progress in that regard. And I think that's good.

I also think that it's important for us to recognize and not only recognize, but very much appreciate the heterogeneity of this disorder.

And I think that is represented in the diversity of perspectives that you had in these meetings. You know, there is no question that autism is a diverse and heterogeneous disorder and that what we're really talking about are a number of different disorders that we all kind of still call “autism.” And we really need to take that heterogeneity and apply it across everything.

There are people sitting at this table who have had kids who have done remarkably well. And there are others who have had children who are still very much challenged, and our community is divided on that. And we all have our children in our best interest, and we try to do the things that we can. And some kids do remarkably well, and other kids don't. And we need to figure out why that is. And I heard some bits and elements and some of the initiatives that you all talked about today, and I think we're making some progress in that regard.

The other frustration that I think you're hearing from the parent community is that a lot of the things that we've said for many, many

years take a long time before they take hold. And then eventually there becomes a better appreciation. So, for example, 10 years ago a lot of people started screaming, "Gee, this is a lot more common than we thought it was." Lo and behold, we realized that it is a fairly common disorder. A lot of people have said, "My kid has GI problems, and, you know, what's with that?" And we were told, "Well, don't worry. That's just a part of autism." Lo and behold, eventually, there is a better appreciation and recognition. Progression, that's another thing.

So there are a lot of different elements that I think our parent community has been very frustrated about that ultimately kind of bear out and actually are now starting to be better appreciated. And I think if we hold that partnership of how we bring the parents and clinicians and the scientists together and work together and hold each other with a high degree of respect, that's where we're going to be most successful. I think that's, you know, that's our challenge here at this table. I think it's the

challenge of the IACC as well, is to be open and respectful of the different opinions that are out there, because that's where we're going to make the most progress against this disorder, which we all kind of come here at this table with that shared vision and interest.

Dr. Insel: You know, that's very helpful. I think we, in the autism team group, and those of us who have been thinking about this process realize that what we've done up until now has gotten us just what we wanted up until now. But that's not getting us the Plan that we need, and that there has to be another phase where we'll be able to get a much broader input. Otherwise, this is not going to be what we want it to be, which is out there pulling in the very best ideas from as broad a community as possible.

We'll be going back to the IACC to figure out how best to do that, and it may slow down the process a bit. But I would rather do it right than do it quick, and in the Combating Autism Act, they said that you need to have a Strategic Plan, but they actually didn't give us a date. So if

we have to delay this a few weeks or a couple of months, that's fine with me. This has got to be for the whole community, not for NIH or CDC or some part of it. Geri, you have a comment?

Dr. Fischbach: Well, I'm not sure how you want me to put it. I know it's part of the initial planning group. I didn't attend any of the meetings. It's really wonderful to hear the outcome from those meetings how much got done. I just have a couple of general observations. One, I think the NIH has been remarkable in including a broad community to help think about these Plans -- broad scientists, broad advocacy groups, broad parent groups. And this is a beginning.

I don't think that you can think of this or any Strategic Plan as a final document; the flexibility of it is really critical. So you may write and submit to the IACC and to Congress a Strategic Plan, but that ought to be looked at every so often, maybe every year, and revised and updated, because what we're thinking now is just not going to be what we're thinking a year from

now. I'll bet you a big bet that we're not going to know two, three, or four risk factors. In another 2 years, we'll know 50, somewhere between 20 and 50 genetic factors that impose increased risk of autism, interactions with the environment.

And first is, how are we going to use that information? I think you have to be realistic. It may shed light on diagnostic processes, but there are huge ethical issues that are raised, which are not discussed so far in the Strategic Plan. What do you tell parents, and what good will it do? What will this information add?

Will it help in terms of therapeutic categorization? I actually doubt it right now. There is not a disease I know of that doesn't have a remarkable degree of heterogeneity. And dealing with that heterogeneity can be an empirical process. And I think that the issues that are being raised here is an urgency on those parts of the Plan that deal with experimental therapeutics. That we don't have to understand mechanisms, of course, to begin some

high-throughput screening on either cell- or animal-based models, and think about this in terms of small clinical trials.

And maybe they can be based on comorbidities, but they can be based on experience with other disorders, and with some clues coming out of the genetics. So I just think we have to be realistic. When I looked at this list and heard the report, there is a wonderful overlap between the groups. And I'll bet we'll be able to boil this down to 10 or so major efforts with a lot of subdivisions in each one. But I think you have to recognize that the Plan is just, it's an initial Plan.

It's not going to be, to me, a final answer, and I hope it remains flexible as we go forward. So the impatience we hear, it's not going to resolve every one of these issues. And I would just put in a big plug for adding, and when we come to those areas, say, whether it's cell-based assays, or animals, or early clinical trials, more really experimental therapeutics, almost mechanism independent for now.

Dr. Insel: It's required to be updated on a regular basis. So that's in the Plan. What we're really talking about, as Joyce said in the initial discussion, this is Strategic Plan 1.0. Knowing that 1.1 will be not too far behind. Dr. Giannini, you had a comment?

Dr. Margaret Giannini: Yes, I want to agree with what has been said down at this end of the table. And I think that I've been to some of the workshops, and what I hope will be in your planning for the short term. The long term, we've heard of yours, and I think it's remarkable with all of the initiatives that are in here, and they're all important. But I do think that there is an urgency with the comments that were made earlier down at this end of the table. I didn't hear, and maybe it's premature, that you don't have the heavy hitters that are going to be responsible for the coverage of these services at the table from the beginning.

And for instance, like CMS would, I know, because I've worked with them, if they have evidence-based information, that would be the

kind of thing that they would cover. Is that not so, Ellen, in many ways?

Ms. Blackwell: Well, it depends.

Dr. Giannini: Yes. But I think it's a good start to show good will that this Committee, or whatever the process is finally going to be, that's going to work early on to plan with some of these short-term things, with the Department of Education, with CMS, and possibly even SSA, Social Security. So I think that partnerships in whatever we do, whether it's this Committee or any other committee, as I do it every day, is you've got to depend on partners if you're going to get really anything done.

So I would urge for that to be done. As far as the Strategic Plan, there has been some comment that you'll be looking at it, and I would assume that in your Strategic Plan you're going to have performance measures and timelines on what's going to be accomplished. So it's recordable and observable so that if it's not working, it can be fixed.

Dr. Insel: So it's going to be your plan?

These people are just providing a starting --

Dr. Giannini: Well, I'm assuming that's inherent and that's a given.

Dr. Insel: Yes, so it will be whatever the IACC wants it to be. And I'm hoping, you know, we have the Secretary set up the IACC with the understanding that the major partners, both Federal and public family clinicians, all of them would be around the table. So the process that we've put into place is summarize that so there will be something, it will be something we're working with. But by no means would I expect this group to give us a plan that we would --

Dr. Giannini: No, no, no. No, that wasn't the intent.

Dr. Insel: But I really need everybody at that end of the table. That's why I'm so glad you're here. You're going to have to do this; you're going to have to tell us what it is you want in the final Plan that's going to go to the community and the Secretary and Congress. It's, you know, the extent that this is helpful, great.

But what I'm saying is that I'm also hearing from you that this may be helpful but there is another piece that will need to be brought in. And we need to think about -- we won't be able to do it today because it's not an open session.

Dr. Giannini: Of course.

Dr. Insel: But in March, we'll have a discussion about so how do we get that other piece and how do we make sure that there isn't a really spectacular idea up there that we haven't captured that needs to be invented here, so.

Dr. Cindy Lawler: I have a brief comment. I participated in one of the workshops, a risk factor workshop. And it was a very collegial process, and I think the, you know, the diversity of membership on those, you know, working groups, you know should be lauded for that. My concern, I think, speaks to some -- there have been some comments about these are reasonable initiatives. They are fairly predictable. Are we missing -– were there missed opportunities for sort of visionary perspectives because we didn't

include researchers, say, outside of the field of autism? That's sort of another community, and I think we're all patting ourselves on the back here because, wow, we got all these people together and they sort of agreed on these cross-cutting themes. But maybe it's like your family. You know, you're going around to your family, "Do you like me? Do you like me? Do you like me?" "Of course." You know, within the family everything is fine. But maybe that's not a measure of success here.

Maybe the fact that there is so much agreement suggests we weren't thinking broadly enough.

Dr. Insel: That goes to the same comment David made as well about the concern about not having the bold ambitious visionary idea. Craig?

Dr. Newschaffer: Frankly, at this point I agree with that. I just think as the process moves forward, when you think about addressing this issue, when you think about addressing this issue, remember that it's not necessarily lack of other voices. The way this process was

constructed, you know, the way people who do this for a living -- I'll speak for myself -- not the other people around this table, but there are a lot of disincentives toward visionary thinking. The way you go about doing your daily research, you know, some call it preliminary data. Some call it other things.

So when you bring the people who are doers together, with 1 day to work on this, without any prepping that they should be bold and audacious, that dampens their visionary ideas as well. So I think it just needs to be important that when we go to the visionary step, you also go back to some of the people. They'll say, "Oh, they didn't get it" and look completely elsewhere. I think it's important to look elsewhere. But I also think it's important to prod the folks in the group or people like them without that kind of thinking as well.

Dr. Insel: Yes, because at the end of the day, they're the people who may end up actually making the discovery. So you want to make sure everybody is aligned. Ellen, I'll give you the

last couple of minutes, then we should break.

Ms. Blackwell: All right, I just have one thing. I was going to ask, it sort of helps me when I hear you guys talking about kids and parents. I mean, I think it might help us to start talking about people with autism. Because a lot of our parents are in their 80's and 90's, and their kids are in their 50's and 60's. So to me, I just try to refocus as people with autism. Because if we just talk about kids, that cuts out a lot of people.

Dr. Insel: You know what's striking to me as I listen to this discussion is that normally when you do a Strategic Plan, the very first step is you create a vision and a mission. And you get some real buy-in on what that would be. That was never done here, so we kind of went ahead and started putting all of us together without having any real agreement about what is the full vision and what is that picture of what autism should look like in 2018 or 2028. And obviously this isn't the group to do that. But the IACC, I think, is going to need to have some

opportunity to find some common ground where it says, "This is what we really want. And this is what the Strategic Plan is for."

But nonetheless, we've got something here. I think we need to try to get this refined to a point where the IACC can use it. But there does need to be a very different kind of discussion that hasn't happened and I don't think could happen very well at the workshops. And I think once that's happened, then as Craig says, it's the chance to go back and make sure that everyone understands how this could be implemented and how this could become real.

I get the sense we need at least a biology break if nothing else. But I'd like to keep this fairly –- because we're a little bit past schedule. So maybe we could return in 10 minutes. And Joyce, what else?

Dr. Chung: Give me your conflict-of-interest forms, if you can. And lunch will be coming around between 11:30 and 12:00, so we'll have a working lunch, and I'm the bank.

Dr. Insel: Okay.

(Whereupon, the Committee broke for lunch at 10:56 a.m. and resumed at 11:18 a.m.)

Dr. Insel: So the next part of this task is the real work of the day, which is integrating what we've gotten from these workshops into a framework that the IACC can use and better understand. So what I'm going to need -- I think what we've heard already is that the four themes that we used are not the right framework because already there is so much overlap, and there is so much redundancy. So I'd like some thoughts from the group about how best to wrap our hands around these 41, and I think Geri said we'd probably end up with 10 or something like that.

But what are the -– what we'll need to think about are what are the major categories or bins that these initiatives should end up in. And we began doing this before the meeting; I decided it's probably something we should work with you on and let you give us your best ideas about how to cluster these together. So Denise?

Ms. Resnik: In evaluating what I read

independently, and certainly listening this morning, there seem to be two tracks that we can and may want to consider. The first will be some type of resource assessment where we identify what exists, we analyze what exists looking at the collection protocols -- what to look for and so, basically, what's out there. And where can we continue to get more information. Once we identify some design for that and how to collect that data, then looking at another category, which is capacity building, and that speaks to what we've heard this morning about the expanded populations, ethnic backgrounds, age, gender, comorbid issues.

Capacity building also would look at a more robust tissue collection opportunity. So once we know what we're going to look for and how we want to collect it, then we go out there, and we begin building capacity. And then, based on that -- we've heard a lot about, you know, obviously, the heterogeneity where we look at models. And under that category, perhaps, we've got animal models. We've got the biomarkers. We've got diagnostics.

And then once we have those models in place, which again can be fueled by another realm here, but then we can better understand these environmental exposures. So if we have some idea of greater homogeneity in terms of what we're looking at, then how is the environment impacting, you know, the kids, the adults, the people? And then once we know what it is we're dealing with, what are the autisms, then the treatment research, and how we can go with treatment research, and a personalized approach, biomedical, cost-benefit analysis. But it seems that we're all trying to get at, obviously, what is it that we're looking at, and we recognize that in any of our studies, if we don't know what that subject core is made of, and you know, we can sit around this table as I know we do with our different kids, mine including, and they didn't respond to the same treatment somebody else's kids respond to. But if he's part of the study because he's, you know, 16 years old, or 10 years old, and fasted before the blood draw, he counts.

So it seems that if we look at some of those bins, if you would, and then there are things that would run concurrently that could empower those bins. We heard also about the novel therapeutics. Well, in those novel therapeutics, how do we, again, look at how we're collecting assessments, you know, from the outcomes there?

And so maybe there is something that also adds and conveys that sense of urgency, specifically as it addresses the safety of these kids and the efficacy, you know, in terms of, you know, we as parents will try just about anything, many of us will, you know, if it's going to help or we think it's going to help. But you know, the safety issues are huge and the fact that, you know, physicians or docs, or whoever they are can set up shop in a State. There is no oversight and so, you know, how do we help empower these families with good information and keep these kids, these adults, these people safe?

Dr. Amaral: So I think those are great. And I think the one thing that you've left out that

was a guiding principle of all the workshops was trajectory. And that actually encompasses a lot of this, too. Certainly from brain science we know that it's not necessarily the end point of what the brain looks like; it's how the brain has developed over time that deals with, you know, various treatments at different times throughout life, various diagnostics throughout life.

So I would hope that the concept of trajectory, the pathway or trajectories, early onset versus regression, for example, in terms of trajectories, that should be one of your guiding principles as well.

Dr. Lord: I wonder, too. I think this is really helpful is if we, just given the concerns that we're not easily responding to novelty, that we have some kind of cross-cutting approach, which is a place for, you know, novel translations or novel approaches, which, because I think that, you know, at least my experience, whenever you get a group together and there is time pressure, that's where the

novelty goes right out the window. I mean, and so we have to have some, you know, theoretically, you know, for R01s, you're supposed to have -- they're supposed to comment on innovation. But that just sinks right down to the bottom when you're, you know, when people are trying to agree with each other. You've got to get some mechanism for people to do things, to make proposals that are pretty quick, that don't go through three rounds of a study section that's mostly not autism reviewers but can address specific needs as long as it's a valid scientific proposal. So somehow pulling that out.

Dr. Insel: Can I just, I want to make sure I understand what you're saying. So it's not just the novelty in the research projects, but novelty in the way that they're supported and developed?

Dr. Lord: Yes, I'm saying if we're going to support novel projects, and I think, you know, the treatment group did propose, you know, a fast track for translational research, and also, I'm probably mixing up two initiatives. But there

was also one about commonly used but not validated treatments. But I'm saying have a particular mechanism for dealing with those and anything else that's really novel that someone wants to do and let them do it quickly.

So not have as, you know, not have it necessarily go through the system, because I don't think the system does well right now for that.

Dr. Insel: I remember that Kayla -– Peter, I don't know if you had joined us. Dan was involved -- we used to debate whether to do an “X Prize for Autism.” You remember this?

Dr. Geschwind: Oh, sure. Yes.

Dr. Insel: And there was this -– we never did that -- but there was a long discussion about whether we should have, you know, a $10-million-dollar prize for somebody who worked out. In this case, I think we were talking about the genetic architecture of autism or some, you know, something about the cause that could explain this mystery.

I mean, there are just ways of thinking

about this very different from the traditional funding mechanisms of how one goes about this. Geri?

Dr. Dawson: So just following up on these ideas about the novel treatments and also the fast-track translational work. And I think that I'd be curious, Lyn, if this also addresses some of the issues you were bringing up earlier, which the group felt that it was very important to rapidly study treatments that are now developing out in the community that have not been well empirically validated. They may have safety issues associated with them. But the whole idea is that this is a place where novel ideas are coming to the fore, right? And people are using these interventions, but there haven't been enough even efficacy trials on these.

So I think that when we start to see these interventions being used in the community -- and they offer promise, right, for actually making a difference -- it's very important that we have a mechanism for studying those. So that was one of the initiatives. And then the second one

was that sometimes there are just interesting ideas, whether it's these kinds of ideas that are these novel treatments being commonly used or others that have a lot of promise. And they're a little bit out of the box, out of the mainstream.

And if there is kind of a rapid mechanism for doing some pilot studies that would be just, is this going to be a fruitful direction to head, rather than, you know, more of the traditional NIH model of having to build up a lot of pilot data and, you know, have a program that you can support that line of work. So that was the fast-track mechanism.

Dr. Insel: So again, I just want to make sure I hear what you're saying. So it sounds like one issue would be to think about having a bin that looks at the process for supporting science, for supporting research, and developing a process that's quite different than what we have now, whether it's public, private, partnership of public and private. It could be a bunch of things. But that wasn't in any of the -– I guess

there are a few comments in here that would speak to that. But I'm still looking at what are the bins that we want to have to put these 41 into?

So that is one, though, that is a little more visionary and bold according to David's criteria. But I don't think we talked about it, because as Denise was saying before, we were kind of really into tactics. You know, we were down in -– what are the next experiments that need to be done, not stepping back to say how can we do this in a different way to get to different results.

Me. Resnik: You need to turn your mic off, Geri. Thanks. Thank you. Well, two things. When you talk about the novel therapeutics as they can empower our understanding of some of the models, but we understand that in assessing the novel therapeutics, we come up with the same issue of we don't know really what we're dealing with in terms of the subjects that are responding well versus those that are not. But, you know, maybe we can come at it from both ends.

