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INTERAGENCY AUTISM COORDINATING COMMITTEE

SUBCOMMITTEE FOR
BASIC AND TRANSLATIONAL RESEARCH

STRATEGIC PLAN QUESTION 4 PLANNING GROUP

CONFERENCE CALL

NOVEMBER 13, 2013

The Strategic Plan Question 4 Planning Group convened via conference call at 2:30 p.m., Susan Daniels, *Executive Secretary*, IACC presiding.

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PAUL WANG, Autism Speaks

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PROCEEDINGS:

Dr. Susan Daniels: Thank you. Welcome to our listening audience, to members of the IACC, and to our invited experts joining us today for the call of the IACC Strategic Plan Update Question 4 Planning Group.

We appreciate everyone being here, and we're going to be talking today in our second part of the update to the Strategic Plan for Autism Spectrum Disorder Research of the IACC.

I would like to start off today by taking a roll call just so everybody knows who is here on the phone with us today. So the members of the IACC that are part of this are Anshu Batra, who is not going to be available today.

Idil Abdull? I think she might be joining us later.

Tiffany Farchione? Tiffany, are you with us?

Dr. Tiffany Farchione: Yes. Yes, I am.

Dr. Daniels: Okay, thanks.

Dr. Farchione: Sorry, I thought you were just

naming people. I didn't realize you were doing roll call.

Dr. Daniels: I just wanted to ensure that we could hear everybody that that everyone knows who's here.

Dr. Farchione: Got you.

Dr. Daniels: Lisa Gilotty for Tom Insel?

Dr. Lisa Gilotty: Yes, I'm here. Thank you.

Dr. Daniels: Thanks. Scott Baddish is not going to be available today; he had a conflict.

Paul Wang?

Dr. Paul Wang: Yes, hello.

Dr. Daniels: Hello.

Jeremy Veenstra-VanderWeele?

Dr. Jeremy Veenstra-VanderWeele: Yes. An amazing pronunciation.

Dr. Daniels: Oh, thank you.

And Amy Wetherby is not going to be with us today because she also had a conflict.

I'd like to have each of our external invited participants briefly introduce yourselves and, you

know, your background and how you relate to this Group.

So, Dr. Paul Wang, can you introduce yourself?

Dr. Wang: Yes. Hi, everybody. I'm a developmental behavioral pediatrician, formerly worked in academics doing a combination of research on language developments and also clinical care, in which I participated in the care of many, many children with autism spectrum disorders, as well as other developmental disabilities.

Since then, I've worked in the biotech industry at Seaside Therapeutics, trying to develop a drug therapy that might benefit core symptoms of fragile X syndrome and autism spectrum disorders as well. And a month ago, I joined Autism Speaks, where I now serve as head of medical research.

Dr. Daniels: Thank you.

And Jeremy Veenstra-VanderWeele, can you give us a little bit of background on yourself?

Dr. Veenstra-VanderWeele: Sure. So I am a [Inaudible comment] psychiatrist by clinical training. I did work in molecular genetics as I was doing some of my clinical training and then did a postdoctoral research fellowship in molecular neuroscience and have since moved into working in genetic mouse models related to autism and also remain active clinically and also do translational work looking at a variety of different medications in autism, as well as in fragile X syndrome.

Dr. Daniels: Thank you. And I'd also like to have Lisa Gilotty introduce herself because she's not usually a part of the IACC group.

Dr. Lisa Gilotty: Hi. My name is Lisa Gilotty. I'm a program officer at NIMH. And I manage the Institute's autism portfolio.

Dr. Daniels: Thank you. And I think everyone is familiar with the members of the IACC. And we will have bios posted for all our external invited participants on our Web-site prior to the meeting

on Friday, our workshop that will be taking place all day on Friday for the Strategic Plan update. And we already do have bios posted for all the IACC members.

For those who are listening on the phone, if you go to the IACC Web-site and go to the Meetings and Events page, if you look up this meeting that's happening on November 13th, from 2:30 to 4:30, you'll see a link for Materials. And there you can access all the same documents that the Committee has in front of them that I emailed to them. So you can follow along.

So to give you a little bit of background about our task today, the Committee decided this year that they would like to do an update to the Strategic Plan that entails an accountability exercise or an evaluation of progress on the Strategic Plan.

So the Strategic Plan has been in place for 5 years, since 2009. And at this point in time, we have portfolio analysis data from funders across

the entire Federal Government and private funders that are working on autism research. This mostly includes private foundations, not pharma organizations. And so we've collected these data.

And on the last phone call, the Question 4 Planning Group -- and Question 4 is about Treatments and Interventions -- this Planning Group went through the funding data that we've collected over the past 5 years to look at the status of each of the individual objectives of the Committee named for this question area.

And these objectives represent gaps in the portfolio that were seen by the Committee when they started work on the Strategic Plan, and over time they've added more objectives to the Strategic Plan to try to fill those gaps. And those areas are in addition to what was already going on in the portfolio in other areas.

And so, we have -- I've provided you with another document that is the Conclusions Table, which basically summarizes what we discussed on

the previous call; which was only the IACC members from this Group.

And so what our task is today is, we're going to go through each of these objectives, briefly recap what was discussed last time in terms of the status as it relates to funding of projects across the different funders, and this time we want to get input from our experts about the status of the field -- What has been happening? What advances have been made in these fields? What are the current needs, gaps, opportunities, and barriers in each of these areas? -- to try to get an assessment of the health and status of these areas in terms of actual research progress.

So the table that you have in front of you has these laid out for you, all these objective areas, and there are 12 of them for this question. And so we will try to go through them relatively efficiently so that we can get through our call within 2 hours. But we've had other groups that have had 17 objectives to go through, so they all

made it through theirs. So I'm confident that the Question 4 Group will be able to make it through all of these.

Do you have any questions before we get started, any other background information that would be helpful?

[Pause]

Dr. Wang: Susan, it's Paul Wang. I just want to check. We're starting with the file labeled Question 4 Cumulative Funding Table?

Dr. Daniels: No, we're starting with the other one, the one that's called the Conclusions Table.

Dr. Wang: Okay.

Dr. Daniels: It's the other table. And then I also included in your packets that I mailed out to you the listing of grants from 2011 and '12. And I just put that in as background and reference, just in case somebody needed it during this call, because on a couple of the previous calls, people have wanted to refer to those documents. And they are documents from the previous call. But we won't

be specifically trying to look at those today unless we need to find some information. Did you find it?

Dr. Wang: Conclusions by Objective?

Dr. Daniels: Yes.

Dr. Wang: Great.

Dr. Daniels: Great. Okay. So let's start then with the first objective, 4.S.A, which is, “Support at least three randomized controlled trials that address co-occurring medical conditions associated with ASD by 2010.”

And the IACC recommended budget for this was $13 million, approximately, and the Committee members of this Group last time saw that around $17 million had been expended in this area and determined that the recommended budget had been met.

And more than three projects had been funded, but these projects are basically just a start on what needs to be done in this area. And the projects included trials of sleep interventions,

cognitive behavioral therapy for anxiety, and treatments of seizure. However, more work is needed to address those co-occurring conditions more thoroughly and to address other co-occurring conditions.

And so we wanted to get a sense from you who are on the phone as to what is happening in the field in terms of RCTs for co-occurring medical conditions and what we want to see happen and how we might be able to address any gaps that might be in the portfolio.

Dr. Veenstra-VanderWeele: So I was actually curious with this one. So sleep and anxiety are here, but hyperactivity appears down below someplace. And it may be that that's just -- I just looked through the 2012, alright, I forget, actually the 2011 portfolio.

