U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

INTERAGENCY AUTISM COORDINATING COMMITTEE

SUBCOMMITTEE FOR BASIC AND
TRANSLATIONAL RESEARCH

CONFERENCE CALL

WEDNESDAY, MARCH 6, 2013

The Subcommittee for Basic and Translational Research met via conference call from 2:07 p.m. until 4:33 p.m. Thomas Insel M.D., and Geraldine Dawson, Ph.D., *Co-Chairs*, presiding.

PRESENT:

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

GERALDINE DAWSON, Ph.D., *Co-Chair*, Autism Speaks

SUSAN DANIELS, Ph.D., *Executive Secretary*,
Interagency Autism Coordinating Committee (IACC)

ANSHU BATRA, M.D., Our Special Kids

LINDA BIRNBAUM, Ph.D., National Institute of Environmental Health Sciences

COLEEN BOYLE, Ph.D., M.S. Hyg., Centers for Disease Control and Prevention

NOAH BRITTON, M.A., Bunker Hill Community College

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

DENNIS CHOI, M.D., Ph.D., Stony Brook University

PRESENT (continued):

JAN CRANDY, Nevada State Autism Treatment Assistance Program and Nevada Commission on Autism Spectrum Disorders

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

DONNA KIMBARK, Ph.D., U.S. Department of Defense

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

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

SCOTT ROBERTSON, M.H.C.I., The Autistic Self Advocacy Network (ASAN)

ALISON SINGER, M.B.A., Autism Science Foundation

TABLE OF CONTENTS:

PROCEEDINGS:

2:07 p.m.

Dr. Susan Daniels: Well, welcome everyone to the call, to all the Subcommittee members, other Committee members and members of the public who might be listening on the phone call.

We are convening here in snowy Washington and hopefully many of the rest of you around the country are having better weather than us.

But we hope that everyone is well, and I'd like to have Tom Insel and Geri Dawson help get us started on the call.

Dr. Thomas Insel: Thanks, Susan. As those of you who are on the phone just heard, actually government is closed today so we're doing this in a conference call mode where everybody's in a different place.

Maybe a little harder to coordinate but I think we'll do our best and I appreciate everybody joining us.

We will take roll here in a moment. I

just wanted to give Geri a moment to also welcome everybody and then we'll get on with the agenda.

Dr. Geraldine Dawson: Welcome, everyone, and fortunately, I'm not snowed in. I'm here at my office at UNC and I think we've got a great agenda that - and a very ambitious agenda for the next few hours.

I'm really looking forward to the discussion and I wondered also, Tom, if you might comment on whether the sequestration has affected anything related to the IACC at this point. And so I don't know if you're at liberty to talk about that, but it has come up recently as a question.

Dr. Insel: Well, today seems to be what everybody in Washington is calling the "Snowquestration" because of the storm, but at this point, other than very long lines at the airports and long lines in some government buildings - I was on Capitol Hill yesterday and almost missed a hearing that I was a witness at because I couldn't get into the

building because of the lines that were going around the block.

But within the IACC and within NIH at least I can't point to anything that is different. We are on a continuing resolution budget. We've been on that since October 1st and that continues to be true until March 27th.

So the date that all of us are thinking about was not the sequester March 1st date but the March 27th date, by which we need to have a new budget and that's really the key point because if that doesn’t happen then we’ll go into a government shut-down mode, which will certainly have an impact on everyone.

Dr. Dawson: Great. Thank you.

Dr. Insel: So the reason we're not at work and the reason there's no government today has nothing to do with the sequester. It only has to do with the snow.

Susan, do you want to go ahead and take the roll and we'll see who's with us on the phone?

Dr. Daniels: Okay. So I'm going to first go through Subcommittee members that were expected to be on the call, and then we'll try to also take attendance for any other members of the Committee, who might have also joined. So, Linda Birnbaum?

Dr. Linda Birnbaum: Here.

Dr. Daniels: Coleen Boyle?

Dr. Coleen Boyle: I'm here.

Dr. Daniels: Denise Dougherty? I guess she's not a part of the Subcommittee, but not here. Tiffany Farchione?

Dr. Tiffany Farchione: I'm here.