So, you know, where we prioritize and how

we build up, you know, that track of research on the novel therapeutics -– again, it powers maybe these different areas is one comment that I wanted to make. Second, what we were talking about during the break is again, this is very tactical in terms of, you know, the research and trying to create the process and bins. But there is another layer that really speaks to some broader strategies, and I think it speaks to the visionary kind of thinking, bringing people who are not the same suspects around the table, and that engagement. And those groups that are already investing and, certainly, Simons is, significant dollars in research, and how do we engage them as part of a strategic initiative for us? How do we engage them in this process and early in the process to have some of the out-of-the-box thinking, but also so that we can continue to engage them throughout as we get toward implementation? And there is, you know, and which groups, and if we haven't identified them are out there that are already investing significantly in infrastructure that will help

leverage whatever investment NIH makes in research. So I don't know if we really tapped that.

Dr. Insel: That may really be more the job of the IACC because there, we've got the partners in place. But it does fit into this first category you mentioned about resource assessment. At least initially having the landscape in front of you. So one of the things that the Committee will have to do before they can finalize any sort of plan is to actually see what's currently being done. And Autism Speaks has shared with us already their portfolio. So there is a way to, once we have the bins and the different elements in them, we can begin to link up with where the current investments are. We're doing this at NIH, and the NIH Autism Coordinating Committee that Alice represents here is working right now on trying to come up with the full list of projects. I think CDC is doing that as well. So we'll all be able to, I hope, I don't know if it will be by March 14, but soon thereafter have that landscape in one place

at one time to be able to see what's currently being done, where the gaps are.

Ms. Resnik: I have a process question for you. And that is you acknowledged earlier that, you know, IACC will identify the vision and mission for the Strategic Plan. Tactics typically follow what you set out to do. And so was there an assumption on the mission, vision of what this Plan is supposed to do before we got into, you know, looking at the specific research initiatives?

Dr. Insel: No. No, and I think that's the discussion that has to happen going forward. And they've got to decide, or we've got to decide as a group, what it is that we really want to accomplish over these next -– it's a 5-year timeframe that we've been given. So much of that is laid out for us. The Combating Autism Act provides some of the language of the kinds of things that the Congress expects. But what has not been developed yet by the Committee is a clear vision statement of what it is everybody agrees would be most important. Alison?

Ms. Singer: I think another way for us to think about setting up the bins that could work either -- I think it works in parallel with the bins that Denise has set up -- is to really look at it from the standpoint of the families who are experiencing autism as opposed to just looking at it from the standpoint of the science.

So I think when we think about what families experience when they get the diagnosis, the questions that they're asking when they get a diagnosis is, first, "Why does this -– why did this happen to my child?" Then they ask, "What am I going to do to help my child?" So that really focuses on the treatment. Then it's, "Well, how do I actually go about getting these services, and are they actually available to me? Where do I go, and how do I get there?" Then they ask themselves, "What is my child's future going to be like across his or her lifespan?" So what's in store? And then I think after our children are settled a little bit, we start to think about how can we work to prevent this from happening to other children, including any subsequent

children that we may have or our grandchildren.

Dr. Insel: Can you see some of these 41 items fitting with those?

Ms. Singer: I do.

Dr. Insel: That's great.

Ms. Redwood: Another thing that we discussed back several months ago was coming up with some guiding principles. And I think it's essential that we go back and identify our mission statement and our goals. But then I think we need a group of guiding principles that each of these 41 will have to address or fall under. Whether it's the sense of urgency or that all of these have some type of treatment arm associated with them or a goal in sight when we come up with these plans. So I think we need to think about that as well. And I know, David, you mentioned some guiding principles I think we all have. So maybe use those to inform the Strategic Plan.

Dr. Insel: Any others besides urgency treatment as a -– Geri?

Dr. Dawson: Well, it might be useful to identify things that we feel are barriers to

progress. So I know that it was mentioned, for example, the need for some kind of a screen, diagnostic measure, that could be used at a population level that was more rapid or, you know, outcome measure. I mean, these are the things that aren't quite as sexy, but they are absolutely needed if we're going to make progress.

Some of them are resources, so the brain tissue bank I think is an obvious one that -– so when -– I think if we look at either barriers or resources that we feel like if those were put into place, would just accelerate. Because we actually don't know the direction that things are going to head in some ways. So it's important not to just focus on specific hypotheses but also to develop resources where a lot of creativity would be facilitated.

Dr. Fischbach: I heard several people, including Cathy and, I think -– sorry to mispronounce your name –- talk about a shortage of trained clinicians to see, to interview, make diagnoses, and to do treatment. If that's true,

there ought to be some training program as part of their resource assessment. Didn't you tell me that sometimes it takes 2 months to schedule a visit at a clinic with no --

(Laughter)

Dr. Fischbach: Twelve months? That's unthinkable. I mean, how can you do any diagnostic?

Dr. Insel: And that's in places with lots of resources like New Haven.

Dr. Fischbach: So somehow think about how to provide training opportunities.

Dr. Dawson: That initiative on looking at how to translate the known treatments into the broader community, I think, is partly focused on that issue.

Dr. Insel: Right, right. So if we took just the last few comments that I'm hearing, if we go back to Alison's conceptual structure, you could think about having almost a matrix here where you could look at what are the barriers or challenges in each of these areas and where the opportunities are. And hopefully the idea would

be the 41 will somehow, whatever it is -- I think you said, Geri, it's probably going to end up a 10 or a 12 -- but whatever it is that came from the workshops could be mapped onto this, I would think. How do people think about this?

Dr. Fischbach: It's a great idea.

Dr. Dawson: That's a great idea.

Dr. Insel: So Alison, you said that you had already seen how they matched up? You want to just try us out on a few and see?

Ms. Singer: Well, where do we start?

Dr. Insel: Just give us any --

Ms. Singer: I guess the, "Why does my child have autism?" it's, yes, really looking at the biology and the cause.

Dr. Insel: So what would be --

Ms. Singer: The ideology as we say in our --

Dr. Geschwind: So in part, so it would -– I mean -- it's interesting because then maybe in a third dimension, in a way, one can have these other issues that were raised like -– you know, so there are resources that need to be developed,

and then there are kinds of questions that need to be answered in a way that are related to this.

So from a resource standpoint on the why, the thing that came up, number one, was post mortem brain and tissue acquisition initiatives, you know, from that, which is already ongoing. You know, so I'm just starting with a low-hanging fruit to kind of begin. So I'm not sure if -– you know, has a three-dimensional. You know?

Dr. Insel: Yes, that's kind of a matrix of –- so that's what I was trying to get at before, Dan, is that if you think about the kinds of initiatives that are in here, there are at least three different flavors. There are capacity building and resource issues, whether it's workforce, which actually isn't in here but could be, or issues around building repositories, databases, a whole bunch. There are probably five or six such issues at the 41.

There is another set that is very tactical, like let's go out and find a biomarker or a set of biomarkers. And then there is another set

that, to me, has a slightly different flavor, which is more related to what Denise was calling the “resource assessment,” the State of the States issues, the issues around defining the costs of autism, looking at the current landscape. And that's a research question. I mean, what does autism cost the United States? That's entirely a research question that only a few people are looking at, and it would be very important for informing policy.

So there is a whole other category. And I counted maybe 3 or 4 of the 41 that fall into that. So what I'm struggling, what the group -– we've been talking about this a little bit -- is what are the right bins? And it seems to me that what Alison has given us is kind of one axis of this, and then you could think of another axis that would look at these other kinds of things, like capacity building and specific projects.

Dr. Geschwind: So maybe put like within each of these, you have challenges, opportunities, kind of for each. And then these other bins that you just talked about, like things that are

tactical or resources or mechanisms. Kind of getting back, you know, and so that across the top you would have something like resources, the tactical, the mechanisms. And then for each it would be kind of challenges, opportunities or challenges, and plans for each, because those are the kind of --

Dr. Insel: That's the third dimension.

Dr. Geschwind: Yes.

Dr. Insel: Got it.

Dr. Dawson: Now, where does translational fit into that?

Dr. Geschwind: Kind of under how, I would think at some -– how can I help them? How do you -– or what?

Dr. Dawson: But, I mean, there wouldn't -– but you were saying there were three types of initiatives, capacity resources, tactical, and resource assessment.

Dr. Geschwind: Oh, no. I mean, that was just an example, yes.

Dr. Dawson: So I was wondering how does --

Mr. Resnik: It was after we established what

–- I mean, going back to the other page -- after we looked at what the models are, then we look at the translational component because now you've got good material to work with -- good subjects, phenotyping of those. And then you look at how it translates.

Dr. Dawson: I just want to make sure that we don't lose the urgency and get into too much infrastructure building. I mean, I think it's really important to do that, but also to keep pushing to the front end of, "Okay, what can we do now, or what are the things that we need to address now?" I mean, both sides are really important.

Dr. Geschwind: So maybe that should be another, you know, right after --

Dr. Dawson: I don't know.

Dr. Geschwind: I think a lot of -– I'm sorry.

Mr. Bell: I was just going to say, wouldn't there be an opportunity once you build a matrix like this to identify what is currently being done and then to identify what are the things that should be on that urgency list, meaning

these are things that we should do right away? And whether it's through a public-private partnership, or one group says, "You know what, we'll do that, or we'll create a mechanism by which we can do that." Whatever, I mean, to me that's kind of the process that we need to get to is what does the Plan look like, and then we start dividing it up and saying, "Okay, how are we going to accomplish this Plan?"

Which I think, if we were to go back to the matrix, is what was lacking. Here is the matrix, and now let's just assume it will happen.

Dr. Insel: Although there, there was a short-term, long-term. So that was one axis, but it's not clear that -– but your part about the implementation wasn't there.

Mr. Bell: Right.

Dr. Insel: I also like Lyn's idea that you would probably start this thing off with a set of guiding principles, which would have to kind of go through the whole -– the whole document. We are saying these are the things that we are committed to.

Mr. Bell: It's already been done.

Dr. Insel: Oh, yes?

Ms. Resnik: Actually, it's not that it's been done and distributed, but when Alison and I have to reevaluate the matrix, we did, I think, identify six guiding principles, and I actually have a copy of that if you're interested.

Dr. Insel: Should I put them up, or maybe we should put those on the --

Ms. Resnik: Well, clearly one is a sense of urgency. Another is that spirit of collaboration, and that's value-integrated, cross-disciplinary approaches, teamwork, sponsorships, clearly defined roles and responsibilities.

Dr. Insel: Hold on, hold on, hold on.

Ms. Resnik: But in terms of the bucket, it was spirit of collaboration.

Dr. Insel: So the first one was urgency?

Ms. Resnik: Yes.

Dr. Insel: Collaboration.

Ms. Resnik: So the main headers, spirit of collaboration was next. Another was engagement,

and that speaks to families -- engaging with families and existing programs. Another was alignment, and that spoke to short-, mid-, and long-term objectives aligned with integrated funding priorities, review processes. Another was return on investment. And then the sixth was accountability. And each of these has a brief description.

So sense of urgency, spirit of collaboration, engagement, alignment, return on investment, accountability.

Dr. Insel: And the last one is accountability. And you can take out the second line, Steve.

Dr. Stephen Foote: Collaboration?

Dr. Insel: Yes. So is that something that the workgroup would like to send forward as -- along with whatever recommendations are made as these sort of guiding principles? Did these capture? These --

Mr. Bell: One other suggestion or idea or concept, and it may be included in one of these, is a sense of open-mindedness that there always

is this value. And it could be included in there, I guess. But I just feel strongly that everyone has to be open to the idea that, you know, there isn't anything too crazy or whatever that, you know, within reason we need to keep an open mind as we evaluate a number of different ideas and concepts and theories and hypotheses and what have you; that, you know, you just need to be very openminded about it.

Ms. Singer: I'd like to throw out “consumer focused” so that as we're evaluating the different opportunities, we're always thinking about the application and whether there is relevance to people who are living with autism.

Dr. Lord: This is sort of from the totally opposite perspective. How about plan for replicability? So building in, because there have been so many findings in one place that then just peter out. So building into things a way for someone else to try them, you know, once they fail. That seems particularly important if we're going to really try to do novel things.

Ms. Resnik: That may go under

accountability.

Dr. Lord: Yes, you're right. That's probably as said.

Dr. Insel: Cathy, before you brought up innovation and novelty. Is that a guiding principle for the Plan, or is that something that's more of an add-on in maybe 5 percent?

Dr. Lord: Well, it may go with open-mindedness, actually. I don't know if that's what Peter, is that what you're -– or are you thinking more --

Mr. Bell: No.

Dr. Lord: No?

Mr. Bell: Not really.

Dr. Lord: Okay.

Dr. Geschwind: I mean, it's interesting because there's, you know –- in my mind this may reflect a lack of open-mindedness. There is a tension between the ultimate open-mindedness and what part of what I think about accountability, not kind of consumer research accountability, but the idea that ideas and any concept is okay. Except for there has to be a

sense of accountability. In other words, there is an idea there we can all agree, we don't know anything about it. Have to test it.

Once it's tested, there is accountability, you know, and all of that. So it kind of -– there is a tension there. But I see it's a nice tension. It's an important --

Dr. Fischbach: Maybe what Cathy was trying to capture with reproducibility is just some notion of rigor or excellence or -– it's just different than urgency, relevance, open-mindedness. You just want to do the very best laboratory and clinical science. So that's a very high standard. I think that should be a criterion. And I actually don't see -– the return on investment is not quite at the same level as all those others. I'm not sure what that means, return on investment. I'd rather see something like excellence. What do people mean by return on investment?

Ms. Resnik: And excellence could fit in or could be the category instead of return on investment. But it was about prioritizing and

funding research that represents infrastructure, capacity-building initiatives, has direct impacts on individuals with ASD in their families and leads to effective treatment approaches and interventions. And the portfolio of investments will dovetail serially and in parallel together to meet the stated goal.

So it was the idea that, you know, whatever we put in, we're going to look to how we leverage. And that also -– the return on investment -- also means leveraging as we talked about earlier with resources that already exist. Which, you know, maybe falls under a broader heading of excellence. But those are ideas that I think should be in the mission or vision, what you're suggesting.

Dr. Insel: David?

Dr. Amaral: Tom, the one other one that I would suggest is a critical path or clear-cut goals. I know one of the things that's influenced me about, as the MIND Institute was started, is these people who are successful out in the private sector always had a direction of where

they wanted to get to, and they figured out how to get there, the critical path to that goal. And I don't see that, yet, in this list.

Mr. Resnik: It could be critical path. The other word we used was “alignment.” So it was short-, mid-, and long-term objectives will be aligned with the integrated funding priorities, review processes, and timelines, and resulting data would be shared in a timely manner. So I think we were trying to get at that under that heading of alignment.

Dr. Newschaffer: When I was thinking about return on investment, I was thinking -– I thought it meant something a little different. And I thought it got to what Dan was saying. In many ways I see that this tension between open-mindedness and accountability as sort of assessment of risk and reward, which is sort of a way of thinking about likely return on investment. So I don't know if that risk/reward concept is something that's worthwhile. I mean, it tends to be pretty useful because you think of low risk -- low rewards are easy, low risk,

high rewards are easy -- and the other two tend to be the ones that you have to think about. And, you know, urgency is something that can be used to be factored in as another domain along with risk/reward. But that's what I thought you were -– was part of thinking about return on investment. And I don't know if it's something that should be captured elsewhere, or if it will slide in under that.

Ms. Resnik: It could be. These are just concepts to work from.

Dr. Insel: Geri?

Dr. Dawson: Just more on the return on investment concept. The way I think about that is that there needs to be a mechanism for examining the impact of what you've invested in and deciding what's your metric, right, for whether it was successful. So it could be things like, you know, did it lead to opening lines of new research, or influence, you know, knowledge in the field in such a way that it opened up, you know, other ideas? Or it could be did it actually impact people's lives in some way to improve the

quality of life?

But without that circle where we then say, you know, are we going to keep putting money here, right, that's a good place to invest over time? Then I think that, you know, we don't have any way of really evaluating whether it was a good investment.

Dr. Geschwind: Is that accountability? Is that the same thing?

Dr. Dawson: I think it's very much a part of accountability, yes.

Dr. Fischbach: So you don't want this list to grow too long. It's providing principles; it's not trying to -– Steve, does the fact that you didn't write down excellence or rigor mean we're going to ignore it?

Dr. Foote: What I'm hearing is this: We've got eight keywords here. There are many ideas that could fit underneath these eight keywords, and Denise has already roughed out some of the text that would explain what she meant or what she and Alison meant by these keywords.

Dr. Fischbach: But where do excellence and

rigor and reproducibility fit?

Dr. Foote: So I think the question's better addressed to Denise, whether that's included in the text that she --

Dr. Geschwind: I thought it fit under -– like I think this R01 and the excellence fit under accountability as a larger kind of catchphrase.

Dr. Fischbach: Accountability is fuzzy. Accountability is asking what were the results, are they, relevant to the greater mission, should we change -– that's not the same as excellent. You can do sloppy science and use bad data just for the sake of getting something done and writing another grant.

Dr. Geschwind: I see.

Dr. Fischbach: And that's not what I'm talking about. I'm talking about recruiting the very best scientists in the world to do really, really good clinical or basic research.

Dr. Insel: And Denise, the relevance is relevance to what?

Dr. Fischbach: Autism.

Ms. Resnik: I just -– that wasn't --

Dr. Foote: Relevance to the consumer.

Ms. Resnik: The way I put it was consumer focus.

Dr. Fischbach: Yes, consumer --

Dr. Insel: Anything else? These are things you'd want the IACC to take into stride.

Mr. Grossman: Under the return on investment, I think one of the aspects I didn't hear in the description that Denise read out is that we have to have sustainability -– define return on investment on there, that certainly we need to sustain that in some way. And that's one of the issues that's running amuck in the applied research sector, is that as you do all this great research and you find out that it works, who’s going to pay for it?