But it seems to me like there's actually quite a lot going on in this area, and much of it is straight adaptation from what is known about the same symptoms in the absence of autism spectrum

disorder. And I guess to me, it feels like it's quite a lot and maybe enough for some of these areas like hyperactivity.

And in other areas, perhaps there still needs to be more, like CVT for anxiety, where there have been some significant advances.

But I think it's sort of a challenging area when the core symptoms are such attacks on families to be instead investing in things that address noncore symptoms. And I do some of this work. So I'm a little torn here, and hopefully you can pick that up in my tone. But it was striking when I looked through the funding.

Dr. Daniels: And who was commenting?

Dr. Veenstra-VanderWeele: Jeremy.

Dr. Daniels: Jeremy, thanks. Other thoughts?

Dr. Veenstra-VanderWeele: Actually, yeah. It isn't the stuff that's listed in the conclusion. It's more thinking about how much funding has gone to the treatment of hyperactivity in autism spectrum disorder, using things that have already

been shown to be effective in hyperactivity in ADHD.

Dr. Daniels: Right. And I think in terms of the background of this objective, I think in the Committee there's been a real concern about co-occurring conditions. And 5 years ago when we started, I think the sense of the Committee was that this was a real gap area, and so they wanted to fill it in.

And I think one of the messages that came from the last group was that it does look like there has been effort to fill this area in. So I think that you're making those kinds of observations. Other thoughts about this? Are there areas that are missed that still need more attention?

Dr. Wang: This is Paul Wang. I completely concur with Jeremy that we should not in any way neglect or shortchange treatment research for core symptoms, because we are just so poorly equipped there with any kind of evidence-based treatment.

At the same time, we know very well that there

are, you know, a whole panoply of medications that are being prescribed for various co-occurring conditions. And it also behooves us to better understand which -- better understand the safety and efficacy of those treatments.

For myself, I think that sleep is really at the top of that list. In my clinical training, I was taught that, boy, if a family is reporting multiple problems, multiple behavioral issues with their child, got to start with sleep. Otherwise, no one will have any energy to deal with any of the rest. That might be a bit of an overstatement, but I do think that sleep is high on the list here.

And what I am not entirely able to discern from the table is whether the funding of research on interventions for sleep really spans the age range that it needs to. You know, it's one thing to have an RCT for adults or high-functioning adolescents who are having difficulties with sleep, but quite another to study those in the

younger population.

Dr. Veenstra-VanderWeele: Not surprisingly, I completely agree with Paul. And this is an area also where unlike for hyperactivity where we have a lot of evidence outside of autism spectrum disorder, we really don't have a lot of research in terms of treatments for sleep in the general population that easily translates into autism, at least in pediatrics.

And I think that's an area of significant growth, but it needs to grow more and expand beyond the research in melatonin, which is important, but that's mostly what I saw when I looked at the grant funding.

Dr. Daniels: Thank you.

Are there other comments from anybody?

Dr. Veenstra-VanderWeele: I would say, again, anxiety is an area where we really don't know a lot about treatment in autism spectrum disorder, and those treatments have not been easy to adapt. So I think that's another area for further work.

Dr. Daniels: Okay. Good. Well, thank you. If we don’t have any further comments, we can move on to the next objective, 4.S.B: Standardize and validate at least 20 model systems, such as cellular and/or animal models, that replicate features of ASD and will allow identification of specific molecular targets or neural circuits amenable to existing or new interventions by 2012.”

And on this one, the Committee subset that met last time felt that the recommended budget had been met and exceeded, and there were a number of projects in this area, over 90, that were supported to develop animal models.

Some of the members of the Planning Group were a little bit concerned. They felt that perhaps this area has been too highly prioritized in comparison to other areas that are more close to translation to the community. And so what do you all think about this? We'd be interested in hearing your thoughts about this area.

Where have we come in 5 years of animal models, and what are the current needs?

Dr. Veenstra-VanderWeele: I'm happy to start. Paul, do you want to offer your perspective?

Dr. Wang: Happy to defer to you.

Dr. Veenstra-VanderWeele: Okay. So I do work in animal models. And so I have, I suppose, a conflict of interest here that I should just acknowledge out front.

As a clinician, I would say that we don't have that many things that have already been discussed, proposed make sense that are ready to take into large-scale treatment studies. We have some, and those need to be prioritized. But from my perspective, where cancer research was 20, maybe 30 years ago, where we're just starting to have animal models and cellular models that are actually tractable and can develop new hypotheses based on those.

I think, given the state of the knowledge in the field, it makes sense that this is where the

investment is. And I think it will probably need to continue to be here for some time until we have more things that are actually ready to translate.

If you take the fragile X syndrome model as an example, there was roughly 20 years of work and still ongoing work in that animal model, as well as some work in cells and fruit flies and so forth. But work in the mouse then led to largely industry-sponsored studies that promised to actually transform treatment.

But that's a long time. It's 20 years in between the start of the animal model and actually seeing things that may come to the clinic. So I'd be hesitant to pull back on this funding and just fund things based on an idea that we think we have right now.

Dr. Daniels: Thanks. Are there other thoughts?

Dr. Wang: Paul here. I don't have as much expertise on animal models and research there as Jeremy does. And I do not have any specific comment on the level of funding here.

I just want to voice what could be considered, I guess, a cautionary note. And I think it's something that Dr. Insel has spoken to in the past. We have to be very careful not to overestimate or to expect too much from the animal models.

We really don't think we can create an animal that has autism and so we should not expect that we would correct autism in a mouse or a rat or any other kind of animal with a treatment that should not be a precondition for potential, at least, advancing that treatment into human studies.

So you know, a rather simple and perhaps naive comment, but I just wanted to share that. Tiffany, do you have any comments from an FDA perspective about the need for animal models?

Dr. Farchione: Well, I don't know that I necessarily have comments about need for animal models, per se. I mean, the main reason that we usually look at animal data is, you know, to have a couple of preclinical toxicology models, you

know, before doing trials in humans. Those models don't have to be a disease model; they just have to be, you know, two different species looking at toxicology. So no, not really.

Dr. Daniels: Okay. Thank you.

Ms. Idil Abdull: Hi, this is Idil. Can you guys hear me now?

Dr. Daniels: Yes. I can hear you.

Ms. Abdull: Oh, good. I've been trying for half an hour to get on. They kept putting me on listen-only mode.

Dr. Daniels: Oh. Sorry to hear that. Anyway, glad you could join. Do you have a comment on this?

Ms. Abdull: So I've been trying just to get on. But initially, on the first question, which was that co-morbidity, that's when I realized I wasn't able to speak. But I basically just have a question for any of the experts, and that is for the sleep issues. So you know, the Question 4 says, which treatment and interventions will help?

And we said that on the last call that in terms of the funding that has been met, and there's been a lot of research done on it. But as a mom who's on the ground, if I go to a doctor and I say, "My son with autism doesn't sleep more than 4 or 5 hours a night," what would you say?

Because they're not telling us on the ground that this intervention or this treatment is going to help for sleep issues with children with autism that have -- you know, that have sleep problems? So what would any of the experts have problem with that?

In other words, like, we've done a lot of research with the funding. But it's not translating real treatment and real intervention, in my opinion.

Dr. Veenstra-VanderWeele: So I get -- this is Jeremy. I get asked that question a lot, meaning, what can we do for this particular child who's having sleep difficulties? I would say that what's been funded has primarily addressed difficulty

with sleep initiation and has done less to address difficulty with night awakenings and decreased duration of sleep.

We just haven't had a lot of research with that. And I think that's one of the things that needs to happen.