Dr. Daniels: Alice Kau? No.

Operator: And I'm sorry. This is the operator. Would you like me to open all the lines?

Dr. Daniels: No.

Operator: Okay, sorry.

Dr. Daniels: Thank you. Donna Kimbark?

Ms. Donna Kimbark: I'm here.

Dr. Daniels: Walter Koroshetz? Tom Insel is here. John O'Brien is not on the

Subcommittee. Anshu Batra?

Dr. Anshu Batra: Here.

Dr. Daniels: Noah Britton?

Mr. Noah Britton: Yo.

Dr. Daniels: No?

Mr. Britton: Yo, I'm here.

Dr. Daniels: Oh, you are here. Okay. Obviously, if you're answering hopefully you're here. Matthew Carey?

Dr. Matthew Carey: Here.

Dr. Daniels: Dennis Choi?

Dr. Dennis Choi: Here.

Dr. Daniels: Geri Dawson is here. Lyn Redwood?

Ms. Lyn Redwood: Here.

Dr. Daniels: John Robison? No. Alison Singer?

Ms. Alison Singer: I'm here.

Dr. Daniels: And then I heard Scott Michael Robertson. You're on this call?

Mr. Scott Robertson: Yeah, I'm here.

Dr. Daniels: Jan Crandy?

Ms. Jan Crandy: I'm here.

Dr. Daniels: Idil Abdull? And then is there anyone else, who is on the call from the Committee that I haven't called?

Okay. I think that we have our attendance, then.

Dr. Walter Koroshetz: Hi. This is Dr. Koroshetz. Sorry, I was in listen-only there for a while.

Dr. Daniels: Oh, hi. Thanks.

Dr. Insel: We have a relatively open agenda, and that was by choice. This is in some ways the follow up to a discussion we had at the last IACC meeting, where we were realizing that much of the work of the IACC could be done by the two Subcommittees, and part of the work that this Subcommittee has been doing up until now had to do with mostly the updating of the Strategic Plan.

And we'll take in a moment a few minutes to just review the minutes from the last meeting in November to make sure that everyone approves of those minutes or can edit them as needed.

But the bigger issue for this afternoon will be to think about what we do going forward and to get ideas about how you want to operate as a group and what you have to accomplish, and to think about how to prioritize that because we don't have endless time or endless resources.

So we'll need to have a very thoughtful discussion about most important things that we can accomplish. Whatever we do, obviously, goes back to the full IACC, but our sense is that a lot of the heavy lifting can take place in these Subcommittees. And this one, which has to do with the research side of things, can then begin to frame the issues that we would take to the full Committee when we need to actually have an action agenda and to get something that is supported by the full Committee.

Susan, anything else you want to say about the agenda today before - any other work that we need to accomplish besides going through the minutes from last time?

Dr. Daniels: I think you covered what we need to talk about in the agenda.

Dr. Insel: Okay. Geri, anything?

Dr. Dawson: No, I think that sounds right.

Dr. Insel: So can we say something about the minutes? Those went out, I think, earlier today. Do we have comments, questions, issues about those that you want to revise?

Dr. Daniels: Yes, we had one from Lyn Redwood on one item and that's already been corrected. But if there's anything else?

Dr. Batra: Susan, this is Anshu. I just have a small correction on - let me skip to it, I'm sorry. It was under question two. Discussion of question two, Page 4, first paragraph, where it said Dr. David Amaral's group shows the increased brain growth but not in girls or in boys without aggressive autism. Is that supposed to be regressive autism?

Dr. Daniels: Ah, thank you. That was a mistake from the transcript so thanks for pointing that out.

Dr. Batra: And then the next where it says which may indicate a marker of aggressive autism. So there's two changes there in that sentence.

Dr. Daniels: Okay. Thank you. Anything else? Okay. I'm not hearing any other changes. Are all in favor of accepting these minutes as written?

(Chorus of ayes.)

Dr. Daniels: Any opposed or any abstaining?

Mr. Britton: Yes.

Dr. Daniels: So the minutes are accepted with this change and the one that Lyn Redwood gave me earlier. Thanks.