Dr. Trevathan: Let me make a statement, mainly because I'm one of the people on the IACC and the workgroup. I want to make sure my impression is accurate when we take this back to the larger, to the other group. I think this is terrific, by the way, this list. But one of the

things that Dan said that's not on the list, the low-hanging fruit issue, and we need to make sure we're all thinking the same thing.

One of the factors that involves urgency, the collaboration, which I think has to be across government agencies in the public and private sector, and the return on investment is we've got these already existing or starting infrastructures like ENAs, cadres, National Children's Study. So I'm assuming that one of the things that fits in all these areas, if we're going to move quickly, and we don't –- and be responsible and have high return on investment, we don't reproduce infrastructures that take a long time. And we look at how we can enhance these things that already are built up, maybe sometimes having different emphasis or whatever to try to accomplish the goals set out.

That fits under several of these headings. It's not specifically stated it will build on existing infrastructure rather than build new ones that may be inefficient. But is that assumed under all these?

Dr. Insel: Was that spirit of collaboration would be kind of leveraging what's between groups and --

Dr. Trevathan: Yes, that we have all of us that have been involved in building and working on these different infrastructures, which take a lot of time. We sit down at the table together and look at what we can do together.

Dr. Insel: That's very much in the spirit of the act.

Dr. Trevathan: Exactly.

Dr. Insel: You know, it's they wanted to build partnerships. I'm still wanting to go back to, I guess it was Lee's comment about -– maybe it's relevance. But I don't know if that's, relevance is what you really meant. What you were talking about, what we often call the “gap” -– so we talk about the problem with dissemination, that you have great science that goes into great journals, and no one ever uses it. There is no impact on practice. So is that --

Ms. Resnik: I think that's consumer focus.

Dr. Insel: Is that captured; is it?

Ms. Resnik: I would think consumer focus, and then I mean, because the consumer focus is the delivery and the sustained delivery. I think that that could fall under --

Dr. Insel: Is that what you were saying, or is there something more?

Mr. Grossman: It was more than that just because it's an issue that is one that we're tackling quite frequently in terms of the applied research. We can go and find that certain behaviors or certain interventions may work, but, again, who is going to pay for it? So that's where the sustainability comes in. And I think that you can say that for just about most educational and/or behavioral or psychosocial applied sciences.

And at the end of the day, that's really what –- you could say the same thing for work in a rehab, a voc-rehab housing situation, supportive employment. That entire sector there seems like there are people wanting to do good work in it, and they may come out with good studies and meet their respective rigor. But

there is no way to sustain that, to generalize it so that everybody that's affected can receive the same benefits of that research.

Dr. Insel: So what's the research, since it's a Research Plan, would it be around, let's say, economics or -– it's like science for policy, right? Science to influence --

Mr. Grossman: Right, it's more of a policy issue. We've been having this discussion with some other disability organizations. Some of them are disease specific. There is one cancer group that we've been talking to, and they -– we've been trying to design ways to build accountability into what they feel now is an applied research. For example, they're curing their people, but they still have significant social needs. And some of them are behavioral and mental health issues. And they are not getting people –- they are not getting the agencies to fund them, to fund what they need appropriately.

So this goes beyond the biomedical side, and it goes more into the applied side, which is, you know, CMS, the Department of Education, HRSA,

you know, SAMHSA, and those folks.

M. Blackwell: I think what Lee is alluding to is that a lot of these services or therapies or treatments or whatever we want to call them, are not services -– are not items that are -– they're discretionary. The States -– they are available at the States' discretion. So, you know, and none of these services are entitlements after a person exits the education system.

So I don't know if you guys recognize that, I mean, there are huge waiting lists across the United States for services that we don't even know if they work. So is that kind of what you're getting to, Lee, I mean that --

Mr. Grossman: I mean, it's easy to see return on investment when it comes to a biomedical intervention because if it's proving a benefit, it could be put into a therapeutic type of device such as a pharmaceutical or testing methodology that generally insurance companies would pay for. They see the benefit, and they're willing to cover it.

But in these more abstract ideas, such as the behavioral side, the educational side, psychosocial, which are really life spanned, there isn't that return on investment. A manufacturer, for example, won't be investing in that. And those needs are pervasive. And I'd like to --

Dr. Insel: So I hear you. I'm worried about mission creep here because I think the Plan -- there are a lot of issues around autism, which are not going to be addressed by the Strategic Plan research. What I'm wondering is because those are such important issues, is there a way we can use a Research Plan to give us data that actually could influence those issues? Because that gets to this issue of being consumer focused; it's what people care about.

So, as just an example, we're doing this in another arena where we're establishing what the indirect costs are of some of the disorders that my Institute works on to demonstrate that it's worth spending more on certain kinds of interventions up front to save huge amounts of

costs downstream. We can show that, and it's very compelling economically. That's a research project that we've had to fund to get those kinds of data because they didn't exist anywhere. Is that what you're -– I'm not sure I understand you.

Mr. Grossman: Right, and this is a difficult issue to tackle because it really hasn't been addressed yet. And it's more a public policy issue than it is anything --

Dr. Insel: But what I'm talking about --

Mr. Grossman: -- but the research can support that.

Dr. Insel: Right.

Mr. Grossman: To change public policy.

Dr. Insel: So it goes back to Geri's -– you could do a highly rigorous with absolutely defensible economic analysis of what autism costs the United States in the way that we currently help kids, adults, and families. I don't think that's been done. Actually, it's in one of the 41; some of you recommended that -– a cost-outcome study.

But I guess I thought that that was kind of number two up there, or I thought it was already in there someplace. It's not a return on investment; it's actually the lack of return on the investment. But you'd want to make the argument. You'd use the science, then, to demonstrate the failure of current policies and then hope to drive policy change through that. So, but I'm trying to make sure I understand that that's what you're saying. Maybe you're saying something else.

Dr. Geschwind: Yes, I was just going to say, I mean, you can summarize that under outcomes, you know, if you want to make it a research question, outcomes research. And that directly impacts health policy. I mean, you do outcomes research so that you can push policy one way or another. I mean, you hope –- you do the research. You don't know what the answer is. But the hope is that the answer then pushes policy. So it's outcomes in a broad way.

Dr. Insel: Yes, but it could be -– so there's a whole area of health economics that is a highly

rigorous, very important, which as far as I know hasn't been applied here. It could be one of the categories. Lyn, you've had your --

Ms. Redwood: Yes, and this is a little bit off base here, but I'm focusing on, sort of, the sense of urgency, Tom, and how we're going to address that. And I'm almost thinking we need another mechanism outside of the workshops we've had that's more along the lines of a Manhattan Project where we, you know, acknowledge that the problem that we have in front of us, and we bring together the top scientists in all these other fields that oftentimes don't communicate with each other, whether it's genetics, environmental medicine, toxicology, gastroenterology, and define what we know about autism and what we need to know and what we don't know and what we need to know and use that to define sort of our low-hanging fruit, and I'm just throwing that out there because I don't know that we really captured that in the workshops.

I don't know that we really know exactly if we've brought together one document that's been

updated based on the science we have today defining what we know about autism.

Dr. Insel: That's -- I was interested in this because that's where Denise started in terms of this resource assessment piece. As I -- if I understood you right, that was trying to capture the landscape of what's currently known, what's being done, where the gaps are, and maybe --

Ms. Resnik: And also setting up some protocols for data collection so that we inform more about how to collect so that we can go to the next phase, which is the capacity building.

Dr. Insel: Yes, and that clearly wasn't in the workshops anywhere. I mean, people -- no one came to the workshop saying we need to develop a way of actually monitoring who's doing what and what's not being done and how much people are spending in all these different areas and how they are working together.

Ms. Redwood: I see that as a little bit different, though. I see that as more like a research inventory. Actually, Mark Loxhill has

pulled that together just recently through all the CRISP database and pulled out all the autism research, so he has some nice documents that outline with keywords, whether it's genetics or treatment base, where you can see where the money in your portfolio is being spent on autism. But I guess I see that as being a huge need, too, because we need to know where the money is, what stuff have we got ongoing right now that we can expect some return on next year or the year after next.

But I also think we need to define the state of what we know now. Because that's going to drive –- that's going to drive our research time, like, if we all agree that it's an epidemic, and I know right now that there are people that don't. So depending on whether you accept it's an epidemic or not defines where you go with research. Because if it's an epidemic that's just happened the last decade, then we need to take some of the focus off the genetics and look at environment, and that's an area that I think as you know has not been, you know, has received

a minority of funding.

And so when we define what we know, it's going to help us to drive where we go. If there is an environmental trigger, then it's preventable, and it's possibly treatable. So then our focus gets down to that level.

Dr. Insel: So what you're talking about is I don't think will happen today, here. But it sounds to me like that is this issue of coming up with a common ground that the IACC can identify.

Ms. Redwood: Right. What are our critical needs about autism?

Dr. Insel: I think we need to have a space in which to do that, which we currently don't have. And it should involve, I think, a lot of sectors of the community. And one of the things that I would love to get your thoughts about at the next meeting we have is how best to do that, whether it's through townhall meetings or through broader discussions, either on the Web or in vivo or how we want to proceed with that. Because I agree, I think that there is something

about this, and that's kind of why I went back to saying we actually need to sort of get the mission vision and kind of assumptions clear first. We have to come to some agreement about what's the problem before we get into the tactics of what are the specific experiments. And I think we'll need to do that as an IACC before we can be ready to put out a Strategic Plan.

I think for today, though, it's a little easier. We're going to sidestep that because this group is just here to tell us what to do with these 41 initiatives, knowing that we're going to end up with –- we'll use those, some of those, probably. But we'll probably end up with something quite different. And this was one attempt to get the community that of 70 or so people that came together over 4 days to get their best ideas.

But as you say, we'll probably need to take a different swipe at this and think about a different way to get additional ideas in. What I was hoping for, from today, was at least to have a framework and to have something for people to

begin to look at so that as we go forward and we bring in additional perspectives, people can say add this or take off that or modify this.

So I'm not sure it makes sense, though, for us to take a lot of time today to say what are our common assumptions because this group is not going to be --

Ms. Redwood: I agree. It would be a separate meeting, but I think it's critical that we lay that foundation --

Dr. Chung: I'm hoping we can take a break soon because lunch is here. And we really have 3 hours, less than 3 hours left, so just to remind you about the time. I just want to know -– you can break whenever you feel like. I just wanted to let you know.

Dr. Geschwind: I think that actually can be addressed in the first, you know, in the why did this happen. Those are the research questions, the why. So, and it cuts across other areas that you talked about. We're the ones talking about environmental genetics. And so when people talk about genetics it may be nonheritable genetics,

things caused by the environment that affect the genome.

So I mean it's a broad -– but so the why. So I think if we use that, it actually encompasses all of this. It doesn't get to the Manhattan Project issue, which is -– but it would allow one to, you know, in a way, capture that diversity because it's the why we don't have an answer to.

Dr. Insel: So I hear there is some enthusiasm for this structure. And it has the immediate appeal that it follows some of those guiding principles like being consumer focused and looking at engagement and alignment. Could we grab lunch, come back to the table, and think about how to put some of these initiatives clustered under those?

Dr. Geschwind: Yes.

Dr. Insel: Okay, all right.

(Whereupon, the Committee broke for lunch at 12:12 p.m. and resumed at 12:29 p.m.)

Dr. Insel: I can guarantee you that if at the end of the day we send, you send 41

initiatives to the IACC, and they're not clustered and not organized in any way better than what we've already done, they will be very disappointed. They found the 41 that we sent as just a kind of test run; to them it was pretty difficult for them to manage.

So we need your help in getting these things clustered and organized in some way. Alison has given us this very interesting structure, and what I'm going to recommend is that we start with that and begin to think about the initiatives that are in front of us, the 41 that we've got, and which are going to collapse down because many of them are redundant. But end up with a smaller group that would be in one of these five categories. Maybe there will end up being a sixth one.

But let's start with the first one. Why did this happen? Alison, that's really about looking at etiology, or in the terms here, the etiology, risk factors, issues around some of the things that Dan's group dealt with most of all. Can we get some of the initiatives that you think, maybe

by number, that should go into there? Maybe it would be easiest just to take the --

Dr. Geschwind: Sure. You know, it's pretty --

Dr. Insel: The ones that are blue, Dan.

Dr. Geschwind: Yes. So I'm just going down. I think that collaborative development of streamlined screening diagnostic approaches for any light-skilled environmental epidemiologic and genetic population-based studies would -– is kind of part of the why. It would also feed the others as well, such as prevention with large-scale studies will lead to that kind of knowledge. But you know, we could start by, again, just version 1.0. You know, sticking it there.

Another -– oh, here. Risk factor studies focusing on preconception, prenatal and perinatal, and early postnatal prediagnostic exposures. This was one of the most -- ones that the entire group, no matter what their background was, you know, from a scientific standpoint, felt that there was the least amount

of information. In other words, if you do an assessment of what's known, it's almost zero. And it is kind of critical for a disorder that you think occurs during this time. We have no risk factor exposure information, pregnancy history and all of that.

So that would go under why as well. Twenty-one will go there, too.

Dr. Insel: Which 21?

Dr. Geschwind: Analysis of mechanisms underlining interplay of environmental and genetic factors.

Dr. Insel: Just go down the line, 38 then you just went --

Dr. Geschwind: Yes, irrelevant, immune and infectious factors. But again, we -– some of these might be able to go into areas. So we might want to, you know, balance as we're putting down stuff, for example.

Dr. Insel: There really isn't another area. You know, mainly how to prevent.

Dr. Geschwind: Yes.

Dr. Chung: Is that okay doing it this way?

Okay.

Dr. Geschwind : And I think here, gene-based phenotyping in cognitive neuroscience. I mean anything that basically says risk factor or risk. Yes, I'm just kind of trying to consider that -– I'm not sure one wants to put everything in this box. You know, and I'm not sure. For example, this is one of the, you know, there are a lot of, as Tom mentioned, there are a lot of, you know, stakeholders that come to these meetings. So the large-scale resource of genomic data, you know, is very, very specific.

If you look at that, and if you look at how all the 70 people across all the groups scored these or not all 70, but how the major people ended up scoring these, I'm not sure what we want to do with these scores, but this doesn't come up as high priority of the ones that I just mentioned. But you know, I guess, is the point now just to stick everything in and then we can collapse later?

Dr. Insel: Yes. It will definitely be collapsed.

Mr. Bell: If we're going to follow this paradigm, I actually believe that there are two other questions that come before all of this. And that is, do you have a child and know something is wrong? So you're like, "What is this?" You know, "There is something that seems abnormal here. I need to go see someone and figure it out."

So --

Dr. Geschwind: This is the diagnostic phenotype?

De. Insel: Right, that's a good --

Mr. Bell: =And then actually, once someone says your child has autism, you go through that, well, "What is autism?" And why do you say that, meaning you go through this sense of, you know, well, what does that mean, or what is autism? And then once you figure out well, autism is these sets of behaviors, and what have you, and then I think, you know, the question is well, "How do we go beyond just the diagnostic, and figure out what is the underlying pathophysiology of autism, which is much more of a scientific question. And I think, I don't think many parents

probably think of it that way. But it's probably how we should all be thinking in terms of there is a set of behaviors that’s causing those sets of behaviors. And then I think you go to the point of, well, "Why did this happen?" You know, what caused all of this? So I actually think that there are two other questions that come before this, that will fall into some of the discussions and initiatives that we've had, which is, what is autism? What is this, and because I think that's more of a diagnostic question. And then, you know, what is the underlying biology of autism? It's not the logical question that a parent would say, but it's really what we should be saying, which is, what's going on underneath here in terms of some sort of a biological or pathophysiological issue that's causing these symptoms. It's not very typical of them.

Dr. Geschwind: Well, that makes sense. The second one was when you start using the word “pathophysiology,” it falls under the kind of why questions. I mean the first one is really important, is actually, is not really

encompassed. But by making it something beyond pathophysiology in your number two, or you know, maybe it's relevant. What is this from a parent perspective, you know, "What's the problem with my child?"

Dr. Dawson: Is something wrong?

Dr. Geschwind: Yes, is something wrong, you know, and what is it?

Dr. Insel: Geri?

Dr. Dawson: I think it does go beyond, you know, maybe the genetic environmental factors in terms of, I mean, I don't want to speak for Peter, but I think what you might be saying, tell me if this is right, it has more to do with, "Well, my child is behaving this way. Is it because of, you know, there is GI distress and pain, or is it because there is something wrong with the cerebellum, where overexcitation in the brain, and therefore the child is having problem with sensory input?" Or in other words, trying to actually understand at the level of the biology of what -- why is the behavior acting that -- you know, why is the child acting that way.

And you know, if you look at something like, I remember when I was on a consensus panel for PKU, you know, they had figured out, right, the cause. But they had almost no understanding of the pathophysiology, I mean, at that point.

Dr. Insel: And they have a greater intervention.

Dr. Dawson: Yes, they have a great intervention, right?

Dr. Insel: Yes.

Dr. Dawson: So I'm just saying they really aren't exaggerated.

Dr. Insel: I will point out that the same thing is true with polio; we still haven't answered the major pathophysiological questions about polio. Why do some people get paralyzed and some don't. We don't know why. It's not important anymore.

So I'm wondering if those two, though, could even collapse into something --

Dr. Geschwind: Like is something wrong, and what is it?

Dr. Insel: But it seems to me the question

of what is autism is sort of the -– deals with both of those, or is that not right? Are you wanting to keep this very consumer focused?

Mr. Bell: It's two-dimensional. I think what is autism, at a diagnostic level, what does it look like, and one of the issues that the diagnostic group came up with. And then it goes, the second intervention is it goes deeper to that. How do you go beyond a diagnosis and understand what's underlying?

Dr. Insel: Okay, so that would be the –- so underlying --

Mr. Bell: Problem.