Ms. Abdull: Okay. Then maybe we can say on this, that particular objective, the first one, that even though the funding is there, even though some of the research has been done, it hasn't been done where it produces results. In other words, we don't know. We don’t have an answer to the parent to make sure the child is sleeping through, what to give this kid.

Because research, if I think of it in just layman's terms, it should translate or transfer into reality, into the ground, into the community, into the families. And there are so many co-morbidities and sleep is only one issue but that there isn’t really which one treatment or intervention, after so much money, that parents

are being told that, even if they have -- another thing, I don't know where you guys are, I apologize. But another question I would have is the -- and Lyn is not here. But the GI issues, they have so many problems. And my son is one of them.

But I have not yet seen a doctor who can pinpoint what exactly the problem is, other than he's pointing to his tummy and he's saying, "Owie." So again, what are we telling? We have to have something to tell these families. We've done this research. We've spent this money. Here is how you can help your child. Here is what's going to help.

I'm sure I sound frustrated, because I really am.

Dr. Veenstra-VanderWeele: Yeah. And this is Jeremy again. And I'm frustrated, too. I think a lot of us are. We would like to have more to offer families.

I would say with regard to sleep research that

we do know more about how to help with sleep initiation than we did 5 years ago. And that's based on considerable funding. But I would agree with you that we don’t know much about sleep maintenance and preventing might awakenings.

And then with regard to GI, I would agree with you that that's an area of significant difficulty, although there, too, I think we do know more than 5 years ago. What we know is the sort of GI problems that are common, not necessarily how to treat them.

Dr. Wang: This is Paul chiming in on GI. I think there is still a lot of groundwork, if you will, to be done on understanding the GI issues. We know that, as Jeremy said, the complaints and symptoms that are most common. But I don't think we really understand their etiology. So I think more work needs to be done there before we could satisfy the Question 4 objective on treatments and interventions.

Ms. Abdull: I agree. I agree on that. Thank

you.

Dr. Daniels: And in Question 2, I believe, they have some objectives that talk more about etiology for co-occurring conditions.

And, Idil, did you have comments on 4.S.B, the model systems?

Ms. Abdull: No, not right now. Let me catch up a little bit. I've been fighting with the operator for a half an hour.

[Laughter]

Dr. Daniels: Alright.

Ms. Abdull: No, I don't. Thank you.

Dr. Daniels: Okay. Thanks.

So then, let's move on to 4.S.C: So this one is “Test safety and efficacy of at least five widely used interventions,” and the examples that are given are “nutrition, medications, assisted technologies, sensory integration, and medical procedures -- that have not been rigorously studied for use in ASD by 2012.”

And with this objective, I think the Committee

was really trying to target some interventions that are widely used in the community, some quote/unquote "alternative interventions" for which there's not a strong evidence base, and asking for more research on those.

The recommended budget, the Committee group last time determined, was partially met, and several projects were funding in this area. But more work and funding are needed. And this is an area that the public is highly interested in.

The Group noted that interventions for minimally verbal children are needed, but there is another objective that's focused on that area. But this objective did have some projects about assistive communication technologies, robotics, and speech processing technology to help with minimally verbal children.

So what do you think has happened in the past 5 years in this area, and what is still needed?

Ms. Abdull: This is Idil. I wonder if I can ask the experts just two different ways, so in two

different categories. The nutrition part, I have done everything nutrition there is, I have done from GFCF to the no-carb no-sugar, whatever I heard from the Internet. And that's, obviously, not always research based.

And because parents are trying to pick the needle from the haystack, trying to figure out what's going to work. So I wonder, can we still say we're better off than we were, but we don't know exactly which nutritional deficits or which nutritional changes are better or helpful to children with ASD?

And then the other one was the sensor integration. And that is -- and so it's two things. But the sensory integration, you can have sensory processing disorder or sensory integration disorder and not really have autism, so that could be even comorbidity.

But many, many children, particularly the minimally verbal or the nonverbal kids, have sensory processing disorders. But then that's an

area where even the funders don't want to pay. The insurance companies don't want to pay, Medicaid doesn't want to pay. They don't think there is enough research behind it.

So I just wonder what can we do in that? And in my opinion, I don't think we're at that -- but in the field, anyway, on the ground. But I wanted to see what you guys, the experts, would say. What has been done, and what can you recommend or help us recommend on the -- for the next time?

Dr. Veenstra-VanderWeele: So this is Jeremy. With regard to diet, there actually was a carefully done study of the GFCF diet, and that was reported on. I think that was an important outcome. In some of these areas, there is so much diversity that I think it's difficult to identify which thing to do next. But I think that it's an important area for further study.

The most important thing is to do the studies in a clear enough way, with a treatment manual, with adequate power to be able to detect a

difference so that we can say clearly whether or not this is something that is helpful or plausible.

With regard to sensory integration, I would very much agree. I would love to see a study that tests a manualized intervention in a careful enough way that we can clearly say whether that's helpful or not helpful and which parts of it, potentially, are helpful. And there's just very little out there, to my knowledge, at least. And I don't see anything funded at this scale that would answer the question.

Ms. Abdull: And so, Jeremy for the GF, would this be the research that said there wasn't really enough concrete data to say it does help? So in other words, we can't really say. If your child, this gluten-free, casein-free diet, your child will not have X, Y, Z symptoms of autism.

If I remember correctly, there was a study that said it's not helpful. The research said that it's not going to make anything any significantly

better. Is that the one that you're talking about?

Dr. Veenstra-VanderWeele: Yes. There was a study, and Paul may be able to remind me of some of the details. I think it was Susan Hyman that did some of this work -- that looked at a randomized trial where it was evaluated whether or not the gluten-free, casein-free diet seemed to provide specific benefit with regard to autism symptoms, and they didn't find any significant benefit.

There have also been a number of reviews. And what you're describing sounds more like sort of an expert assessment of the literature as opposed to a particular study. And I know that there have been a couple of people who have published based on the total of the literature as well.

Dr. Wang: This is Paul. Yes, the GFCF study that I'm familiar with was led by Susan Hyman and/or her colleagues out of Rochester. It was not a very large study, and I think an argument could be made that it should have been more robustly

powered.

And I think in light of very recent research that's been coming out on gluten or related antigens for which people with ASD have higher rates of antibodies against, I think it's reasonable to consider looking at that issue again. Potentially running a larger trial, if more expert people than I agree that there's justification for that.

I guess, you know, looking more broadly at this question -- first of all, I agree with Jeremy's thoughts on the sensory integration question. You know, the budget that has been expended here far undershoots the recommendation. It's stated as being partially fulfilled. It's much less than one-half of what the recommendation was.

There's a challenge in here, though, in putting together, you know, really a well-motivated or scientifically justified study. I think sensory integration is an area where we can

look. I think that GI is an area that probably bears examination again.

And I think, as has also been mentioned, the augmentative and assistive communication realm is one that should be very carefully examined, especially with the advances that we've seen in the capabilities of electronic devices for those purposes recently.

I think it's a place we need to look very carefully. I would not recommend any reduction in the area here in funding for this area. I ask why the budget that was recommended has not been met.

Dr. Daniels: So I can comment a little bit on that. This is Susan. In terms of most Government agency funding, most of it is investigator initiated. There is some funding that is related to specific targeted initiatives. But in this case, my guess is that in the investigator-initiated pool, that we haven't probably had a great number of applications in that area.

And I'm not aware of whether there have been

any initiatives. Maybe Lisa Gilotty -- Do you have any comments from NIMH anyway? We're just one of the funding agencies?