Dr. Insel: And that's different than risk factors, which would be, why did this happen?

Mr. Bell: Yes, and which actually goes more into the biology, which is what is the underlying biology. What's happening that's causing these things? And then I think a natural thing is, well, why did this happen? But I just want to be careful with it because I don't think the first thing you do is you come out of a diagnosis, although you never know. But this, well, why does

this happen? You kind of want to know what am I dealing with, what's wrong? And therefore, how do we fix it? And which then goes into the other ones.

Dr. Insel: And that's one place where the community is still completely split. And the people that I hear from, it's everything from this is a disease of synapses, to this is a disease of the large intestine. But some people who say this is not a disease and don't even begin to think of it that way. So I think there is a real discussion to have around even that first question. And there is a research basis for this as well, where the finding of pathophysiology, finding a lesion of any sort, finding an association of any sort would be extremely helpful.

Mr. Bell: Joyce, I think it is what's going wrong, not is something wrong, but what's going wrong.

Dr. Geschwind: So Peter, in that, do you, would you encompass comorbidities, you know, comorbid, like, in the what, kind of?

Mr. Bell: Yes, absolutely.

Dr. Insel: That could also be what's in store, which is the other one that Alison discussed.

De. Dawson: Although they can show up very early.

Dr. Insel: They can be the presenting problem.

Dr. Dawson: Yes, exactly.

Dr. Insel: So if we start with the first one of what is this, any help in getting us to identify some of those?

Dr. Dawson: If you want numbers, that's Cathy's.

Dr. Lord: Eighteen, which is the -– 18, which is categorical and dimensional measures of ASD-associated features, et cetera. I think 32 is also trying to make sure that and the screening is appropriate across diverse populations. Yes, 19 --

Dr. Geschwind: Yes, even 33 could go there. You know, the one that was stuck below?

Dr. Lord: Yes, yes.

Mr. Bell: Wouldn't 33 be more of the second dimension of the act, which is what is the underlying issue that's going to --

Dr. Lord: We need 33 to answer, yes, the second dimension.

Mr. Bell: Because it goes deeper than just the diagnostic. It goes to what is the underlying issue.

Dr. Geschwind: No, but they could be forgotten.

Dr. Lord: They could be the same.

Dr. Geschwind: See, I think 19 and 33 could be, if you think of putting things together, the screening instrument issue is the broad issue, and the subtext there is that a screening instrument has to be, has to work in community settings as well as research settings, and work across different kinds of populations, you know, from SES to ethnicities.

Dr. Lord: I think what 19 is trying to get at, which is just to follow up on what Dan said is I think 33 was focused on, for research purposes, how do we identify populations that we

can study. And 33 -– wait, that was 33 -– 19 is saying well now, if we unleash three instruments, I mean, just as recent recommendations from the Pediatrics Academy as in what happens to, you know, what happens to referrals in the population. What happens, how do people use that, how accurate is it? Is it beneficial; I mean, those kinds of questions. Not just is it actually finding a population you can study. So but they are both talking about screening.

Dr. Geschwind: But I think we could combine them into one that would then take both of those flavors.

Dr. Insel: Along with 32.

Dr. Lord: Yes.

Dr. Geschwind: Yes. So actually take, you know, kind of screening, you know, development of efficient kind of consumer friendly, in a way, screening instruments. Or you know, efficient efficacious screening instruments, and then four different purposes, or kind of with different questions under them.

Dr. Lord: That definitely makes sense.

Dr. Geschwind: So look at their predictive validity in different community settings to support, you know, the large-scale studies. And for the minority and disadvantaged who are hardly represented. Different, you know, SES.

Dr. Lord: Would you put, Craig, would you put tracking of prevalence here, or would you put tracking of prevalence somewhere else?

Dr. Newschaffer: I think I'd put it here.

Dr. Lord: Okay. Let's see, 25 would be -- oh, that's probably more what's in store.

Dr. Insel: Yes.

Dr. Lord: And --

Dr. Dawson: No, she said not to put it --

Dr. Lord: I'm sorry. I think 4 is evaluating diagnostic criterion approaches, which really does overlap with 18. And then I think 27 would go in here, which is just how does the diagnostic process work in the community.

Dr. Geschwind: And a lot of that could actually be collapsed into two things or so, yes.

Dr. Dawson: So Peter, what do you think

that's missing there? Thinking about your, going back to your experience, or any of the parents? You know, how does that feel?

Mr. Bell: Thirty-three still to me feels like it belongs in the next category, because I think it's going beyond just the diagnostic. It's actually helping you understand what the contributing factor might be. If I'm reading it correctly, which is large-scale genetic.

Dr. Geschwind: Well, it's just the development of easier screeners.

Mr. Bell: So it's more the screening and diagnostic --

Dr. Geschwind: It's all about screening. It's actually we took the liberty of -– and it's actually a bridge between our group and the diagnosis group, even though we didn't have a lot of diagnostic experts in our group with the idea of this need to engage the diagnosis community to develop screeners. And the screeners will have different purposes. But one of them is to a large-scale, population-based epidemiologic or a genetic -- it doesn't matter -- studies. But

those screeners will also be useful, hopefully, in community settings.

Mr. Bell: Right, I just would take the word “genetic” out of there, because it's getting --

Dr. Geschwind: Oh, no. We need to collapse it in –- I think going through, my thought would be that you could take all six of these and kind of make it into one or two things.

Mr. Bell: It's two items.

Dr. Geschwind: Yes, and they're general.

Dr. Trevathan: I believe when we were having the discussion, too, although this was in the risk factors, I remember, there was a discussion not only of the importance of this being in the diagnosis but also in terms of interventions. I mean, if we want to have intervention in earlier ages, we have to be able to have streamlined diagnostic approaches in communities, and big populations.

So I remember when we were taking the liberty of thinking actually across a lot of areas of that one.

Dr. Insel: Thanks. Do biomarkers go here?

So let's go on to what's going wrong.

Dr. Geschwind: I mean, the biomarkers could -- I mean, you know, some things go across a few of these. Biomarkers would be one, because the biomarkers would hopefully help tell you what is this.

Dr. Newschaffer: Yes, like PKU.

Dr. Geschwind: The idea of biomarkers is not to identify pathophysiologic pathways, necessarily, but to actually diagnose or kind of categorize patients based on biomarkers. So it's just like a diagnostic screening tool that would, you know, with clinical screening tool, this flavor of biomarker has to do with as a screening kind of approach.

Dr. Newschaffer: Because it's just one flavor of biomarkers.

Dr. Geschwind: Yes, yes, exactly. Yes.

Ms. Redwood: I see biomarkers fitting under treatment, too.

Dr. Chung: So do we want to go on to the next question?

Ms. McKee: Can I make a comment about under

diagnosis? We talked about it a little bit during the break; my specific experience with diagnosis is that my pediatrician didn't want to put autism down because it acts as a barrier for insurance coverage and other services. So they actually are trying to hide the diagnosis so you can get services. And until we include that somewhere, we're kind of fighting against ourselves.

Mr. Bell: It's funny because in California, it's the opposite.

Dr. Geschwind: It varies, yes.

Ms. McKee: They no longer diagnose?

Dr. Geschwind: Because the services are -- so again, it's a crazy thing about in one State you need to get the diagnosis to get anything, but in another State. You got it, you can't, yes.

Dr. Trevathan: And I might add, just while we're on this topic, this is what we were discussing. And in fact, there are cities in which we do surveillance where we can see that in some areas, there seem to be incentives to make the diagnosis in others, incentives not to put the diagnosis down, and so being able to see

beyond that as to what's really going on, it's quite a challenge. But you're spot on.

Dr. Insel: Okay, let's move on to the next piece. This is more of the biology. Is that right? What's going wrong, or what has gone wrong.

Dr. Amaral: Yes, I think most of the biology initiatives would go here. So I would probably rank it starting with number 16, the multidisciplinary longitudinal study of infants with autism before age 3. So that's going to be at the time when you've first seen the disorder.

Probably, you know, there is gender difference and biological features of autism as well, early on. I guess now I probably would move the immune infectious factors from wherever we put it into this topic; we didn't have this topic before. But because if it's a dysfunction of the immune system that's leading to it, that may be manifested at early stages. Beyond that, you know, I think probably the post mortem, although it's a little bit tangential, but it would ultimately would give us some insight into

what's going wrong.

Dr. Geschwind: What about the neuroplasticity, does that belong in here?

Dr. Amaral: The neuroplasticity, I think more of in terms of treatment. You know, I mean it certainly could be an etiology as well.

Dr. Dawson: But not necessarily because I think that even with, you know, the same treatments, you get this huge variation in response. So it really does speak to the underlying biology, I think, of you know, and this heterogeneity.

Dr. Insel: Right.

Dr. Dawson: So you know, again, it's hard to get your head around how to write it as initiative, but and then also it's just the mechanisms of neuroplasticity, right. I think that's another issue that's very important to understand, both in terms of kids coming in with risk, right, genetic risks, and then how environment might mitigate the outcome as well as actual biological interventions.

Dr. Insel: So maybe if we put it in, we can

cite it again later. Maybe put it in terms of treatment. The comment I was hearing this morning was trying to capture the heterogeneity. It does seem like a question of what's going wrong is partly embedded there, understanding that this is many different things, and how do you get to the different subtypes.

Dr. Dawson: Yes, that gets into your idea of the comprehensive genetic work up for --

Dr. Geschwind: So I'm having a conceptual brain blockage. Maybe it's due to sugar. I'm trying to figure out why it would put something in the "what is going wrong" and what would make me put it in the "why." Right, like what -– you know, because I was thinking of the why did this happen, as the kind of fundamental.

Dr. Fischbach: Maybe you could think of it as what has gone wrong with the -– there is a loss of synaptic inhibition. And why, it's because neurologic gene is not expressed. So if you could think about it at that different level.

Dr. Geschwind: That's very helpful, yes.

Dr. Insel: As if you talked about asthma,

you could say what's going wrong would have to do with changes in pulmonary responses. But the why is exposure and genetics.

Dr. Geschwind: Right. Okay, thank you.

Ms. Blackwell: If I could just interject about this question. Gail and I were just talking about it, and it's kind of negative. Maybe it should be what is the difference between, you know, why is my family member different? But this is kind of negative language. It makes it sound like autism is "oh." So maybe that should be reworded. Why is this person different?

Dr. Insel: Maybe wrong is atypical.

Ms. Blackwell: Yes, wrong.

Dr. Insel: I mean, if we don't change the language, we'll have to change the language. You can't, you're right; we can't use that word. But for now, I think we'll do a lot of wordsmithing later. I'm just trying -- it's a great point, and we should flag it. I'm not sure what's going on.

Ms. Blackwell: What's different?

Dr. Insel: That's interesting. It sounds like a song.

Dr. Fischbach: But be more specific what's, you, especially must think of in terms of what, you know, in terms of specific regions of the brain, or disconnections. Is this Strategic Plan a place that mentioned them, or is that too deep?

Dr. Amaral: So I guess a lot of those issues came up during the meeting. But we thought it really needs a sort of a global perspective at this point in time. So whether, you know, whether it's the amygdala or the cerebral cortex or whatever, I mean, I think that would be addressed if you're doing a multidisciplinary longitudinal study of infants.

You know, I happened to see the detail, but we weren't dealing with that level in the meetings.

Dr. Fischbach: Which is my feeling is this is an evolving Plan. It might be nice to have some historical record of what people thought in 2008. And whether any of that is held up in 2009. It's such a lack of hypothesis, but you have them in your head, I know. I mean, you're thinking about them.

Dr. Amaral: Yes, even been published occasionally.

Dr. Lord: It also occurred to me that you know what's not in here at all, which has been the bulk of psychological studies -- is sort of descriptions of, you know, sort of theoretical models of how is the child processing, or adult processing, in their environment. So theory of mind and joint attention, and what is it that makes a child look different? And then how do you help make sense of that from the persons or the child's perspective? And I know, you know, when there was a similar exercise to this in the U.K., and the biggest, sort of, conclusion was there were far too many studies of that kind of thing. There were way too many studies of let's show that this kid is different than this kid and this person is different from this person.

But we don't have probably one single initiative except maybe the gene-based phenotyping and cognitive neuroscience, if you attach on, you know, attach on to it, neuroscience, then it sounds better. But there

isn't anything in here about just, you know, theoretical models of what is the social -– what are the social and cognitive deficits of autism.

Dr. Insel: So let's come back to what's missing.

Dr. Lord: Okay, sorry.

Dr. Insel: So I want to make sure that we have a little bit of time for that at the end, because there are a bunch of things that I've heard about today that people wish had been in the list. But I want to see if we can capture and collapse some of these, so that we at least have something organized. Is there anything else to go into this?

Dr. Geschwind: Well, can we go back and look at why? Because we put in stuff in why before we had this first important one? And I'm wondering if some of this actually goes up there, just to take a quick look. Maybe the role, maybe the 38 would go up there.

Dr. Insel: No, I think it's already up there. Isn't it up there, Joyce?

Dr. Chung: It could go in both places, I

think.

Dr. Geschwind: And so the one that Cathy just mentioned, the gene-based phenotyping, cognitive neuroscience might actually go in there.

Dr. Chung: It's six?

Dr. Geschwind: Six, yes.

Dr. Chung: Okay.

Dr. Geschwind: Yes. And so I'd maybe take 38-B out of the second one, so we don't, no, out of the second one. No, this is the first one.

Dr. Amaral: So we keep going down to why.

Dr. Geschwind: Under why, yes. Then take out --

Dr. Chung: Take this out?

Dr. Geschwind: Yes, because it already is up there.

Ms. Resnik: So there could be overlaps?

Dr. Insel: Yes.

Ms. Resnik: I mean, we know that there are. So I think it's okay if you haven't represented in more than one area, and we look at, in essence, that phasing and the different dimensions that

initiative could represent.

Dr. Insel: Yes, I think that we'll end up with some things that we will certainly bridge. Plus to go back to Geri's point, I would imagine that the final document will have text in it that, in front of all these recommendations, that will play out what the challenges and what the current state of knowledge would be, where the major questions are, opportunities, those kinds of things.

Dr. Dawson: I just -– before we leave, no, no. What's going on, I'm just wondering if whether we've really addressed some of the more novel, you know, perspectives like oxidative stress, and where does that fit in the things that are up there? And I just want to make sure that they've gotten --

Dr. Amaral: Well, there were certain, this number one, multidisciplinary, number 16 was really a very broad-based kind of analysis, looking at immune and environmental factors, and other things as well.

Dr. Dawson: Okay.

Dr. Amaral: I mean, it's not specific, but it was encompassed.

Dr. Dawson: So if there were, you know, theoretically, an RFA in this area, it would list those kinds of things as potentially things to study in the context of a study like this.

Dr. Insel: But if it wasn't clear to you, it's not going to be clear to others. So we keep --

Dr. Dawson: I just wanted to throw it out there.

Dr. Insel: You know, I think it's a good way to do it, Joyce, just to make a note on the --

Dr. Geschwind: Thirty-five, improved identification and characterization of autism in adulthood could fit into a couple, but it would also fit into what an autistic adult looks like. That might go into one as well.

Dr. Insel: I think that's what is this?

Dr. Geschwind: Yes, I think that's what is it. I mean, because --

Dr. Insel: Or is that --

Dr. Geschwind: It's 35.

Dr. Insel: It might be what's in store.

Dr. Geschwind: Well, you know, unfortunately, it's actually both, but I think it's really important to put up here because it gets through each training issue. Let's just, you know, adult neurologists, for example, are seeing a lot of these people as a psychiatrist, having no idea what it actually is. So that's it. I would almost say what is this, what is adult --

Ms. Singer: I think that also speaks to the fact that many adults are being diagnosed for the first time as adults.

Dr. Geschwind: Yes, right. Do you want to do anything with diagnosis in that? Or no, that goes in characterizing and improving the diagnostic process in the community, and all that stuff. In the very first one, okay?

Dr. Dawson: And does the tissue thing go in there?

Dr. Geschwind: Yes.

Dr. Dawson: Is it there?

Dr. Geschwind: That isn't there yet. Sorry.

Dr. Dawson: Okay, sorry. Yes, there it is.

Dr. Geschwind: Okay, kind of confused.

Dr. Dawson: How about this, is there more than this one? He took some out.

Dr. Geschwind: Would methods development for biologic exposures and biomarkers go in there?

Dr. Dawson: Yes, definitely.

Dr. Geschwind: That's 30? I'm sorry, that's 20.

Dr. Dawson: Yes.

Dr. Geschwind: We have to figure out where to put number 10, which is the new paradigm. I know where that one --

Mr. Bell: It seems like the second one, what’s the underlying -– what's going on.

Dr. Geschwind: So maybe that would go in the what's that?

Mr. Bell: You get a diagnosis, then you do a G Profile to determine if they fall in that 20 percent, or whatever it might be.

Dr. Geschwind: Yes.

Dr. Amaral: What about the risk factor

studies and other special populations? Would that be under what is happening?

Dr. Geschwind: Yes, 34.

Dr. Dawson: 34, did you say?

Dr. Geschwind: Yes, it's right in the middle there.

Dr. Newschaffer: Some might send them from the perspective of time trends. We could argue that 7 could also go into it with that. So it's 7 from the perspective of time trends, but you could also argue for what -- from the perspective that Geri was raising earlier about characterizing frequency of different clinical symptoms in a population-based sample; that's what enhanced surveillance would do. So that's a little fence rider between the two.

Dr. Chung: Where would you put it?

Dr. Newschaffer: I think we can put it either place. So if you're right there, you can put it there.

Dr. Insel: We want to move on to what did I do.

Dr. Dawson: So we've got the efficacy trials

for comprehensive intervention. We've got the cost-outcome studies of intervention models. We've got the identification of biomarkers to guide treatment selection and evaluation. Sorry. Biomarkers, too -– is that what number again?

Dr. Insel: 12.

Dr. Chung: 12?

Dr. Dawson: Yes.

Dr. Chung: Okay.

Dr. Dawson: Although you might note that Geri Fischbach said this has never worked. I heard it. And then the next one is efficacy and safety of commonly used but untested treatments.

Dr. Insel: That is so close to number one.

Dr. Dawson: No.

Dr. Insel: No?

Dr. Dawson: Not at all. They are almost the opposite, but are we reading it wrong?

Dr. Geschwind: Are you thinking of the biomarker one or --

Dr. Insel: The efficacy trials for comprehensive intervention models and the

investigation of efficacy and safety.

Dr. Dawson: Okay, let me tell you about what those two things are.

Dr. Insel: I'm sorry. I didn't finish reading it. You're right.

Dr. Dawson: Okay, all right.

Dr. Insel: That's the urgent one.

Dr. Dawson: Okay. Well, they're both urgent. Okay, State of the States could go there.

Dr. Insel: Because I thought maybe State of the States would go in "how can I implement?"

Dr. Dawson: All right. Oh, okay. All right, sure. That makes sense. I think the development of the better outcomes measures, which is part of 18, kind of an overlap, interventions for older children and adults.

Dr. Insel: The animal models one.

Mr. Bell: Did you have 41?

Dr. Dawson: Oh, did I --

Mr. Bell: The intervention of prevention --

Dr. Dawson: Yes, I'm getting there. Mine has –- I'm looking at one page where that's the last one, the listed -– anyway, the next one is role

of comorbidity and the treatment of ASD. And that would be both, you know, psychiatric and medical, animal models and cellular systems for developing treatment. I've got a lot of work to do in the treatment area, as you can see. Let's see, we have identify and evaluate models of effective dissemination of evidence-based practice into community. Yes, that would actually go under how to implement. Sorry.

And then I guess this one is implement 2, fast-track mechanisms to facilitate translational treatment research. You know, I don't have the numbers.

Dr. Geschwind: Forty, that's 40.

Dr. Dawson: Oh, 40. Okay. I do have the numbers, great.

Dr. Geschwind: Halfway down.

Dr. Dawson: And then 41 is intervention and prevention approaches for infants and toddlers at risk.

Dr. Insel: Can I get a 30 in there, novel treatments?

Dr. Dawson: Oh, sorry -– novel treatments

for course symptoms. Yes, thank you. Any others I missed?

Dr. Lord: Do you want to -– Geri, 25 it overlaps a lot with 18, but it's another one that's about outcome, phenotypes for outcome. Where is that?

Dr. Insel: I think that was a what, I think that should have gone under, what, 25?

Dr. Dawson: Yes, so maybe that should go under the -– 25, should go under the first one?

Dr. Insel: Exactly, that should go in the first one.

Dr. Dawson: Okay.

Dr. Insel: I believe this --

Dr. Lord: I think 37, which is develop resources to coordinate large population-based research, I think that was the people that suggested, that were interested in outcome. So I don't know if that would go with how or -– it's not really treatment. It's number 37. I just don't want it to get lost.

Dr. Chung: Where does it go?

Dr. Lord: I don't know. Craig?

Dr. Newschaffer: Eleven is the one that actually I thought you would– 11 is the one, did we capture that one already? Emerging of administrative databases. It connects a little bit to some of the points that Lee was making on the outcomes research.

Dr. Lord: So maybe it's 37 and 11, and it's --

Dr. Insel: I think we're probably going to have to have a separate category, because it's not going to fit into any of these.

Dr. Lord: No.

Dr. Insel: That's really not for the consumer; it's for the scientist.

Dr. Dawson: Okay, so a separate place for those.

Dr. Trevathan: Okay, and what about 35, improved identification and characterization of adults?

Dr. Insel: There are a couple of those that --

Dr. Geschwind: That was put into number -– that was put into --

Dr. Dawson: Number 1, what is this?

Dr. Insel: Yes, there it is. Okay, how can I implement?

Dr. Dawson: So that's State of States, which is 15. And it's also identify and evaluate models of effective dissemination of evidence-based practices, 29, sorry. And then also 36, I think, fits into that, evaluation of community-based interventions. And by the way, the idea behind that, I didn't really talk about that, but it is that there really are a lot of interventions that are out there -– social skills programs and vocational programs and so forth that have had no research in terms of their efficacy at all. 36, yes.

Dr. Insel: Can I ask you about some of these, because in some ways, this field is so far behind that it's, you know, you should be able to learn some things from other fields. And where most of medicine is now, it's kind of getting past the sort of traditional efficacy trials and thinking much more about personalized medicine approaches, identifying, you know, those

outliers who respond to a treatment where there’s no mean difference between groups, that kind of thing.

Was that part of the discussion at all, thinking about can we capture this individual difference and predictors of response? Since we know this is already such a heterogeneous group, you certainly don't want to do just the classic efficacy kind of trials.

Dr. Geschwind: I think the one that had 18; actually in blue on the first page, number 5, it says the whole thing -– severity outcome and treatment and pharmacological response. But it really, I mean, that's what it is.

Dr. Dawson: Yes, the other place is that if you read the actual initiative for number 1, where you're looking at, I think it actually should be effectiveness trials, but maybe it's still efficacy trials. But anyway, there was an emphasis on looking at moderators and --

Dr. Insel: Yes, and I saw that. So I think again, I think we're going to capture that in the text someplace. That was in the spirit of the

discussion at the meeting. Okay, anything else for implementation? We're ready to go onto what's in store.

Dr. Lord: 39, actually 39 just probably should read children and adults. And then we've already put 35 up in "What is this?" but it's relevant for families of children to know what happens in adulthood.

Dr. Insel: Does the comorbidity piece come in here as well?

Dr. Dawson: It does. Actually, it really should, especially psychiatric.

Dr. Geschwind: And on some level, diagnostic, anything related to etiology; we don't know yet, but the thought is that different etiologies may have different trajectories. So I'm wondering if there is a way to -– you know, so one hope, the hope of a clinician is doing a genetic test, is that the genetics will help you. We don't know this though, would help you actually tell somebody about what's the appropriate treatment, what's the prognosis. But I'm not sure.

Dr. Lord: So maybe make a note. Should we make a note, because I think that's -– that's part of an unstated of 39, of using anything that might predict those trajectories?

Dr. Geschwind: Yes, using any phenotype, environmental or genetic, kind of. Yes, for 39, like the developmental trajectory. So how do you get to understand it -– so I guess the delineation of the factors that predict.

Dr. Insel: You guys gave that a pretty low rating. Was that because you thought that it had already been covered someplace else, or just --

Dr. Newschaffer: Which had more language like that. Right, David, the one that was put up much earlier?

Dr. Insel: I'm sorry. Excuse me.

Dr. Newschaffer: The one that was put up much earlier.

Dr. Dawson: But that's before 3.

Dr. Insel: Yes, that was before 3. It was limited to that period of --

Dr. Newschaffer: Before 3, okay. Right.

Dr. Geschwind: So this one is -– Tom, where

did this one end up?

Dr. Lord: 2.89.

Dr. Geschwind: One of the interesting things is when you look at some of these numbers, there are so many things that need to be done. You know, now looking at this, nobody would say that's a, you know, a 2.9. That's kind of a pretty critical question. So you know, but then you --

Dr. Insel: It's the state of our ignorance.

Dr. Geschwind: Yes.

Dr. Dawson: And I think, you know, I guess personally I feel like we've been studying development for a while, not well, and there is still so much more to know. But I think what we're going to find out is there is this tremendous variation. And you know, if I –- if we had to take the resources, it seems like we need to focus on, you know, what's going on, how do we prevent it, what are the treatments?

And so it's not that it's not important, it's just that I don't think it's going to lead us to the answer to do a lot more descriptive longitudinal studies personally.

Dr. Insel: It will be -– that's a very helpful comment, I think especially for those things that are, that the group gave us fairly low mean scores for. If you have reservations about any of these things, you think you really don't want the IACC to run down this path, and that's not quite so negative. But I think it's a good warning sign to us that we ought to be thinking about this as not just much more descriptive, or thinking much more about, kind of, interventions, the preemptive approaches, and doing something to interrupt the very early trajectory. That's helpful to know.

Dr. Dawson: And I think if the descriptive work is really linked into questions around mechanism, biomarkers, early diagnosis/prevention, then I think, yes, it would take us to the next step.

Dr. Lord: I guess I would disagree because I just think that we don't really know. I mean, we have a lot of personal accounts of like how many kids really do grow out of autism. But we don't know so we can't really look at it terribly

well if we don't know who. And there are a lot of things that are sort of urban legends about what happens as people get older.

And I think that you may want to link some of those trajectories, I mean, just as Dan was saying, to other to bio -- not just biomarkers, but biological phenomenon. So I think part of it is, you know, we all have a huge emphasis on the biology, and that doesn't have any biology in it. So I think it just got ducked.

Dr. Geschwind: But it could be easily connected. Because, you know, it's likely that there was very early, the zero to 3, kind of study that got a very high priority. I mean, this is totally hooked into that. There may be things at age 1 that are related to what happens at age 10.

Dr. Insel: But I'll bring you back to some of these that are at the very low end. So if there are ways you want to see them reshaped and made more relevant, more in line with what the principles were, those guiding principles, that would be helpful to us.

So you probably have about 15 to 20 that are

on the low side of 2.5. So those might be worth, some of them, coming back to. We're ready to go onto what else is -- what's in store. Is there anything else there, Joyce, that you think you need? Okay, that's the prevention piece.

Ms. Resnik: I wonder if this is where we can add in some of our, when you look at number 11, or number 37 in terms of resources to coordinate large population-based -- that when we think about prevention in the future, what is it that's going to empower that research? And maybe that's where, because I know you were looking for another category to put some of these resource infrastructure kinds of pieces. Maybe that's where we can place it.

Dr. Insel: Well, that's a great idea. This could be capacity building, including workforce -– I don't think there is anything in here that addresses the workforce, is there? Interesting. That's amazing. But I guess it's none of the groups.

Dr. Dawson: Well, no, the dissemination into the community is definitely addressing the

workforce.

Dr. Insel: Okay, okay.

Dr. Dawson: Yes, that's what it's all about.

Dr. Geschwind: It is a really -- I mean, just to diverge on that for one minute, I think somebody mentioned before, earlier in the day, you know, all of these policy issues. Let's just say that somebody said I'm going to give you, you know, $10 billion dollars to treat autism with tomorrow; we don't have the people to actually get the treatments that would actually be at a level that would be effective in many places in the country.

Dr. Insel: Do we have the treatments?

Dr. Geschwind: Well, in some -- you know, for some, I think, I mean, we really have to ask Geri. But you know, I mean, moreso. I'm not a treatment expert, but I think in some cases there is stuff that we could certainly be doing that could be more widely disseminated than it is that would help. I mean, like this -- not to get too, Mike, you know, with, like, these programs that are like the early childhood.

Dr. Insel: Can you turn your microphone on? You guys want to be quoted on this?

Dr. Geschwind: I mean, you know like we know there are like these vastly different trajectories of kids, and some kids get early intensive intervention and just do beautifully, and a lot don't. But that early intensive intervention done by really, really –- it has to be done by people, you know, to be really be effective, the most effective, by very, very skilled, trained people, and for that segment that will respond, I don't know if it's 20 or 25 percent, that's not a small amount. But it's not going to cure the issue. That's why we're doing research. But at the other level, there are these, you know, I'm aware of, you know, behavior-, cognitive-based intensive therapies that need to, you know, that could be disseminated and would help a group.

And you know, but there aren't even people even to do it out there. There aren't people who are trained to rep a level of --

Dr. Insel: There is a piece this week in

Science; I don't think it's out in print, but it's out online about treating autism online with virtual-reality kinds of interventions. Again, something that never came up, I think, at the treatment session. But thinking it completely, this goes back to the discussion, I think from Lyn, about innovation and you know, thinking about completely different ways of approaching this, and what we've been doing.

Ms. Blackwell: And I think it goes back to Lee's question about who is going to pay for it. Even if we figure out what the treatment is, who pays for it? Not just who does it, and whether or not there is workforce capacity, but are there funds to pay the people to deliver the treatment? So, and then that's a huge issue where I've worked.

Dr. Dawson: So you know, to me it seems like that there are several, you know, key pieces that research can address, that make progress toward this. You know, one is good clinical trials. Because I've stood in front of those insurance companies, and that's the first thing they say

is, we want to see the evidence, right.

And so that's, I think, very important. And not only looking at the outcome in the children, but the collateral impact on the family. So what I've been able to argue successfully up at Microsoft, it was based on arguments of the impact on the family, because that was going to be the employee, right. And so I think that we, you know, good studies about outcome and efficacy are really important. And then you have to make the argument to insurance companies, and they have to decide that they're going to go along with that.

And then you get the issues of dissemination. And there are several issues there. I mean, training of the workforce is one. You know, the feasibility of these. You know, so parents having to stay home and try to coordinate these is another aspect of it. So you know, there are a lot of pieces of it. And each one, I think, is a research question, except for maybe convincing the insurance companies.

Mr. Grossman: In the treatment models, we

did go over these issues. And I think it -– what it boiled down to, because we were limited, to only six, was that we threw it all into the category of cost-outcome studies, number 9. That would address all these issues, because we felt, you know, at some point you're going to have to have an economic basis for this, which again, brings up the whole sustainability and the pay-now-or-pay-later type of concept that we're all struggling with. And to Dan's question, we are spending more than $10 billion dollars a year, now to service this community between what CMS, Department of Education, and States, and others are doing now, and it's, I think, by anybody's means, it's not an efficient use of the money, and certainly not addressing the needs of the community.

Dr. Insel: And that's been addressed, because what that doesn't take into account is the largest economic loss, which is unemployment of people who stay home from work to take care of a child for sometimes 18, 20 years. So you start to put those numbers together, and you

realize there is –- this is actually conspicuous that this hasn't been done well in this area where it has been done quite well in so many other medical disorders.

So this would be great to capture. It goes back to Geri's comment. At some point, there has got to be the text that says, well, we actually have -– what we really know, what we've done, and what's the state of the art in 2008. And I think it needs to be said that this, in 2008, though, an awful lot is being spent for direct care. There is -– we don't know about what the indirect costs are. And we don't even know, I think carefully, what all the direct costs are yet.

Dr. Fischbach: I bet in terms of daily disability, whatever that stands for, would rival depression over the lifetime.

Dr. Insel: Well, not quite, because the prevalence isn't as high, but it's up there. It's going to be up, you know, it would be probably rivaling a lot of other chronic disorders, chronic disorders that start before age 3 and last a lifetime.

So, yes, it's going to be huge. The difference here is that you've pulled in whole family systems, so and that's been very hard to model for any of the other disorders.

Dr. Fischbach: Geri, can I -– I want to describe everything you said, which I agree with. But is that going to be part of a meeting, what's next to gender research and these social issues? Is that -– I think it's very important.

Dr. Dawson: Yes, that was included in our group, so for example, the cost-effectiveness, the cost-outcome studies and also looking at models of dissemination.

Dr. Fischbach: But in terms of workforce, it seems to be one interesting thing to study would be our nurse practitioner, as a fact, as physician.

Dr. Dawson: But that's exactly what the dissemination kinds of studies look at. They look at, you know, who needs to be the deliverer, what kind of training do they need to have, what kind of technical assistance you need to provide the people in order for them to maintain the

skill level, and how can you do that in the most efficient way. And in other disorders, they've developed models and they train. They compare this model versus that model and see, you know, what works. But we haven't done that kind of research. And partly it's because in terms of the things that we do believe are effective, like early intensive behavioral intervention, even that science is still fragile, shall we say. I mean, there are some good studies, but you know, we still have to put a little bit more data behind that. And you know, we have a study now that will be coming out in the next couple of years. And hopefully that will be good.

Dr. Insel: But there, too, this cost issue. I have never seen a good analysis of the --

Dr. Dawson: No.

Dr. Insel: -- cost of that kind of an intervention, which is expensive, and extensive. And doesn't work in some proportion of children.

Ms. Blackwell: I can tell you what we're paying for over in Medicaid -- about $80 to $100

an hour, 40 hours a week per child. So that math is pretty stunning. So when you think of a State having to assume that kind of a burden for a service that as you just said, Geri, doesn't have any long-term data behind it, it's pretty scary. That's a lot of money.

Dr. Insel: And we have -– so the Congressional Budget Office did a study and released it about a year and a half ago, maybe 2 years ago, on education costs. So what the Department of Education is bringing us -- stunning. They compared autism to many other disabilities, someone can probably remember it better than I can, but it's a pretty impressive number that hasn't really -– all of this needs to be put into some general context. What about so -– I'm sorry.

Ms. Singer: I was going to say I, unfortunately, have to go. But when we looked at the what can we do to prevent and preempt, you know, other than the infrastructure questions, I think that's an area where we may not have come up with enough ideas because right now, I think,

under that category, maybe Joyce, you can -– we only have two infrastructure-building ideas about prevention and preemption.

Dr. Insel: Number 41 is intervention and prevention approaches for infants and toddlers at risk for autism. And that seems like the core of what this could be.

Ms. Singer: I think another thing that would go into that category is really searching for environmental triggers and eliminating them so that we prevent that way.

Dr. Insel: Which number is that?

Dr. Geschwind: 23.

Ms. Singer: And then I think there is another one that speaks directly to gene-environment. I think we're looking for environmental triggers. I think that has to go under prevention and preemption.

Dr. Geschwind: And so 23 ends up being also early on because it's getting to the what or the why, as well as the prevention. But I think it's okay to have them in both places\;, in a way it kind of emphasizes how important they probably

are. At some level, when you understand the why --

Ms. Singer: Then you can fit in.

Dr. Geschwind: Hopefully you can, yes.

Dr. Trevathan: But one thing on the prevention side that you don't want to forget is that once you start doing things in the environment, what interventions in the environment and community, that's where this tracking or prevalence tracking really comes into play, because we haven't had the opportunity to do this yet, but you'd like to know whether the intervention you did actually had an impact in the real world.