Dr. Gilotty: We have -- we have a set of autism announcements -- program announcements -- that certainly cover the treatment applications for these areas. There have been a number of projects funded over the years, but I suppose they were all lower budgeted projects.

I think the instructions that Susan gave, along with the tables, were helpful in that, you know, the amounts of money were really not -- you know -- they weren't informed, necessarily by -- I mean they were projections into the future. So it's hard to go back in time to that point and think, "Well, what should something have cost?" We know what it did cost.

And so I think it's maybe better to look at the actual studies that were funded and the findings from those studies rather than the specific dollar amount.

So the overall dollar amount isn't as meaningful to me as the comments that were made, which I agree with, that you're making, that there really hasn't been as many clear-cut findings in a number of these areas as we would like, and there's still work to be done.

So I guess it's all a long way of saying, no, there's not a very specific announcement, for example, on sensory integration treatments. But, clearly, we solicit applications in those areas, and, clearly, applications are funded in those areas. It's just that work still needs to happen.

Dr. Daniels: So a point of clarification about the budget recommendations, too, especially for those who are a little bit newer to the IACC Strategic Plan. So Congress requires in the Combating Autism Act that the Strategic Plan provide recommended budgets for each of the recommendations that are made. And so groups of program officials and people from various funding agencies were gathered to estimate what it might

cost to do what was prescribed in these objectives.

And the objectives were seen as a floor rather than a ceiling. So they were the minimum amount of work that would be needed to be done to try to jump-start some work in these gap areas. So they were by no means supposed to be the maximum amount of work that could be done, but just to get started, what would be the minimum amount of work that needed to be done, or types of work, and what was an estimate of how much this might cost, to give some guidance to funding organizations and agencies as to what it may or may not cost.

And in reality, sometimes things cost more, and sometimes things cost less than these projections. But that was the intent. They were not directives to agencies to spend a certain amount that they -- you know -- that was required.

Ms. Gilotty: Do you mind if I make one more comment?

Dr. Daniels: Sure.

Ms. Gilotty: I really -- I mean, the point [Inaudible comment] about -- that a number of studies were smaller and potentially underpowered. And in thinking about the objectives in the Strategic Plan, they are supposed to be four gap areas, you know, not for the most well developed or things that we've already got a handle on, clearly, because if we already had a handle on it, it wouldn't need to really be in the Strategic Plan. So the idea is these are supposed to be forward-thinking objectives.

And possibly one of the reasons that many studies might be smaller for a number of these objectives and they might seem to be somewhat underpowered is that these are generally considered to be new areas. And so the thinking would be that we'd want to fund smaller studies, more pilot work in the area, more exploratory work, to see if more research is needed.

If we get promising findings, then we'd want to invest more, we'd want to invest in something

larger. But you know, to begin with, you don’t start off with a gigantic study if you don't know that -- you know -- you need to know if you're going to get a signal, so to speak, in an area before you'd want to pursue that signal.

Dr. Daniels: And on the last call, there was a recurring theme throughout the objectives for this particular question that there was some observation that a lot of the studies were small and potentially underpowered. And so that was something that kind of resonated throughout this entire chapter. So you might see that again as we move through this.

If it's okay, we'll go ahead and move on to 4.S.D: “Complete two multisite randomized controlled trials of comprehensive early intervention that address core symptoms, family functioning, and community involvement by 2013.”

And here, the Committee members who were on the phone last time felt that the recommended budget had been met and exceeded. And in about

2011 and '12, about 20 trials or so were supported, but it appeared that the trials were small and potentially underpowered.

And they talked about whether larger trials might be more likely to produce definitive results. So what do you feel is going on in this area of research? And what needs to happen here?

Dr. Veenstra-VanderWeele: So this is Jeremy. I think that we don’t -- it's important to optimize the particular approach that's being used. And I think there is still a need for some smaller scale studies in order to pick what seem to be the active components of treatment. But I would say that what we really need is things that are adequately powered to answer questions.

And this is one where I think that the topic area calls for things that are powered to really answer the question definitively. And it seems like that hasn't been emphasized to the degree that you might like, although I would say that we have seen some of those studies in the last few

years. So there was very reasonably sized, although still not, certainly, overpowered study of the Early Start Denver Model, that's been published. And there's another one that's sort of in preparation. And I think those are very important studies.

But they are all -- all the studies in this area tend to be smaller than we would see, say, for a medicine.

Dr. Daniels: Other comments?

Dr. Wang: This is Paul. I completely concur with Jeremy's comments. You know, the original stated goals, I realize from quite a while ago of running two studies, are perhaps even embarrassingly low. And it's very appropriate that there has been a more vigorous effort in this area than had originally been anticipated or intended. So it's great to see that.

But, yeah, absolutely, these trials need to be robustly powered.

Dr. Daniels: Great. Anything else from anyone

in the Group on this? What about in terms of addressing core symptoms, family functioning, and community involvement? Did you feel that those areas are all being equally covered in terms of what's happening in the field?

[Several speakers]

Ms. Abdull: Go ahead. Go ahead.

Dr. Veenstra-VanderWeele: No, you can go ahead.

Ms. Abdull: I was going to say about the early intervention because that really drives so many -- I mean, there are over 30 states, even over 35, if I'm not mistaken, that are pushing for early intervention, and they're saying we want ABA because we have the research.

But the research is so small and it's such a small, you know, young, very young children, even earlier than the Denver model. It's for young kids. And so the longer we don't have research, the less -- then the more children are not getting the help. Because again, policymakers want to see

this research that is randomized, that's repeated, and the same results were gotten before they can say, "Okay, we're going to pay millions of dollars of an allocated budget from this state to pay for this XYZ intervention."

And so while, you know, the funding looks a lot, based on what IACC recommended, it's just really not enough to drive policy in the early-intervention one.

And then on the community and family involvement, I would say we're lacking on that. I don't see a lot of families where that research is included, so family involvement, as we know – everybody knows that autism doesn’t just affect the person. It affects the whole family. It affects the whole community, even.

And at least in the Somali it's affecting, like relatives all the way back home. And there isn't a lot of involvement; there isn't a lot of inclusion. A lot of family members don't have a say because there isn't research that says, if you

include the family, it will benefit.

So I would say we haven't met that objective, Susan. I don't -- in terms of funding, yes. But in terms of outcome that people on the ground can say, not really. Even the interventions that a lot of the states have passed, that's just really basically parents pushing legislators and saying, "If you don’t do this, we won't vote for you." It's not really -- it's not even research based. They're just -- legislators are just doing this because they don't want to be voted out.

And I would love to see a large clinical trial, more than, you know, a few dozen kids, that has concrete results, that would drive policy, not state by state, but just nationally, so that whether it was in Alaska, or you live in California, you live in Minnesota, you don’t have to figure out which state is going to pay for my child's therapy.

[Pause]

Dr. Veenstra-VanderWeele: This is Jeremy. I

would echo the overall sense. One of the things that's challenging for me as I read this question -- and you really just highlighted this nicely -- is that it mixes three things that are quite different: so, address core symptoms. And I think that's where things have gone and really where -- because it comes first, where you feel like this topic is going.

But addressing family functioning and community involvement feels to me almost like it's a separate area and that it might be helpful to capture that separately.

Dr. Daniels: And we actually just had our Questions 5 and 6 call this morning on services and lifespan issues. And they weren't talking about trials. And the trials are the reason that this is in this question, because it falls under interventions. But they were talking about other types of research involving looking at family functioning and community involvement that were not necessarily multi-site RCTs.

So that is one area of overlap which we face, which is just one of many.

Alright, so, if you don't have further comments on that one, let's move to 4.S.E: “Convene a workshop to advance the understanding of clinical subtypes and treatment personalization. Examples: What are the core symptoms to target for treatment studies?”

And we're looking for some information on whether there has been a workshop. I don’t know. Paul, if you know, has Autism Speaks done anything in this area? I'm not aware of anything NIH to this point has done on this.

Dr. Wang: No, I don't recall anything really focused on the question that's posed here. There was a workshop on a related topic, and that was one for identifying outcome measures.

Dr. Farchione: Yeah, that was exactly the one that I was thinking of when I read this as well. But it's not exactly what the Question is talking about.

Dr. Veenstra-VanderWeele: There's an effort from the Foundation for the NIH -- I think that's what it's called -- that is centered on biomarkers in autism spectrum disorder that comes a little closer to this. But it isn't -- and it is oriented toward treatment, very much so, actually. It's not completed yet. As an effort, I think it's still moving along toward producing a white paper. But it's not explicitly this.

Dr. Daniels: Right. And so, with this one, at this point in time, there hasn't been a workshop on this particular topic, but it's something that, you know, may happen in the future, depending on which agencies decide to look into that.

But we can note the FNIH effort and the outcome measures workshop as being somewhat related. And this is one of those cases where, in the portfolio analysis, the funding might not show up there because that funding is mostly related to grants. And some of these types of activities don't take place through grants.

So the next one is 4.S.F: “Launch randomized controlled trials of interventions, including biological signatures and other measures to predict response, and monitor quality of life and functional outcomes in each of the following groups: five trials in infants and toddlers by 2013; three trials in school-age children and/or adolescents by 2013; and three trials in adults by 2014.”

And in this area, the recommended budget had been partially met, according to the Group that met last time. The investment in projects under this objective is making good progress toward the recommended amount, with over 20 projects funded. However, more work is needed and the theme again of possibly trials being too small and underpowered.

So this is another one, also, where there is a mix of different types of trials that are called for here. So what is your thought about what is happening in the field here?

Dr. Wang: This is Paul with just a question. How does this objective relate to the ones above it, which also address trials? You know, obviously, you could run a trial with or without looking at biological signatures and other measures to predict response. So are the things listed here totally independent of the other objectives above?

Dr. Daniels: So this is one of those challenges in the process of coding the portfolio. So for this objective, it needed to be related somehow to biological signatures to end up coded to this objective. So it's possible that there are projects that are somewhat related that fell in another area, because each project is only coded to one, to prevent double-counting of funding.

So that has been another recurring theme throughout the Strategic Plan, that there is overlap between the objectives and between questions in some cases.

Ms. Gilotty: Just as with, that, you know,

there are certainly projects in 4.S.F that would -- it's the same thing. So there are projects in 4.S.F that could potentially have also counted under 4.S.D, and there are projects in 4.S.D that potentially could, you know, easily be counted under 4.S.F.

But it's a matter of coding what you think is maybe the primary component of the study. But, you know, if there could be -- if you could code a secondary component, then obviously you might have coded the other objective as well. So yes, there's often quite a bit of overlap.

Dr. Daniels: And that's why this particular discussion is really important, because the portfolio data, while they're helpful, they're not the whole story. And these kinds of nuances wouldn’t be captured through just looking at the portfolio.

Dr. Veenstra-VanderWeele: This is Jeremy. I think here the comment about the trials being too small and underpowered makes me less nervous or

concerned, in part because I think we're just at the cusp of being able to use biological signatures, certainly, in this way. I think we're closer to being able to use some behavioral signatures or other indicators to personalize treatment.

This is something that I hope we see emerge more over the next 5 years. But it doesn't surprise me that it's small. And I guess sort of like the point Lisa made earlier, we would want to see the pilot work before we saw larger scale work.

[Pause]

Dr. Daniels: Other comments?

Dr. Wang: Just a comment that I think we can expect, as we go forward in time, that a very large proportion of RCPs of any kind of treatment will potentially incorporate, you know, some assay of biological signatures and measures to predict response.

So the job of coding into these separate

categories will become more and more challenging.

Dr. Veenstra-VanderWeele: Yeah, I have to agree with that, and that's what we’re hoping for. That's what we hope the future holds.

Dr. Daniels: Thanks. That's helpful.

So then, let's move on to the next one. 4.S.G: “Support at least five studies on interventions for nonverbal individuals with ASD by 2012. Such studies may include:

Projects examining service-provision models that enhance access to augmentative and alternative communication supports in both classroom and adult service-provision settings, such as residential service provision and the impact of such access on quality of life, communication, and behavior; Studies of novel treatment approaches that facilitate communication skills in individuals who are nonverbal, including the components of effective AAC approaches for specific subpopulations of people with ASD; and Studies assessing access and use of AAC for

children and adults with ASD who have limited or partially limited speech and the impact on functional outcomes and quality of life."

And on this one, the Group felt that the recommended budget had been met, and there were about 11 to 16 studies funded from 2010 to '12, but that work needs to continue in this area.

This is another one that overlaps with the services portfolio. So what do you feel is happening in terms of the progress in this field? And what things need to happen to keep this moving?

[Pause]

Dr. Veenstra-VanderWeele: This is Jeremy. I think this is clearly an area of significant importance. One of the interesting things about the *DSM-5* is that verbal function -- verbal communication ability -- comes out of the autism criteria. Despite it coming out of the criteria, I'd say it's still an area for significant work and something that I think has been growing, which

is really encouraging, but an area where families and children really struggle quite a lot.

Dr. Wang: This is Paul. I'm less familiar with work in this area than on some of the other objectives. I see here again the challenge in coding that you have faced. And you know, the comment that I made previously on 4.S.B, where the budget was undershot, I can see now that some studies relevant to 4.S.C might have gotten classified here under 4.S.G because of their use of assistive communicative devices.

Dr. Daniels: Right.

Dr. Wang: So I understand better the point that you've made about coding. Just a general comment here that, yeah, I do absolutely support continued work in this area. We know that, historically, research on autism has been more concentrated on higher functioning individuals than on the lower functioning and on adults, in general. And it's certainly very important to see continued work here in the low-functioning

nonverbal population.

Dr. Daniels: Great, anything else from others in the Group on that one?

Okay. Let's move to 4.S.H: “Support at least two studies that focus on research on health promotion and prevention of secondary conditions in people with ASD by 2012. Secondary conditions of interest include weight issues and obesity, injury, and co-occurring psychiatric and medical conditions.”

And the Group felt that the recommended budget was partially met. And a small number of projects were funded, but further work is needed to address some of the specific issues described in this objective.

And I should mention that there is overlap with Question 5 in this area, as it has an objective that's also related to prevention and health promotion activities.

Dr. Veenstra-VanderWeele: I really struggled to separate some of this from 4.A, whatever it is,

the first objective. I guess I'm not sure how psychiatric and medical conditions are secondary. I can see how weight issues and obesity could be secondary. And I can see how injury could be secondary.

But this is one where I have a hard time separating co-occurring from secondary.

Dr. Daniels: Yes, this [Inaudible comment] in other, Strategic Plan, too, where there were topics of interest, they tended to sometimes get repeated in multiple objectives.

[Pause]

It talks about the research in this area, what areas might be doing well, and other areas that still are gap areas that need additional work.

Dr. Wang: This is Paul. Jeremy, you may know better than I do here, but I believe there is a study that Evdokia Anagnostou is PI in Germany is a collaborator on to look at the use of metformin in patients with ASD who are taking antipsychotics and the effect on weight.

It seems to me it would be appropriately listed here under 4.S.H. I don't see it. It's part of the AIR-P package.