So that's -– at the end of the day, that's the real goal we all have for prevalence.

Dr. Insel: We will call this the Singer model, henceforth.

Dr. Trevathan: So that's number 7. That's number 7 up there, as part of the prevention.

Dr. Insel: Anything else for prevention? Tracking is going to be key. Anything else you want to put in here? Lee?

Mr. Grossman: I'm just trying to correlate what's here on our list because there is a lot that could be added to prevention.

Dr. Insel: Yes, we're going to do that in 2 minutes if we're done with this list. So I don't hear any other nominations. I assume we'll have to look and make sure we got everything that we wanted onto these categories -- what the group will do, because I think there is still a lot of redundancy. I think these can be collapsed. I suspect at the end of the day it will be more like 20 initiatives across these five, six categories, rather than 41. Unless there are any other comments about this approach and how we will develop this, can we move to this final discussion about what's missing?

Based on discussions that were had at the group discussions, anything, science that has come up since then, issues that you know people are concerned about, or ideas from the IACC that you've heard today? Are there things that we should put up here that are not in this, amongst the 41?

Ms. Redwood: Tom, there was a recent article out on mitochondrial endophenotypes and autism that just came out, that I think is very interesting. And I don't hear much discussion regarding metabolism, oxidative stress, mitochondrial abnormalities. I think that's an area that also could be very fruitful for autism research for identifying potential targets for treatment.

Dr. Insel: Can I add that to the list? There is something called a -- I just saw this. Someone wants to do the mitochondrome; they do these whole full studies of mitochondria across a bunch of diseases. Autism wasn't listed as one of them, but interesting idea.

Ms. Redwood: That looks like the area of toxicology. I mean, there are just reports, after reports, after reports from parents that when they test their children for heavy metals; they have large amounts of lead, cadmium, mercury, all sorts of heavy metals. And then if you look at, you know, the work of Jill James with oxidative stress and lower glutathion levels,

our children may be more vulnerable. So I think that's an issue that really needs to be investigated, too, is what are some of the environmental toxicants?

There were some wonderful recommendations that came out of the IOM workshop on autism in the environment. And I just don't think those really got incorporated as much as they could have been into the 41 issues that we came up with.

Dr. Newschaffer: I do think, just to comment on that, I do think that the titles don't capture that, but some of the text does -- biomarkers, you know, talks about some of the biomarkers with nutrition; I know they talk about metabolic. I know the longitudinal risk factor study talks explicitly about collecting biomarkers. They have to be biomarkers of various exposures, be they metals or other neurotoxicants. So you may not have made it into titles, but I do know that there are a number of initiatives that in the body text definitely went to that from the risk factors group.

Dr. Trevathan: Okay, that's definitely in

number 21, on the genetic environmental factors.

Ms. Blackwell: We did one on novel treatments, too. Stuff that was untested that we sort of meant to pick up some in that category.

Dr. Geschwind: So my sense is that these are very specific, kind of, honing down to the level of granularity that is actually encompassed in probably about a half dozen of the kind of why and what questions -– but can be mentioned if they are kind of clear and cross-cutting research issues within the text, and you know, would definitely fall in just as people -– the titles and stuff are more general than the, you know, don't get the specific genes, or specific environmental things.

Dr. Insel: David?

Dr. Amaral: So under the brain initiative discussion, we also were talking about collecting samples of other tissues. And this hasn't really been vocalized yet, but I really do think it's important to have a comprehensive approach to drawing blood samples, blood samples from the children and blood samples from the

parents and to actually have the ability to quickly evaluate environmental factors, or you know, this work coming out both from Hopkins and from our group about maternal antibodies. We've been stymied to really make that, I think, a real solace finding because we haven't been able to survey a large enough group of mothers who've had children with autism.

So if there was a national database of blood samples of individuals who've had one or two children with autism and actually a group of samples of women who haven't had any children, we could do a study, you know, in a very short-turnaround time. So I think somewhere in this, there should be the sense of having some resources for looking at environmental factors and other kinds of nongenetic etiologies.

Dr. Geschwind: So that is actually number 28 that got a very low score. That is exactly what 28 was meant for, which is a kind of resource development thing. So I think that's why it got further down because it's not a kind of, you know, sexy, novel, you know, out of the box. It's

kind of this, you know, a resource that would allow one to test for things rapidly and have appropriate– the key is appropriate -- control and comparison groups. That's where things get really, really tricky.

Ms. Redwood: Hey, David?

Dr. Geschwind: Yes.

Ms. Redwood: We've talked about getting more brain tissue. I know that NICHD and the University of Maryland are collaborating for the brain tissue principle, also collect extracranial tissue. And I think that's important, too, to start looking at other organ systems, whether it's the terminal ilium, the adrenals, the thyroid. We need to be looking at those and collect tissue outside of the brain.

Dr. Insel: And the process and what I think the Strategic Plan can help with is laying out kind of best practices, sort of a consensus view of what should be collected, and how it should be collected. This is a problem we're having with some of these large-scale longitudinal studies where they're collecting so little from 100,000

people. So at the end of the day, you'll have a diagnosis, but you won't have a gamete to go back to.

So what would be really a great activity, we won't be able to do it today, but it would be to come up with the best way to do these kinds of things. What to collect, how to collect it, how to store it, and how to, you know, how much is fixed, how much is frozen -– all of these issues. And they have to be worked out so and, sort of, to provide a standard that everybody can follow.

Dr. Fischbach: Actually Geri and I had a brief conversation about this. And who should collect. I mean, can NIMH develop, or the whole NIH develop, a more common or shared autopsy or banking procedure wherever the event occurs, that there is a team there 24 hours a day? It doesn't have to be labeled autism. It could be somebody ordinarily collecting samples for Alzheimer's disease. But is that possible, to get different teams to at least take in the material?

Dr. Insel: I think so. We had that already for Alzheimer's. And of course, you know, we have done exactly what I described for DNA collection. So we have standards for that, and we have, as you know, these huge central repositories at our Institute alone, which is not a large institute, that have over 70,000 satellites and 70,000 DNA samples.

So those things are very feasible. And the great thing is that they all go into a publicly accessible database that allows broad sharing.

Dr. Fischbach: But it's the brains in particular that has held, you know, so precious and there often, the autism community doesn't have people right on site to receive the tissue. So --

Dr. Insel: Well, David is probably the person who has thought the most about how this might be done. It's a little bit like --

Dr. Amaral: I mean, I really do think it's going to take a national and international effort. I mean, you're going to have coordination. You're going to have to have

local, sort of, chapters all using the same protocol. And you know, I think, as I said before, the ATP has done a great job getting this started. But I don't think there are accepted standards at this point on. And the bottom line is we just -– you know, there are 70 cases. I mean, 70 brain cases, and they are not pristine brain cases. That's the bottom line.

So you know, we just wrote an article in *Trends in Neuroscience*; it is basically saying that until we can get more cases, how are we ever going to deal with the heterogeneity of this disorder? And there is not going to be a single pathology; there are going to be multiple pathologies, and we're not dealing with it. So you know, if there is the will, I'm sure that NIH and the partnering institutions could put together a process that would be enormously more effective. But, you know, you just got to get the thing on.

So there was a very striking moment at the workshop meeting on this. I think it was Eric Courchesne who went into a whole riff about what

it's been like for him to try to do a neuroanatomic study, and how it's just been impossible. And it was a real shock because when I go back to the matrix that was started in 2003, I thought that was the one success that we could show was that we had put together the autism tissue program, and we have now 97 brains. But most of them have not been usable, and they were collected under such various, varying conditions that you can't compare them.

And there are no controls, at least no appropriate controls. So this has to be done in a very different way. There has to be a much more robust effort here.

Dr. Fischbach: So I'm just suggesting a way that –- and I guess there was something that I thought of that might be missing in the Plan, and that is -– and it may be too granular right now, but -- links to other diseases. I mean, were lessons learned from other diseases? There are going to be a lot of things in common with schizophrenia. Autism is not childhood schizophrenia, but we're going to learn a lot

from the genetics of schizophrenia, this 16p, the lesion is turning up as a duplication in many cases of schizophrenia. And if there were common sites for collecting brain tissue -- I know the need, but I don't think we're going to set up just an autism-only series of sites, but if there were trained pathologists available who could deal with the tissue and distribute it to the appropriate bank for storage, it would be helpful.

Dr. Kau: Tom, there are only two banks in existence that collect autism brains. One is ATP; the other is NICHD's brain and tissue banks. And I know John Bacon and Ron Zilci, the VI of the Maryland Bank, working closely together. You know, and we're trying to collaborate and set standards. But I think making it a priority would help the process. You know, because --

Dr. Dawson: And I can say that I've only been in Autism Speaks for 2 months or something now, but it is, if not, the top thing on the list. It's at the top. And so it is something that I think would be really worthwhile, all of us, getting

together and trying to develop a Strategic Plan. And if the IACC believes this is something that is useful, that of course, helps, too.

But I think it's absolutely essential. And as I look at this list, and you know, the state of our knowledge, I think in general looking at this issue of resources and tools is really important because there is just a lot of basic resources that we need in order to answer the questions in a lot of tools, whether it's the screening tool, or some of these other things that we've talked about, that if we had these things, the tool for being able to gather some of the environmental exposure data.

I mean, those are going to, I think, really accelerate our knowledge at the same time that we do more targeted hypothesis-driven work.

Dr. Insel: I think, Geri, what you're hearing from IACC is it's not just brain collection; it's broader tissue.

Dr. Dawson: Absolutely, right.

Dr. Insel: So that we look at a range. And you know, right now, you know, the huge interest

is in having skin fibroblasts, which could easily be stored, and you know, easily then dedifferentiated. And it may turn out. I mean, all of this is happening so quickly. It may be that a year from now that is the most important thing to have because you can --

Dr. Dawson: No, we've been talking about that quite a bit, yes.

Dr. Geschwind: So I'm just going to highlight that as a really key easy tissue to get. And I'm just wondering, with regard to all of these longitudinal studies, and all the other kinds of studies that we're talking about, and this was brought up before, whether we do want to attach something on here, that when these kinds of studies are being done, that there will be some kind of attempt; or you know, we don't want to lock people in. But there should be attempts to collect biomaterials. You know, that has to be kind of an integral part of it, of any large-scale project that's going on.

Dr. Insel: Including clinical trials.

Dr. Geschwind: Yes, yes.

Dr. Newschaffer: When involved in these kinds of efforts, it's also critically important that the standards be in place, too, you know. You'd like standards to be in place before, you know, to inform those efforts within fault.

Dr. Insel: This is where -– so NIHS, and I think Cindy just left the room, but she can -– you know, NIHS can really be very important here. And helping us to define what those standards might look like. Other things that were not on the list?

Dr. Gail Houle: Tom?

Dr. Insel: Yes.

Dr. Houle: This is taking us in a little different direction. But back to some of the dissemination and usability of the intervention research, I think it would be good if we could maybe copy an idea, but modify it and look at promoting something such as a What Works Clearinghouse on research-based interventions for children and adults with autism.

You know, we had talked about there being work out there; the levels of evidence are

different for the studies that are out there, and somehow I think if the IACC could, at least the part of the IACC that was interested in the intervention research piece, get together and promote or look into promoting resources for a kind of What Works Clearinghouse for what we know about research based intervention.

So that's a completely different direction from the tissue banking part of it. But you know, it is some of the work that's supported with some of the funds that, and some of the work that you all do. Another thing is the capacity building in the systems implementation for the practices that would tie into, kind of a What Works Clearinghouse of practices and interventions. And along with that, he had touched somewhat on some of the incentives and disincentives where the actual implementation of research-based practice. And so that could even be another area that we can support some work in. I see that going out.

Because I think, you know, there is a lot of interest, direct interest on the part of

families and practitioners, and perhaps some standard of what works. And some of the research that's going on, I know at Centers of Excellence, and what not, if they could be formatted in a way and categorized and networked in such a way that it could get out there and be better used.

Dr. Insel: In terms of setting standards for that, I'm not sure what if Autism Speaks has walked into this arena or not, but trying to define what we would call “evidence-based or therapeutic” intervention. We have pretty good standards through FDA for drug interventions and autism; I think we're now limited to a single drug that they have approved, but for psychosocial interventions, there is no such FDA. How has Autism Speaks thought about what they tell parents in terms of evidence base?

Dr. Dawson: Well, I mean, if you do look at for example, the 100 Day Kit, there is, at this point, really a description of the range of services that parents might consider. And so I think it does reflect when I said I think that the evidence for early intervention is a bit

fragile. And that's because we haven't, for example, ever compared two different early intensive behavioral interventions. So you can't say up on the 100 Day Kit, we should do this specific kind of early intensive behavioral interventions. But it does say, okay, here are some flavors. You know, there is pivotal response training. There are discrete trials and so forth.

And we suggest that you do engage in these and at this intensity. So that's state of the knowledge. That literally is the state of the knowledge.

Dr. Insel: That's unbelievable to me. Just, I can't think of another area that we deal with in which there is so little evidence base. I mean, core therapeutics.

Dr. Kau: Actually, there is one study coming out of your institution, it was very good. But comparing two approaches, they were very similar, joint attention versus symbolic play. You have shorter outcomes of --

Dr. Dawson: Well, no, but there are quite

a few that are on these targeted, so joint attention versus symbolic play; yes, there are quite a few. But I'm talking where these comprehensive programs that are, you know, 25 hours a week that you do for 2 years or 3 years. So we haven't compared the Denver model and the Lovaas model, or the floor routine versus –-

Dr. Kau: Right, I mean on the larger scale.

Dr. Dawson: Yes, but there have been actually quite a few targeted, more short-term studies.

Dr. Kau: And those are exciting. That's all we have so far.

Dr. Dawson: And they are very exciting, yes. So I think that that part of it, and that's why that was put in terms of these efficacy trials for comprehensive intervention models, right, because that's where we are.

I mean, there is one multisite study that's beginning that you're a site in, and we're a site in, and we have our randomized clinical trial that's coming out, and then there have been a few others that have been published.

Dr. Kau: And this -– each side is required to have a treatment project. So, and that's coming, that funding is coming to an end. So I'm sure that some data will come out of that.

Dr. Insel: We just really need some novel ideas here. When you were talking I was thinking about when I was a resident; that many years ago, there were extensive debates about just these kinds of issues for the treatment of peptic ulcer disease, which now we do a triple therapy. It's just someone has got to be thinking about other approaches besides choosing slight differences in behavioral interventions. Lyn?

Ms. Redwood: Tom, one of the things we talked about was the end of one study and studying the recovered children.

Dr. Insel: That's not on this list though.

Ms. Redwood: No, that's not. I was wondering if that might fit in somewhere, because I think there is a wealth of information that could be garnished from trying to let them recover to no. Did you do 40 hours a week, or did you do Lovaas, or Denver, or did you do biomed along with this?

So I just think we're missing an opportunity there because these are documented recovered children, and we're not taking advantage of what was done to get them there, to try to learn what we can do to get more children there.

Mr. Grossman: In this area, it's going to be very, very difficult to design a study that's going to address through a proper evidence base what applied research really worked, what applied researches are effective.

We've taken the approach more of establishing what best practices should be or what standards should be. For example, we've adopted for educational purposes, the NRC's, I mean, the National Research Council, which Gail and Cathy worked on so extensively as the best practice methodology to follow.

I think it's really going to be hard for us to really establish an evidence base in any of these things as they are because of the heterogeneity and developing a large end to truly study these. There is enough evidence, though, out there. And it might come through in

more of a consensus-based agreement than an evidence base of what we need to do for these kids, for the applied research side.

Dr. Lord: If you really want to do them, they are so expensive. I mean, they don't fit in an R01 model. That's the hard thing. I mean, what we're involved in really is comparing one very comprehensive treatment with not much. And that's three sites, and we're hoping to be able to look at heterogeneity, but we -– to do two active treatments would be probably more than double because we would have to match up the treatments in some ways so that they are different.

So it becomes, it just -– I mean, I think they are very important, but they escalate into millions of dollars for very small ends, very fast.

Dr. Insel: So that's why Lyn's suggestion, which was brought up at the, at your, workshop, but didn't end up on this list, needs to be thought about, because this is not that expensive to at least document children who have

recovered and to try to provide, try to get some sense about whether this is a subgroup. I mean, we certainly would do this with any form of cancer, where you have, and you do have people, I know of one now who has, I know, adenocarcinoma of the lung who has 4 years out without any treatment.

Most of what he had has regressed. No one knows why, but it would be very interesting to know how that happened. And I think that would be -– it's not a study, but it's what you do in an exploratory fashion so you can set up a hypothesis for your next study. And we haven't done it. And you know, we know so little here. It just strikes me that there are lots of places where we just haven't gone yet, and I think it's important to get a list that really captures all of that.

Dr. Geschwind: I mean, along those lines, a lot of parents say their kids get better with fever. I always wonder if it's just because they're just feeling sick so aberrant behaviors, you know, active outward, or is it actually

really getting better? So if that's the case, I mean, that's out of the box a little bit, but that's where you can get a lot more than that of one to do those kinds of studies.

But maybe it's -– you know, maybe a clearinghouse for all -– and you know, Peter mentioned this before, this open-mindedness issue. There were all these things that my introduction to autism was through Portia Iversen. It's like I was hearing all the stuff that she would tell me, and a lot of it just kind of turned out to be, you know, true at some level. You know, her observations, and then you --

So I'm wondering if there is a way to kind of have some kind of funnel for these observations in a scientific way, to kind of collate them, some kind of Web resources, you know, something where they can come together, and then signed, you know, people actually on the research end can have access to them, who might not get exposed to them, to begin to then propose research ideas.

Dr. Insel: Hasn't IAN done that already? I

thought IAN was -– no, they're not. So what about adding that to the list as, you know -– so I hear two things. One is trying to capture the experience, as Lyn says, and what people are actually doing, and what's worked, and what hasn't in the community, and finding out whether it turns out to be a clearinghouse or some other kind of a Web resource.