Dr. Veenstra-VanderWeele: Yeah, yeah. And to me, that's part of the challenge with having H separated from A. I don't actually -- I think the AIR-P shows up under A. And that particular project within the AIR-P really fits this, although it also kind of fits how A is described.

Dr. Daniels: Right. And so that probably is one of those challenges in coding, where some projects, especially these multi-faceted projects, if they're fitting into one objective, it's hard to sometimes see that areas are being covered elsewhere.

Dr. Veenstra-VanderWeele: Yeah. Particularly here in -- I know I just sort of said it. But I just have a hard time saying that co-occurring psychiatric and medical conditions fall here in prevention, in secondary conditions versus above.

What I see as different here is health

promotion and prevention. But I really don’t see that emphasized so much in the projects. I think that is an important area, and that may be something that we just have so little on that it's hard to see that as the focus. But I think that is something that we should really be thinking about.

Dr. Daniels: And the AIR-P is in 4.S.A.

Dr. Veenstra-VanderWeele: Yep.

[Pause]

But I guess maybe the comment would be to take out that description of secondary conditions of interest and really focus on health promotion and prevention.

Dr. Daniels: Okay. Great, let's move on to 4.L.A, 4 long-term A: “Complete at least three randomized controlled trials on medications targeting core symptoms in people with ASD of all ages by 2014.”

And on this one, the Committee subset that met said that the recommended budget appeared to have only been partially met. Ten to fourteen studies

were funded, but they were small and likely underpowered. Most investment is needed on these kinds of projects in order to get meaningful results.

[Pause]

Dr. Veenstra-VanderWeele: Paul, what do you think there? This doesn't include the investment that's happened at the industry level, which is sometimes funded -- what you'd describe as [Inaudible comment] philanthropy.

Dr. Daniels: Right. We don't have any PhARMA groups in the portfolio analysis, and we don’t have individual family foundations.

Dr. Wang: Yeah. I mean, this is, I think, an objective that the field is really -- has been laying the foundation for and is an area that we're moving progressively toward, and I anticipate we'll be much more vigorously engaged in in the future than we have been in the past.

You know, this is where you -- in the case of novel medications, you want to see, you know, some

evidence of target engagement, some evidence of, you know, some type of related efficacy in animal models. You want to see the kinds of animal safety that Tiffany referred to before. You want to have, you know, that adequate motivation and justification before you move it into human trials.

So you know I can well understand that this is an area where momentum is still building. You know there are also drugs that are on the market, you know, approved for some other uses that are being studied in the ASD population that would not need, you know, all that kind of preliminary preclinical work on. Some of that, I think, was classified elsewhere in this exercise.

But I guess I'm just saying that I anticipate that we will have more strong opportunities to provide funding in this area in the years to come.

Dr. Veenstra-VanderWeele: Yeah, I would agree with that. I think here, too, Lisa's point about pilot studies -- it makes sense that these would

be small studies initially. But we would certainly like to see larger studies.

Dr. Farchione: Yeah. And I will say, even just from our perspective, we've seen a lot of like smaller investigator-initiated things coming in, and not -- I'm trying to think if I've even got anything, really, from pharma that I've seen. But, you know, the kinds of stuff that we're getting now, kind of small proof-of-concept stuff.

But I will say that at least there's -- you know, also I guess I'm actually addressing core symptoms. People are getting the message that, you know, improvement on the CGI is not going to be enough to say that this is treating autism. They have to give us some kind of indication of what symptoms are going to be targeted. So that's -- I think that message is actually getting out there, and that's good.

Dr. Veenstra-VanderWeele: On that point, I think one of the things that would be really nice to see here is funding that addresses treatment

research -- treatments that we think already do engage target and actually do move symptoms, to evaluate how we measure that change.

And I think, here, if we do have treatments that show evidence of efficacy, say, in fragile X syndrome or in tuberous sclerosis, we are really going to benefit from follow-on work to understand what outcome measures we can actually use to measure that change.

Right now, we really -- we don't have great outcome measures that we can say are sensitive to change in core symptoms, because for the most part, we don't move core symptoms. And that's why, you know, you have the investigator saying, "The kid seems better."

Dr. Farchione: Right.

Dr. Veenstra-VanderWeele: But we don't know that we capture it in any other outcome measure other than something like the CGI.

Dr. Farchione: And you're never going to get an indication based off of a CGI.

Dr. Veenstra-VanderWeele: No, no.

[Laughter]

Dr. Daniels: Great. Anything else from that one? Okay. Well, let's move to 4.L.B, which is, “Develop interventions for siblings of people with ASD with the goal of reducing the risk of recurrence by at least 30 percent by 2014.”

And the Group felt that the recommended budget had only been partially met and only a small number of projects funded. And the intent of the objective has not been met at this point.

Dr. Veenstra-VanderWeele: So, I mean, I guess it's more than 10 percent of the recommended budget, but it's way under being met. And I think this is an area that we should see things emerge in in the near term and I think something that NIH should be encouraging.

We now have abundant studies of early intensive behavioral intervention, as well as abundant studies -- and they're not as well powered as we might hope -- but abundant studies

showing that sibling risk is significant, larger than we thought it was. And I think we're ready for this area to take significant increases in funding.

Ms. Abdull: Hi. This is Idil. So in this area, as someone who's from a community where some of our families have not one child with autism, but two or four, there isn't -- from the ground, again -- there isn't just that intervention. And even sometimes, if the second or third child of a family takes them for early intervention or early behavior therapy, they still have autism. Not just even autism, but more classic nonverbal autism.

So I just wonder if there's something more that can be done here, because clearly, there's a lot of siblings that are being hit hard, and some of them even with the early intervention that they are getting.

And so I hope that there is a way for this to be more specific and to really prevent it. There are other ways to prevent it other than early

intervention, because I don't think that always works.

Dr. Veenstra-VanderWeele: I think that's an excellent point. And I think we need to know what works and to what degree it works so that we can think about other options.

Dr. Daniels: Okay. Any other comments on that one? So let's go on then to 4.L.C: “Conduct at least one study to evaluate the safety and effectiveness of medications commonly used in the treatment of co-occurring conditions or specific behavioral issues in people with ASD by 2015.”

And with this one, the Group thought that the recommended budget was partially met, and there have been a small number of studies of pharmacological interventions for these conditions.

So what do you think about the state of the field here?

[Pause]

Dr. Veenstra-VanderWeele: I guess here, too, I

struggle to separate this from A and H. I'm not sure where the differences are. And you know, I think that if you take the funding and aggregate it’s still too low, too low for what was laid out, that it's just hard for me to separate the different areas.

I think I would remake my point from A, though, that we have a lot of studies looking at medications that are already in active use and known to work for ADHD but are adopted into what is now defined as ADHD and autism spectrum disorder. And to me, that doesn't seem like as big of a priority as some of these other areas, like sleep, anxiety, and so forth.

Dr. Farchione: I agree.

Dr. Wang: This is Paul. A similar comment as others have said. This should continue to be a priority area, that hopefully it will receive very healthy funding going forward. As others have said, there are a lot of mediations that are being used off label. We don’t truly understand their

efficacy in the ASD population. So it's very appropriate to be supporting their study now.

Dr. Daniels: Anything else?

Ms. Abdull: This is Idil. When you said "off label," I thought of alternative treatments or nontraditional treatments. There are lots of medicines that don't have any research. And sometimes, families go outside the country to Mexico or Costa Rica to get these medications.

And I just wonder, because it lacks the research, but families are so desperate and as Dr. Insel always says, these families are on fire. And we are trying to figure out which host to buy or what -- and so the need outweighs what's happening. And it just creates a lot of unsafe things. The off-label and off-the-market or under-the-market or black market, whatever you want to call it, a lot of these medicines are not safe because we don't have research.