Let me ask you a second kind of related question about that. If an idea emerges, let's say it's fever, or let's say it has to do with talks and exposure, many people think that the current peer-review system would make it impossible for NIH and maybe Autism Speaks to fund such an idea. Whether that's true or not, is there a feeling –- that's true. Okay.

So is there a feeling from this group that one of the things we ought to be thinking about here is a kind of safe haven for supporting that kind of work –- a place where it may still use peer review, but of a different sort, a kind of high risk but high payoff. We're not talking about 80 percent of the investment, but that some

money be put aside for ideas which maybe kind of sound wacky, but if they worked, would really have a huge impact. Kind of like a pioneer award or something like that.

Dr. Dawson: And in fact, at Autism Speaks, we do have what's called the high-risk, high-gain initiative. And it's exactly for those kinds of ideas. And I noticed, this is just a little bit off topic, but the Gates Foundation, they just put out an RFP recently, and it is worded exactly like this. We want to see proposals that probably -- that may not pass peer review at NIH that really are proposing things that have not been proposed before. And we promise very rapid turnaround in getting these pilot studies funded.

So it might be worth even looking at that RFA. It was very well worded. But I do think there is a place for that, and there needs to be a safe haven for those --

Dr. Insel: So let me make it really specific, because what I'm wondering is if you, as a group, as the workgroup, would want to

recommend that to the IACC as something, you know, this is not tactical. This is very strategic. But if you think that the IACC ought to, in their Strategic Plan, suggest some -– I don't know what to even call it -- but a sort of separate strategy for getting very high-risk innovative ideas into the funding stream. And it could be a partnership. We could do it with Simons or do it with Autism Speaks.

Dr. Fischbach: Actually, I think everyone is interested in doing that. We have the pilot programs; you just have to be careful that wacky ideas aren't just wacky ideas. You know, and there has to be some review and some judgment exerted about this. But it's wonderful to think about how you get people who maybe have not thought about this before. You know, people who are working on circadian rhythms or just some other different approaches to say they'd like to, in their system, try to --

Dr. Lord: I wonder, too, if you could have -– I mean, my experience was that I'd probably get an email once a week from somebody who is,

like, I'd like to -– you know, “I want to study zinc, and I'd like you to study zinc with me,” and I think that often what you may have people -– I have no idea, you know, how good these ideas are not, but they don't know where to start. So having some mechanism for people who have these unique ideas be helped to know how to set up a reasonable study. Because I think that's -– you know, they're horrified when they find out that you have to have a standard diagnosis -– I mean, they just can't believe it -– and some kind of blinding procedure.

I mean, some people know some standard aspects of scientific methods, but sometimes they don't. So I think going along with it, it would be really helpful to have not just come here and apply, but if this is what you want to do, you know, this is, you know, you would get sort of like -– I think there used to be, or there may still be education grants where people got help setting things up so it wasn't just, you know, you're on your own. You pass or you don't.

Dr. Houle: There are different kinds of

technical assistance, either pregrant application phase or the grants themselves. I mean, for large States, we had State planning grants to plan how to apply for a grant and use the money. But for smaller, you know, grants, there are field-initiated kinds of ideas. Maybe what you had. And some are so small that they don't have to go through all the reviews that another one would have to go through for a larger grant competition so that innovative ideas can commend new ones.

And then I think we all have the SBIR where ideas that may not get funding by a large company because they're for a low-incidence population; like the people of the deaf/blind population, in a small way, are fundable -– in those areas. But you know, whether the criteria for application, the funding agency could probably, within limits, make that either as tight or as flexible if it had to be terms of your design, you know, whether you require the control group, match control, or whatever.

I think these details could be worked out

if people had the will to actually go with that.

Dr. Insel: Peter?

Mr. Bell: I was just going to say that if this is a big issue that we have faced; and you know, a lot of people can be critical of the types of steps that we fund, or the NIH funds and so forth. And oftentimes, it has nothing to do with the idea that they are trying to test, but rather how they propose testing and the methods they use, and that, you know, we obviously want to make sure that we're funding good science, because there is no reason to fund bad science to come out with a conclusion that no one is going to believe anyway.

And so one of the things that we tried to do this past year with our treatment grants is we had a webinar that literally just put on the table, you know, this is what a good clinical trial would look like, and these are the components that you need to include. And we really were trying to help as much as possible, particularly those people who were not as adept at writing a proposal or designing a clinical

trial, to give them as much assistance to have the most success possible.

Now, we haven't had a chance to review those grants yet, but you know, I think your point, if I'm understanding correctly, is a really good one. Is there a way or a resource that we could create to help, quite honestly, increase the quality of science, of research that is in this field and that we're getting better types of studies to really answer the questions that I think we all want to answer?

Dr. Insel: Take a look at the current issue just out of *Neuron*. On the cover article about autism, which was a completely wacky idea, there were two groups that came together, a clinical group from Alabama -- Tuscaloosa, Alabama, at Clarence, and Read Montague at Baylor. They happened to be friends, there was a personal connection, so that's why this actually took off. I don't know who funded it. Maybe -– did you guys fund it, Autism Speaks?

Dr. Dawson: Oh, no; I was saying he was one of my students.

Dr. Insel: But they come up with what they argue could potentially serve as a biomarker for autism. It's a really fascinating project that just, you know, so it's not all -– I think these are both very good. I mean, these are people who are well trained, you know, state of the art for neuroeconomics. But he had never thought about working in autism before. So sometimes it's just bringing people who are very far afield together and letting something exciting happen. Geri?

Dr. Fischbach: Tom, maybe there is a way to generate novel ideas by asking people from different disciplines. I mean, if you had a program whereby you brought some really extraordinary people in cancer biology, or immunology, unrelated to autism, to come together at a workshop with the idea of learning about autism, and then writing proposals, either bringing their students and writing proposals at $100,000, and maybe that can be done jointly in a public-private partnership.

But from their disciplines, I mean, after all, a lot of this stuff we're learning now;

copy-number variants came from cancer research and some microscopic chromosomal abnormality. But I think that's the way to generate really novel hypotheses –- people who are not terribly versed in autism, but who might want to think about it. They would come to a meeting if there was some gold, a pot of gold at the end of the meeting to say those who were successful, or might even ask them for joint applications between two lands.

Dr. Insel: So again, is this something that you would want to recommend the IACC put into a document? They're thinking about not only how to change the workforce in terms of service delivery but changing the workforce in terms of the research community. Should there be -- you know, we tend to focus on developmental neuroscience and genetics but much less on -– the number of really Nobel-level immunologists who work on autism is probably -– maybe there is one, maybe there are none -– I'm not sure. There are very few people who have solved tough problems in development, who are working in this area from

other areas.

And you know, if you think about disorders like asthma, like juvenile diabetes, like even food allergies, which also appear to have increased enormously in the same timespan, they're dealing with a lot of the same issues, but they're coming at them with different sets of tools and often different kinds of biology. And if you think that's a useful place for us to build partnerships, that might be one of the other things to suggest in this Plan.

Dr. Dawson: Extremely useful, extremely useful.

Ms. Resnik: So what I've been hearing is clearly that IACC is going to create our mission and vision. We've given them a bit of a headstart perhaps on the core values. And then they will work on the strategic objectives. But right after that, when we talk about these strategic initiatives, it seems that our workshop topics actually did deal with those, you know, viable headings and organization for some of the specific strategic initiatives; and then after

that, we might look at the assessment. The assessment would be the state of knowledge; the assessment would be perspective on other diseases, overcoming obstacles, capitalizing on strengths and resources. And then the tactical plan as organized by the “Alison method” of organization, by consumer focus, is one trajectory to go down with the tactical plan. The other could be organized by the research plan. And based on all these, you know, things that would empower, obviously, by the consumer plan, what makes sense, which may go back to something, you know, like this in terms of the resource assessment, or the capacity building, but you know, what are the logical steps in -– and then right after that, although they can be part of it, is this communication outreach and engagement plan, and that speaks to training and education. That speaks to the Nobel laureates. That speaks to, you know, based on this is what we believe to be our Plan, which does incorporate innovative ideas, then how do we engage, but we also want to think about engaging them,

hopefully, earlier in the process.

But there is definitely an outreach plan to parents, because we want those families, you know, involved in the studies, in the enrollment, in the tissue banks, and all those things. And then after that, truly the phasing plan or action plan in terms of managing expectations.

So I think that -– I mean, everything that we've talked about certainly has its place. Whether they can all be categorized under your tactical initiatives, which I don't know that's as practical as maybe looking at the broader plan and giving IACC feedback on some things they might want to consider in the other categories that will make up that integrated Strategic Plan.

Dr. Insel: So I'm not sure what to say in response. There is this communication piece, or this piece of making sure that this is much more of an inclusive process. I think I'd like to move way, way up in your scenario to, like, now. So because I think that, you know, for us, one of

the things I keep hearing in this discussion is that this is a national emergency and that families everywhere ought to be involved. They all should be signed up for tissue collection. They all want to be in these longitudinal studies. They all are to be looking at their other children who could be at risk.

And I think the way to do that is kind of the way the cystic fibrosis community did it and the way the pediatric cancer community did it. You know, just make it a national community. Make it, you know, so that every patient becomes a partner. Every family is involved. And we haven't, we just haven't done that.

Ms. Resnik: So I could imagine something like the Autism Speaks, you know 100 Day Kit, which has been created. But one for research so that if you have an individual on a spectrum, these are the things that you would want to engage with; they are the things that you would want to consider in terms of your engagement with the research community -- and to really give them tools and portals, in which to get onto the

research track.

Dr. Insel: What do people think about that?

Mr. Grossman: I really think it's going to be hard to do that. The reason is that the families are struggling so much; they need to be involved in research is a very, very, very low priority compared to their daily needs. And that's, I think, that's reality. Certainly they'll want to be involved, but if it's -– they're only going to be involved to the point that it's going to help them on that daily basis. And you're going to find minimal support, and people are going to be looking at what their life standings are.

Dr. Insel: You know, what would be helpful –- because this is a very fast-changing landscape –- but in the last 8 weeks, we now have two great examples –- tuberous sclerosis and neurofibromatosis of developmental disorders. At least one of them really does involve 30 percent of the kids have autism that look like they have suddenly become very treatable in adults -– I mean, treatable within a medical

sense. So that based on what we know about the pathophysiology of these disorders, specific chemical lesions have been found, small molecules have been developed, and first in mice that -- to almost a complete recovery in mice -- and now in clinical trials -– extremely promising. We're just a little behind that for fragile X and for Rett syndrome, where the mouse studies have been spectacular -– even better than what we saw in these other two disorders. And they are now moving into clinical trials. And we'll have those data within a few months.

But, you know, I think that's a story that hasn't been told, and these are disorders that where a large number of the kids with these very rare disorders actually do have autism as well. That's an incredibly hopeful kind of change in the science. I was telling the story to one of my colleagues who is an institute director at NIH who said it's like a miracle to think that you could take what we used to call mental retardation syndromes and take adults and actually recover a huge amount of cognitive

function. We really get something that looks like recovery.

Dr. Fischbach: This is so interesting. Is the autism in neurofibromatosis one of the outcome measures of this trial?

Dr. Insel: So it's only in TS. It's only in TS where --

Dr. Fischbach: And that is an outcome measure?

Dr. Insel: No, well, it's not in the first trial. They have been looking at learning; this is done in the U.K. And none of this is published. We've just seen the data in the last month, but it's amazingly exciting. And they get, you know, they get regression of growth of the tumors as well as having cognitive recovery. But we don't know whether how many of those kids actually had autistic syndromes.

Ms. Blackwell: Can I just speak as a parent for a second, and I'm not going to be CMS for a minute, but I just want to go with Lisa that when a parent gets a diagnosis, they're not even going to, you know, why did this happen? The first

place the parent goes is what can I do. Okay, and so usually for most people that means interface with the school system or, looking at your kit, you know, what intervention works? And then the third thing is how do I pay for it? This is what I elect to do.

But all this research stuff is definitely, I agree with Lee, that's way in the background, and it's way in the future for a lot of people thinking about brain donation and tissue donation. It's a place you don't come to until much later on after you've sort of dealt with the, you know, how do I access services and treatment? So I just hate to see those get too far down that road away from what we're supposed to be doing, what advocates want us to be doing.

Mr. Bell: I'm going to give you a different opinion, and I think this is the diversity in our community and the heterogeneity of attitudes, and so forth. And Ellen, I'm not disagreeing with you, I just don't think that it's universal across the board. I think that there are a lot of parents who immediately go to the, "Who did

this to my child?" Particularly if he had a regressive child and you saw your child disappear in front of you, and you're like, "I want to figure out why this happened."

There are other parents that eventually move out of that and get into the mode of how do I make my kid better. And there are a lot of parents who say, "How can I help? How can I contribute?" And you know, if that means participating in research, or having biospecimens available for people to look at, and so forth. There are a lot of parents out there -- that's what they do.

You know, we have hundreds and thousands of them that show up at walks every year who -– they're there because they want to be a part of the answer. And you know, unfortunately, this thing now affects 1.5 million kids and families. There is going to be a heterogeneity of that. So I'm not -– please don't get me wrong. I'm not dismissing what you're saying. I just don't think it's universal. I think there is a range of feelings about what parents, where they go to.

And --

Dr. Fischbach: Ellen, I don't also get your point. I mean this is not an either/or situation, I would hope. I mean something has to be done about services and all the things you've mentioned. But it doesn't mean that the research did take a second, backseat.

Ms. Blackwell: No, I totally agree. I think it's a definitely a many-pronged effort. But we work with States every day that are trying to figure out, as Gail said, what works -- what works for kids, what works for adults, where should we invest our dollars? And you know, so, and dollars are very limited. So it is important for us to try to thread out, you know, where these investments should be made.

Dr. Trevathan: Since Ellen took off her CMS hat, if I can for a minute take off my CDC hat and be the pediatric neurologist. See, it's harder for me to do that, actually. But I'm very interested in Tom's idea about this. As someone who has been a pediatric neurologist, and brain tumor programs working with children's oncology

group, and doing work with Rett syndrome in the early years, and saying what happened, the brain unit gathered the parents as a unified group to push and be together on clinical research. It's really what changed the landscape in both of those groups.

And I understand what Lee is saying, but if your child is diagnosed with a malignant brain tumor, you are no less devastated and have needs for dealing with the immediate issues, but yet that group has somehow over the years been transformed so that the system sort of pushes the development of science and new treatments and so forth. So it's -- I really like Geri's idea about bringing in people, you know, investigators from cancer and some of these other fields. So I'm listening to you all talk, and I'm wondering if the same sorts of interactions might be really useful in terms of some of these groups.

I mean, what is it, because I don't know the answer, what is it that happened in the oncology, children's oncology community that caused this culture to be able to come together very diverse,

very fragmented diagnostic, and more heterogeneous than autism but be able to -- be able to make this push with children's oncology? How did Cathy Hunter and people like that and Rett syndrome pull together parents and families to sort of have this push together for science.

This is very effective on both counts. And I don't know if you've had those interactions. I'm sure Autism Speaks, you guys have thought about this, and Simons, but this is a powerful force if you can get it put together.

Mr. Grossman: Well, you know, I don't think it's an either/or, and I don't think Ellen believes that either. I think what we're looking for is a balance, and if you want more engagement from a community, there has to be an equal investment in their day-to-day needs and in the lifespan needs. I think that you'll get much more support for the scientific endeavors that go on. Because both parents kind of go through this transition of, "Yes, I want to find a cure. I want to do something, anything I can," and then they hit a certain level where they go, "Jesus, what

am I going to do when I die, for my child?" And "How am I going to get him a job? Is he going to be stuck at home?” -– those types of things.

So it's, you know, I think what we're talking about is just finding a balance. And if it’s in the research agenda that we can find more of a balance, that would be even better. I think that there will be a lot more support toward what's happening biomedically if the applied science also has an equal footing in this.

Dr. Insel: If I could just add a thing to what you said, Lee. I think just for the sake of the IACC members who are here, the rest of you don't need to hear this, but the IACC has had none of that balance. The only thing that this group has dealt with so far is the Research Strategic Plan, understanding that's some proportion of what that Committee needs to deal with. There is a whole other important area that still needs to be dealt with that hopefully we can start to address at the next meeting. Denise, you have a comment?

Ms. Resnik: And I agree exactly with what

you're both saying in terms of -- and I count that under engagement in terms of providing families what they need today, tonight, the school year, and that's through the model that we developed at this Southwest Autism Research & Resource Center. But we're there to provide services for families, to help empower them to make good decisions, and as a result of that, we have a very robust research program because we're able to engage and enroll families in our States because they want to give back, they want to help. And you know, we're making it easy for them to try to do that at a variety of levels.

So clearly, in a 100 Day Kit or whatever, the idea was that I suggested, I mean, there would be different levels of research and engagement, but you're absolutely right, we have as part of the engagement plan, you know, have enough of the services research in the plan that there are some on-ramps for them to engage where they are getting some immediate value, at least to be able to make a decision. Do I have 3 more years of this therapy, or do I need to get off

the highway here?

So I agree that the engagement plan could be part of the services research, if you would, or you know, the carrot out there, but definitely need to have a balance. I still feel that if we're going to crack this code and do everything we say, we have to find a better way to engage more and more families and not make it such a burden for them to participate.

Dr. Insel: Geri?

Dr. Dawson: Well, I was just thinking about why parents may not, in some cases, be motivated to participate in research. Although I would say my experience is that so many parents actually are very, very motivated to do so. But I do think when it's not the case, it has to do with the fact that they are not finding the work relevant to the things that are important to them and that the research is in some case very disconnected from providing help and service.

So, I mean, if you really look back at the several years of research that it has undergone in NIH for the last, you know, 20 years, there

really hasn't been that much in the area of treatment. It's mostly been focused on other things. And I think if you look at the CF Foundation, that was a set of hospitals, right, where clinicians were treating children and families and really engaging them in their care and in building from that relationship into a research community.