And I would hope that the funding is recommended a lot more, and I would hope that you

do really large studies to see about which medications work for which core symptoms so that families are not trying to think, it might be unsafe for their children.

Dr. Farchione: I'll just add one other thing that I would say. You know, in terms of looking at comorbidities and things like that with anything -- so if you're saying you wanted to look at a medication to treat anxiety in autism. You know, one of the things that we're always concerned about is the issue of pseudo-specificity.

But I think this is a condition where you could actually make a reasonable case that you're not dealing with pseudo-specificity, because some of these things, being qualitatively different in that population.

So -- I mean, I'm not -- I'm just saying that me as a reviewer, I would be open to that. I'm not sure what the overall Division perspective is because I'm sort of speaking off the cuff. But I think this is somewhere where you could make the

case that pseudo-specificity might not apply.

Dr. Veenstra-VanderWeele: I think that's a useful point and particularly when we think about things that are actually seen. And in some cases, the majority of kids with autism spectrum disorder, like anxiety, for example, where we really have very little, currently, with any evidence behind its use.

So I think that there are some opportunities there.

Dr. Daniels: Great. Thank you. So we're on the last objective here for this question, 4.L.D: “Support at least five community-based studies that assess the effectiveness of interventions and services in broader community settings by 2015. Such studies may include comparative-effectiveness research studies that assess the relative effectiveness of: Different and/or combined medical, pharmacological, nutritional, behavioral, service-provision, and parent- or caregiver-implemented treatments; Scalable early-

intervention programs for implementation in underserved, low-resource, and low-literacy populations; and Studies of widely used community intervention models for which extensive published data are not available.

Outcome measures should include assessment of potential harm as a result of autism treatments, as well as positive outcomes."

And on this one, the Group felt that the recommended budget had been partially met, and there were about 30 to 45 studies that have been supported, which is greater than the initial target, and that, though work has been done, the projects do not cover the scope of interventions in the community.

And on this one, it's another situation of a number of different things being called for here that are quite different.

So what do you think about the status of research in these areas, and where we are and where we need to go?

Dr. Veenstra-VanderWeele: So this is Jeremy. When I read comparative effectiveness or think about effectiveness research, I think about what oftentimes is termed "translation 2" or T2, which is taking things that we know to have efficacy. And usually, academic medical center setups where it's oftentimes very highly trained people providing the treatment in a way that could never be implemented in the community and then bringing that out into the community setting.

I think that that is really emphasized in the bullet points 1 and 2; bullet point 3 is a quite different thing. And it seems to me, just in scanning what's included in this area, we're not really emphasizing those things that we have good evidence for, which would be early intensive behavioral intervention, here. And instead of doing that, we're emphasizing things that are currently being implemented, which to me seems like it runs the risk of showing not a lot.

And I think we really need -- and I think

those studies are important at times to show initial signal -- to then move into something that can be studied more rigorously. But I think we really want to emphasize here taking things that we know work in an academic setting and moving them into the community. And I just don't think we're doing nearly enough of that.

Ms. Abdull: This is Idil. I wonder if I can ask some of the experts here, particularly the [Inaudible comment] early-intervention programs and implementation, the underserved and low-resource, low-literacy populations. And do you think we have enough? Because we know that underserved communities, there are still those disparities. So the results are not showing up on the ground again.

But I just wonder if you had any ideas of how to change that. And we talked about this earlier on the Questions 5 and 6 -- that we know disparity exists. We're not really sure why, and we don't really know how to address it and have a solution

for it. I wonder what your thoughts were on, what can we do here? What can IACC recommend so that underserved communities do not always stay underserved communities?

Dr. Veenstra-VanderWeele: Yeah. I think with regard to this -- there are lots of things that can be done outside of Question 4.

With regard to what really fits inside treatment research as opposed to research that's looking at the underlying reason for disparities, I think what this Question, to me, seems to call for is implementing some of these treatments that would, say, have evidence behind them in a way that evaluates whether they can actually be done in the settings where, you know, people may have fewer resources, there may be fewer resources behind the treatment itself. You may have a lower level of training of the therapists themselves.

Whether doing the treatments in that setting shows the same benefits that we think that it shows in a university clinic setting.

Dr. Gilotty: This is Lisa. Points are really well taken, and I was looking through the list. This particular objective has a lot of overlap with Question 5. Actually, you know, your description of taking what we can do in a sort of rarified setting of a lab with, you know, absolute experts, and the importance of moving that into the community and testing out those interventions in the community is really the definition of services, researcher service delivery systems, research, which is Question 5.

And there are things I know to be coded to Question 5 that could have been coded to this as well and things coded here I know that actually could have been coded to -- you know, so it's a matter of, you know, there's a bit of overlap. You know, I agree completely with the importance of studying these and studying them in real community settings. And how they actually unfold in real life, I think, is pretty important.

And I think -- it is public knowledge, so I

can just say that, you know, you were asking earlier about if we have any initiatives or any new plans in the works. And there's a set of RFAs that was on the street earlier this year -- and it just closed, actually, and we had a few applications for it -- that is actually focused in these areas.

And including -- and it includes focus on underserved communities. So you know we'll at least have hope that we'll be able to support, continue to support in the future, you know, studies that are looking at this. But I agree completely that it's an understudied area.

Dr. Daniels: And certainly -- this is Susan. This morning on the Questions 5 and 6 call we actually spent quite a bit of time talking about scalability of these types of programs. So I think this is one that really is kind of repeated from --

Ms. Gilotty: There's a lot of overlap.

Dr. Veenstra-VanderWeele: Yeah.

Dr. Daniels: -- because, you know, it's interest in different areas sat on the different groups coming up with these objectives. Sometimes they [Inaudible comment] that there were some of those areas that were a little bit duplicated.

Ms. Gilotty: It's fine to have it in more than one place so people see it more than one time.

Dr. Daniels: It's mostly a problem when you come down to coding things.

Dr. Veenstra-VanderWeele: One thing that doesn't show up here that I'm curious about, and as a clinician think about a lot, is the benefit of having case coordination or case management, which really -- it isn't exactly treatment or intervention. But I can tell you, when you work with families, this is the thing that they're looking for.

Somebody who can -- and the number of different clinicians who fill this role, but no insurance companies pay for it or they don’t pay for it in a formal way. But I think it's one of

the things that sort of fits in this community-based or effectiveness bucket.

And one thing that we need to know more about, because if families don't have somebody helping them figure out how to get the services, having somebody to figure out which services actually have evidence and are worth pursuing, it's very hard for people to negotiate the system. And I hear that over and over and over again as a point of significant concern.

Dr. Daniels: This is Susan. I think that there is an HRSA project on that. And I'm guessing that it's in Question 5 somewhere.

Dr. Veenstra-VanderWeele: Okay.

Dr. Daniels: That works on the issue of case coordination and management with underserved populations.

Dr. Wang: This is Paul. I'm glad the conversation turned in this direction. When I first thought about this objective 4.L.D, I think I started in the same place as Jeremy thinking

about, you know, effectiveness research, translating therapies that have proven efficacy and sort of more tightly controlled specific settings and seeing if they do generalize into broader, community-based settings.

But I think, yes, there is also this other side of the question. You know what kinds of supports that specifically are executed on a community level? Meaning, not at the home level, not at the school level, but really on the community scale: What kinds of supports are useful? How are they best designed? How can they be most effectively instituted on a community level? That's very much needed.

Ms. Abdull: Hi. This is Idil. So Jeremy, that's such a good question. And I think, Susan, we talked about that, that coordination. So as a mom, you know, the researchers can say this works and that works, but if you don't know it and if you don’t have somebody who's helping you navigate the system.

And then even when the doctor recommends this is going to work, is the insurance company going to pay for the price? And who's helping you navigate the system?

And the reason a lot of insurance companies or even medication pay for this service coordination or the systems working together is that there isn't research that says, that's beneficial, that it's cost effective to do this, that if you have -- if the family has -- a coordinator, service coordinator, then it's better than because that family is going to get their intervention, and they might need less and less and less services later on from the insurance company or from Medicaid.

And that’s a lot of reasons that companies are not paying CMS or Medicaid is not paying. But what I said on the earlier call is that, administratively, we've been able to write a bill and have the governor allocate $12 million, along with the legislature sign for it, which would have

service coordinators or which would have -- the systems will be working together.

So the Education Department and Medicaid, the health department, and the pediatricians -- all of it will work together and try to figure out how to help that family when they are first diagnosed, or ever before, before they are diagnosed if there are some problems, all the way up to age 18.

But that was a challenge advocating for this. It wasn't -- we didn't have research to back us up. So it would be nice to see if somebody can find or if we can recommend specific research on the importance of coordination and the importance of how it would be cost effective later on.

And that's the reason I think you said the insurance companies don't pay for it, not formally. Because I can tell you about someone who advocates for policy change, the insurance companies are always saying, "Well, where's the evidence? Where's the research for this?" And it would be nice to say, "Well, here's the research

and here's the evidence."

Dr. Daniels: Well, thank you. I think that you've all had really helpful comments on this. Anything else before we move to the next phase of the call? We've kept this really pretty well on time, which is great.

Just to comment on the funding that's not specific to any objective, that represents the part of the portfolio that was ongoing before the start of the Strategic Plan and contains all the projects that are not targeted at these gap areas that are represented by the objectives. And so there is a certain core amount of funding there.

And the Committee is talking about changing the name of that from the non-descriptive "Other" to something else, maybe "Core Activities" or along those lines. So that's the last row in that table.

So for the second part of the call, we wanted to spend a few minutes just talking about the aspirational goal for this Question in the

Strategic Plan, which is, “Interventions will be developed that are effective for reducing both core and associated symptoms, for building adaptive skills, and for maximizing quality of life and health for people with ASD.”

And we wanted to get some thoughts from you all about where we are in terms of achieving this aspirational goal and what are the big hurdles that may need to be overcome to get there, and you know, just to talk about the status of that. So do people have any thoughts?

Ms. Abdull: This is Idil. So I just would like to add in terms of the core symptoms or which treatments or interventions are going to help people with ASD that have -- they all have different symptoms, right? I mean, if you met one kid with autism or one person with autism, you met one person with autism.

But for the nonverbal or minimally verbal children and adults with autism, we talk a lot about the [Inaudible comment] devices, which are

great. I just wonder if there are other means that these children could learn. I've heard a lot about different therapies like the RPM, the rapid prompting method, which was developed by SOMA . I think we had Portia Iversen. We talked about that a little bit.

There are many, many things that, you know, help these children that are minimal that never get the research they need and never get the backing that they need. I just wonder if we can go outside the box and let research -- you know, some research that's going to help what parents are already doing.

But it would make it better it would make it easier for insurances and Medicaid to pay for it because they would have research backing them. That has just been one additional overall comment here.

Dr. Veenstra-VanderWeele: So is the question, Susan, what we see as the major advances and whether the priorities remain the same?

Dr. Daniels: Yes, basically.

Dr. Veenstra-VanderWeele: Okay. So, yes, I would say there's a lot to do. These are priorities that, you know, as Idil points out, I think remain potent. There aren't -- we don't have so many answers that the priorities have necessarily changed. I think we've emphasized areas where there are significant opportunities, where there might not have been those opportunities 5 years ago.

But if you look at the key advances in the treatment realm over the last 5 years, I think you would point to the Early Start Denver Model trial, which is still within the last 5 years, which is a significant advance in a treatment that hadn't been studied in that way before. And then the fact that there's more data coming on that, I think, is also important.

I think that you would point to cognitive behavioral therapies implemented largely for kids who are more verbal and have typically higher IQ.

But we now have significant evidence that those are effective for anxiety. There's more evidence for some social skills treatments, but very little of that is game changing in the way that maybe the Early Start Denver Model is.

On the medicine side, I would say, you know, we have evidence now for aripiprazole, which is new. And there is accumulating evidence for medicines that treat hyperactivity. But I would say that those are the only things that we can really point to on that side.

Although there is promising work, there isn't anything conclusive. And I would say our overall objectives would have to remain pretty similar to where they were 5 years ago.

Dr. Wang: This is Paul with sort of a reflection on the question, at least as I understand it. I think that a lot of us on the call would say that we have a developmental perspective on autism, meaning that the manifestations change with time, that the effects

of autism cascade as well, in that, you know, some perhaps single, perhaps multiple early deficit or impairment later manifests itself in more diverse ways, ways that might be identified as secondary symptoms sort of emerging from the core problem.

Now the reverse of that is that I think we would also be very hopeful that if there's a treatment that addresses the core symptoms, that there would be cascading benefits from that. So that potentially, if the core symptoms improve, some of the associated symptoms might improve. Adaptive skills would improve, quality of life would improve, and potentially health issues as well, as sort of secondary symptoms.

So I think that, to the extent that we meet some of the other goals to address core symptoms, we would be very hopeful that this aspirational goal would also be met. We need to see if that's the case or not. We can't assume with certainty that that will be true. But I, at least, would be hopeful that that would happen.

Dr. Daniels: Great. Thanks. Any other thoughts about how we're doing with the aspirational goal? Are there things that you feel, after you've looked at this, that have been missed, that are major opportunities or gaps?

[Pause]

Dr. Veenstra-VanderWeele: I think we have been saying sort of all along where the new opportunities are. They're still within the objectives, but maybe within the objectives, we have shifted this as Paul said beautifully as a field it's shifted developmentally, where there are now opportunities where there weren't necessarily opportunities before.

And I would say one of those things is that we now have more developed reduced models, animal, cellular, and so forth. And those represent an opportunity to translate things.

And then, obviously, there are things that have moved along in their development as treatments, which are opportunities as well.

Dr. Daniels: Great—anything else that anyone wants to share about this? Well, you've all done a terrific job getting through all of these and sharing some really helpful insights. We look forward to having everyone together at the meeting, and some people will be on the phone, on Friday. So that meeting is taking place from 8:30 to 5:00 on NIH's main campus in Bethesda. And it's open to the public, and so people are welcome to come.

And we also will be webcasting it live on the IACC Web-site. And I will be sending out the agenda and some final instructions for you all prior to the meeting. But you don't need to have done any extensive preparation before you come. So I think we'll be able to just tap into your expertise right there at the meeting.

The day will be divided up according to the different questions in the Strategic Plan, and you'll all be welcome to chime in and talk about all of the areas. So it was the hope that, with

these focused meetings on each question area, we could really dig in at a deeper level but that now we will get out of our silos and then all come together and be able to look at it as a whole and be able to give some final feedback to the Committee, as they continue their efforts to update the Strategic Plan for this year.

So, with that, does anyone have any questions? Well, thank you so much for being here. We really appreciate having you, having your input. And we look forward to talking to you on Friday. So, safe travels to everyone, and we look forward to seeing you soon.

[Chorus of "Thank you" and "Goodbye"]

(Whereupon, the Strategic Plan Question 4 Planning Group conference call was adjourned.)