And so I just think that we need to be thinking about the role of treatment research and the role of interfacing between research and clinical service. And I can say when I engaged in clinical research, like the early-intervention trial, or you know, validating the M-CHAT when we're out screening hundreds and hundreds of families for autism, people are so happy to be able to get those services free.

I don't have any trouble enrolling people in those kinds of studies, right, because it's relevant to think, you know, it has a lot of meaning. So I just think we need to always keep that in mind. And if we're doing something like

a brain tissue program, you know, just to be thinking about how to do this in such a way that we're giving back to people at the same time.

Dr. Houle: I agree because the incentives are different, and sometimes the extent that you can make the participation and the research affect their child's set of services they receive, the intervention they receive, it can be a real motivator -– unlike families of children with cancer who are in a life-and-death situation.

So you know, they're going into the research study because it may mean the life of their child. Most people with children with autism don't have that kind of motivation. They are not afraid that if they don't participate, you know, their child doesn't have a terminal illness that's going to kill them. It's not a life-and-death situation, but there certainly are things of a lesser degree than that, that could motivate parents, families of children with autism, and one of those is the intervention services that if they're going to be able to get

better services, they're going to be able to get more services that, you know, the rewards of being able to participate in database service intervention for decisionmaking, and that kind of thing. So I wouldn't -– you know, I would be a little leery of comparing their motivation to that of a family whose child has cancer and could be facing life or death. I would look at those other motivations of populations where people really, you know, want a community of acceptance for their child. That's another thing. Services you can link them to participation in the community. It's a great motivator.

Dr. Insel: So we're coming to the close of the discussion. I want to just make sure there isn't anything we've left off the table that needs to be added? Lyn?

Ms. Redwood: Okay, I saved this for the end because I know you guys will throw rocks at me. Back when the Combating Autism Bill was being discussed, there is a, as you very well know, a very large vocal part of the community that feels strongly that vaccines played a role in their

children's autism. The stories I hear over and over again are children got six or eight vaccines in 1 day, they developed high fevers, and screamed for 24 hours.

They were never the same. They banged their heads on the wall, and 2 weeks later they were diagnosed with autism. In the language that was attached to the bill and the colloquy, it said no stone should be left unturned -- unturned -- in terms of looking for a cause or a cure for autism, including investigating vaccines and vaccine components. And that's something that I know it's the "V" word that must not be mentioned, but I think that we really have to look at that.

A recent survey that came out where they asked parents what they thought caused their children's autism, vaccines was higher than genetics. So I really think that if we don't go there in some way and look at that, then we're not being responsive to the community that feels strongly that there is a concern.

You guys have seen the full-page ads in,

what was it --

Dr. Insel: *USA Today*.

Ms. Redwood: -- *USA Today*, I mean, I just really think that's an issue that I had to bring up because I represent the advocacy community, and I hear this over and over and over again. So I said it. It was the end of the day, so throw rocks at me because I know it's a very unpopular thing to bring up.

Dr. Geschwind: I have a question, you know, related to that. With regard to a research agenda, can one actually then go from there to pose a research agenda that would be satisfactory? In other words, what are the studies and questions that would need to be asked to actually either prove that or put it to rest; because from a research standpoint, that's really the issue here. So if one can articulate that, and it fits --

Mr. Redwood: That has never been done -- comparing outcomes in a large population of vaccinated and completely unvaccinated children. There are reports from the Amish

communities that there is a very, very, very low incidence of autism in unvaccinated Amish. I think the two cases that an investigative reporter found were both adopted from other countries and had been vaccinated.

There is also a very large clinic in Chicago, I think it's called Health Choice or Health First, also several parents or almost the whole practice doesn't vaccinate. Not only do they not have autism, they don't have asthma, they don't have allergies. They don't have a lot of health problems.

Actually, Blue Cross and Blue Shield approached them wanting to know what they did different because they had so few claims coming from this large pediatric practice. So that would be the study that I know the parents, I think there is a congressman who has also asked for this investigation.

Dr. Newschaffer: That just fits with mission 34 perfectly.

Ms. Redwood: Can you do it?

Dr. Newschaffer: Well, that is the more

difficult question.

Dr. Insel: Craig, what's the– fill us in. What was it?

Dr. Newschaffer: Number 34. It was research the studies in other special populations. That's what we talked about -– high-exposure groups or low-exposure.

Dr. Insel: It doesn't mention the "V" word specifically. But it's set up to take advantage of those sorts of natural experiments exactly, and I think that I know that researchers need to be encouraged to do that. You know, I think the question, you know, I think the real question is the implementation questions about studies like that, because they can be difficult. But I mean, the initiative is there. We used to facilitate that if somebody felt that they could pull it off. Geri?

Dr. Dawson: I was just going to say, yes, there are two places where I think that kind of work can be done in the context of this. One is the special populations, and I think the Amish are one that would be of interest. And in fact,

Autism Speaks is looking into that in a proposal right now. And so it's an opportunity, and there are other populations like that as well.

And then the other is in these studies looking at risk factors broadly and whether it's, as Craig has kind of said, following the infants from conception. I can't imagine that you're not going to be getting the vaccine records.

Dr. Newschaffer: We are.

Dr. Dawson: In the context of a very large -- how many babies are in that study?

Dr. Newschaffer: It will be 1,000 babies.

Dr. Dawson: One thousand babies followed from point of conception. So and these are infant sibs; so what we're finding is that a lot of parents are choosing not to vaccinate. So another study that, you know, at Autism Speaks that we've just funded in the context of the Baby Sibs Research Consortium is a feasibility study to look at how many parents actually did not vaccinate their children so that we can determine whether there is enough variability

there that you could answer the question.

So I do think that people aren't, you know, completely covering their eyes here. That for no other reason because people still are very interested in this. And you know, there is no bad idea. There only needs to be, you know, there needs to be good science, though.

Dr. Dawson: That's new, that's a new just to the --

Dr. Newschaffer: It hasn't officially been announced.

Dr. Dawson: That's true; we haven't officially announced it. It's no place a researcher would go in the past.

Dr. Insel: Let me take you one step further. So in the biology discussion at the workshop, there was a little bit of discussion about this emerging area of microbiomics, and the possibility, which has been brought up, not in autism, but I think it's in asthma, that vaccination, current standards of neonatal care, how prenatal children are handled, a bunch of these things may be changing the microbiome,

and then leading to a very different innate immunity pattern.

Actually, the juvenile diabetes people are starting to go down this road, and they want to fund research because they think this may be explaining the increase in type 1 diabetes. So even if you did such a study with vaccines, what you really want to know is –- because not every kid who gets vaccinated develops autism. So is there something about what vaccines are doing that set up a process that we'd want to know a lot more about.

So that's something that seems to me that once, you know, again, it's of huge interest in other areas of medicine that deal with increase in developmental disorders from an immune perspective. And we talked about kind of looking at immune factors. But we now have this spectacular ability to do microbiomics at a very large level and a very comprehensive level. And yes, I don't think anybody has taken that on for autism.

And that actually could be one of the ways

in which, whether it's vaccination or other aspects of early care, things have really changed the most, and that's the way it may be playing out. It may have nothing to do with what's in the vaccines but all the things that have to do with what the vaccines change and the child's sort of microbiologic environment.

Ms. Redwood: That just came out, Tom, the delayed DPT vaccine; I think it was like for 2 or 4 months resulted in a 50-percent reduction in asthma rates.

Dr. Dawson: In what rates?

Mr. Redwood: Asthma.

Dr. Dawson: Oh, asthma.

Ms. Redwood: Asthma rates.

Dr. Insel: Yes, I mean, so that's where, it's that kind of a notion where this comes from, is that there is this critical period in which you set up autoantibodies to the human tissues and they get triggered by different exposures that you have. So it's -- I guess what I'm pushing for is that we've learned the importance of getting beyond descriptive studies to look at

mechanisms, and I think if you know that's where you want to go, then you might as well just start and go there from the get-go.

So if you're starting to do a longitudinal developmental study, then think about sampling from many different parts of the body to get these microbiomic profiles.

Mr. Bell: I was just going to say this has a lot to do with my suggestion that there is an open-mindedness about our guiding principles. And I think that, in fact, Geri was quoted in an AP article by saying that, you know, this is still an open issue in the community, that a lot of parents still very much believe that vaccines play a role. And until that goes away, we should continue to look at it. And I'm paraphrasing there, and I apologize if I go way too far.

But clearly this is an issue that's not going to go away. And there are many people in the research community who are convinced and want it to be taken off the table and no more research put into it and so forth. And that only serves to just antagonize that part of the

community. And I think that, you know, there is an opportunity to do more rigorous studies of this and to look at whether there are special populations or segments of the population that are more vulnerable and what have you.

And so if it means being in our communication or in the communication plan of the Strategic Plan, there is an opportunity to say that, you know, when we talk about environmental factors, that truly means all types of environmental factors. I think that's what you're hearing from -– I don't know what it is, but I would say -- a reasonably significant part of the community is that this is still very much an issue that they feel needs to be addressed and looked at.

But again, I go back to my original heterogeneity, you know. I mean, this is a very heterogeneous disorder, and that could be an issue with part of it but probably is not as big of an issue with a significant portion of the community. Again, I'm kind of going into an area I probably shouldn't, but I think it is something

that needs to still be up on the table.

Dr. Insel: But it's a tough one. I would support that we have that on the table, but at the same time we have to talk about all the unintended consequences. We're dealing with the first multistate measles outbreak in years, and you just want to be really careful that in the effort to be openminded, you're also not doing harm where it's not needed.

So I guess it goes back to Geri's point. I think it's really important to be clear about what we know and what we don't know. And to think about the Strategic Plan as an opportunity to test lots of possibilities and lots of ideas. But it has to –- really has to -- be founded on the very best scientific rigor. And knowing that, you know, there are consequences for going down one path or the other.

Ms. Redwood: But the comment could actually be the opposite, I mean, right now, as Geri said, parents aren't vaccinating because they don't know. So it may be by not doing the science you're actually putting yourself at more risk for

outbreaks of disease. So either way, I see it as a win-win situation to get an answer.

Dr. Insel: It's interesting, because you know, in the discussions I've had with some parents, they want to vaccinate. It's not that they don't want to vaccinate their children -– they want to know how to do it safely. And it may be that -– I mean, there is a way, I think, to frame this that doesn't create so much exposure for all concerned. I think it deserves some further discussion.

This is actually one of the issues that I was thinking about when I said before, we need to, I think there needs to be someplace where we can talk through some of the basics here, some of the areas that have been splitting the community. And we need to make sure that as an Interagency Coordinating Committee that we're actually bridging some of those things and figuring out where the common ground is. Because I think, at the end of the day, we all want the same outcomes, but we may be coming at this from a different perspective. Anything else that

we've left off? Bob?

Mr. Grossman: I got to run, but this is, but there is something you said earlier I just want to have clarified for all of us, is that you mentioned that we're on kind of a 5-year window. Is that a 5-year window just for the IACC's existence, or how does that relate to the Strategic Plan? What we're looking at, is that going to extend beyond the 5 years? I would assume it would be, but I just want to get all that clarified.

Dr. Insel: I'm just quoting for the Act, it dies at the end of 5 years, and it says that everything that's in this Act is no longer, it's no longer supported. I'm assuming by then, under a very different administration and a different Congress, we'll have this thing renewed in some ways. So we're working on -- we've got more than 4 years and a few months left. But it's, for that reason, the Strategic Plan will have a 5-year window, but it gets renewed every –- or it gets revised every year. Anything else? You have done such a fantastic job. We're going to let you out

early? Dan?

Dr. Geschwind: (Unintelligible conversation)

Dr. Insel: You know what I think? I think we may do that. We've got enough comments about where the collapsing is possible. It's often not going to be simply collapsing but taking three items that talk about the same thing from three perspectives and making it one item with three subgroups or something like that.

Dr. Geschwind: Sure, great.

Dr. Chung: (Unintelligible conversation)

Dr. Insel: Yes, and get some feedback.

Dr. Geschwind: Or you guys can do it and then get feedback.

Dr. Insel: Yes, we will collapse and make it readable. We want to have a document that the worker can send on that you're okay with and that the IACC can use. They couldn't use the 41 items, but they need to have something that's more trackable.

Ms. Resnik: Describe our next steps then, and as we think about an April meeting, what you

would expect from this group?

Dr. Insel: So this is the last meeting. We are finished as of today with this group. What we will do, I mean, we will have a discussion and we will collapse some of these things.

Dr. Chung: What's in April meetings to clarify this? What needs to be decided?

Dr. Insel: Yes, so the April meeting is cancelled. If you want to come just to hang out, you're welcome. What we would like to do is because the IACC has some concerns about -- what's that?

Dr. Geschwind: If you have some entertainment plan.

Dr. Insel: It won't be nearly as entertaining as this. We want to revisit with the IACC, how they want to take this forward. And you know, I think as you've been hearing here, there is a lot of interest in making sure we get more public input.

I think the other piece that we haven't talked about and I want to take back to the IACC is the whole implementation part. So if we have

multiple organizations that are investing heavily in autism research, and just as the example of the $45-million dollar biomarker personalized the medicine effort coming out of TGen that will involve autism, we want to make sure that this is all coordinated in a way that we could take a project like biomarkers, and you and TGen would do the proteomics, and Simons Foundation would do the genomics, and it might be that Autism Speaks does some part of the imaging, and we're involved with doing neurocognition or something like that.

But it has that kind of a feel to it. We're going to have to figure out what group will be able to do that, because there, we really do have to have the major funders coming together to figure out how to coordinate the investments. But we're not ready to do that now. That will be at a much later stage. It would probably be after we actually have the initiatives in the form that we want them in. And then to go back and shop them with all of the different major funding groups. Craig?

Dr. Newschaffer: I just want to know who TGen is, or what TGen is?

Dr. Insel: It's Translational Genomics Research. Yes.

Dr. Chung: And it's based in Arizona, led by trajectory --

Dr. Insel: But they've just required -– they've just recruited a Nobel laureate to run this new personalized medicine effort. And amazingly, I mean, it's a fantastic thing because autism is very high up on their priority list. Thanks to Denise. And they've raised a huge amount of money for this effort. And so, this is the kind of thing that we want to be able to coordinate across these different agencies.

Mr. Bell: Tom, what is, in your mind, what does the IACC meeting in March look like?

Dr. Insel: Joyce?

Dr. Chung: No rest for the weary.

Mr. Bell: Probably not the traditional IACC meeting.

Dr. Insel: You know, one possibility is that we –- you know, well, hopefully we'll have some

of this to lay out and to think through with the group, and we're going to need to have a discussion about how people from the IACC want to go forward. At the first meeting, we committed to doing this, you know, the four workshops and a workgroup. And we wanted to be good for our commitment to do that, even though a lot of people have been unhappy with that approach; it's what the IACC voted to support in November.

So now that we've done that, we want to come back and say, "Tell us how you want to do this going forward." So be thinking about what those opportunities might be, and we can have some -- I'm sure there will be some discussion about this before the meeting. Well, we'll use some time at the meeting to bring the “storm” about.

Ms. Redwood: Tom, I have a question, and being new to the IACC, I guess I don't understand sort of the difference between the service community and the research community and how much of the Combating Autism Act. Was there a number in there for services, and because I hear what they're saying with regard to the huge need

for services, but then I was under the impression that there was a bill that was being moved forward. I think Hillary Clinton was championing that for services and that the CAA wasn't going to cover services. So I just really need some clarification on that.

Dr. Insel: So the Combating Autism, in its language about setting up the IACC, is pretty clear that it's not only research, that the IACC is to coordinate all Federal activities related to autism, including agencies that don't do research, SAMHSA. For the most part, CMS doesn't do a lot of research.

So the Strategic Plan, it calls for a Strategic Plan for Autism Research, and that is a fraction of what the IACC is about. The issues that we're hearing about a little bit, and we heard a lot about them at the first IACC meeting, about how do we get better services, and how do we make sure that the service agenda is addressed, is the other thing that we'll talk about at the next meeting. We may need to have something like a Strategic Plan for services --

not for services research but actually laying out what the issues are for the country, in terms of services for autism.

I mean, these kinds of comments about the huge differences from State to State are just so extraordinary, and the issue that we keep hearing about on the education costs are just -- that needs to be somehow captured and explained, and I think laid out for both the Secretary of HHS and for the Nation.

And the IACC could be a place to do that, and I hope it is. What we did in the former version of that Committee is we tasked a small group of people -- I think, Gail, you were part of that, weren't you? --

Dr. Houle: Yes.

Dr. Insel: -- to come up with a kind of services plan. And so that could serve as a basis for this, but you could think of something much more ambitious. And I hope -- I really hope people are willing to do that because I think it is a wonderful forum to bring people together from many different agencies and to bring them

together with families who actually had to navigate this landscape and come up with an important description and also an important agenda for how to go forward.

Dr. Chung: Can I get a copy of the Plan or maybe some of the things that transpired at the last IACC to make some continuity? I'd love to see what you guys came up with.

Dr. Insel: We can get that, too. In fact, that makes me think that we probably ought to make sure, Joyce, that we have a copy of this --

Dr. Chung: It's on the Website.

Dr. Insel: The services plan?

Dr. Chung: Yes.

Dr. Insel: Okay. So it's there. Okay, anything else before we break? This is the last chance since this is the last chance this workgroup will be together. I wanted to take a moment to thank the workshop chairs, who did a fantastic job. And really great to get all of this done in this very short amount of time. And thank those of you who come from far away, especially for the workgroup to help us think

about how to put this together.

We'll be carrying this forward now, with a little bit of work, to the IACC, and I suspect we'll have to loop back with each of the foundations to think about how we can begin doing some of the implementation. But there, I really need the IACC to give us their best advice about how to do that.

Okay, I think we are finished 10 minutes early. Thank you.

(Whereupon, the Strategic Planning Workgroup Meeting adjourned at 2:51 p.m.)