Dr. Insel: Okay. So let's take a look here at the task in front of us. We've got a couple of hours to think through our strategy as a Subcommittee. When we talked about topics to pursue at the last meeting there were three that emerged from the notes we have.

One was to develop recommendations around social communication disorder - this is

this new *DSM-5* entity - to make sure that the people, who get this diagnosis are not inadvertently excluded from access and to make sure that we have the research done to understand what this is and how it relates to ASD. That was one point that was brought up.

The second was to develop ideas for the update of the Strategic Plan. And we talked about that in a number of different ways, whether to begin to prioritize the plan better, to figure out ways to evaluate progress on the plan in more detail than what we've done with the Portfolio Analysis, and also to maybe identify some of the barriers to progress.

Remember, there were 78 objectives and the question was could we find a way to either identify, which ones need to be now front and center or to identify which, ones where we've made progress enough that we can put them aside or where we're really facing barriers. So that was a second big issue.

The third was a statement from the

Committee about the medical needs of people with autism, and this goes to the comorbidities question and that was felt to be especially urgent for people with autism, who had limited communication abilities and how we could take that on as a research area.

Geri and I have talked a little bit about other potential areas of interest, and what I thought I'd do and, Geri, I'd like you to help, is just kind of lay these out as a broad menu here for us to think about, collect some additional ideas and then we can begin to discuss as a group what might be most important for us to focus on.

Geri, do you want to mention anything else that - from the last few days as we kick this around?

Dr. Dawson: Well, I think the one thing that we talked about, and I do think it's on the list - I'm not sure if you just mentioned it - but we constantly are coming up on this gap between what the research community considers to be evidence-based practices and

even areas of research that, you know, have so much done in that area that we don't need to put more resources there.

And yet when we come to the point of implementing those same practices - let's say social skills training as just an example - and we try to get insurance coverage or to have these legitimately recognized as empirically-supported interventions, it seems to always fall short.

And then there's other areas where I think, you know, whether you're looking at it from a research point of view or from, say, an insurance coverage point of view, there's just huge gaps.

So this is particularly in terms of adult interventions or, you know, the review on adult vocational interventions. So it seems to me that that's a very important issue to address.

Some of it may be addressed through policy, where we make a stand that in fact the literature is strong enough to support

something, and other areas I think it really is - it's a way of thinking about priorities.

And when we get to prioritizing different parts of the Strategic Plan, you know, one could argue that this is a very urgent need, that if we can't actually get these interventions out to people and have them covered by insurance that, you know, we haven't done our job.

Dr. Koroshetz: So, Geri, this is Walter. Let me ask, in terms of the evidence base. So there's this kind of hierarchy of evidence that we talk about.

You know, the first is efficacy, which is usually demonstrating, you know - well, it starts out demonstrating in one institution that a certain therapy has advantages over a placebo.

And then the second level is more of a couple of sites that get together and see if they can replicate it. And then there's a randomized controlled trial of, you know, on the order of a couple hundred people. And

that's efficacy.

And then the next step is effectiveness, which is it really working in the real world? And that's a little bit different than the clinical trial. It's more in the real world. And so, certainly, the different levels of evidence is going to affect the payers in different - differently.

So an effectiveness trial, you know, where there's large numbers of patients in a real-world setting, that's very hard not to adopt.

But as you go down the pyramid there's lots more assumptions. So is that what is needed? Is that kind of movement up that chain what we should be thinking about?

Dr. Dawson: Yes, I think that is exactly the movement of the chain that we're thinking about, and unfortunately, in the area of autism, you know, there's very few effectiveness trials.

There are some areas that have a number of small RCTs. There's actually very few large

RCTs, and so what happens is that when you - even depending on who's doing the review, the systematic review, they typically come away with saying that there's still limited evidence.

And I think that the - one of our, you know, Achilles' heels, so to speak, that we're always facing is the fact that autism is such a heterogeneous disorder and so it's often hard, you know, even to get really consistent results or, you know, small sample sizes often end up with moderate effect sizes and so, you know, that's another issue.

But in general there are some pretty well-developed areas in terms of the, you know, at least in terms of small RCTs. But, you know, that often is not enough. And so we just need to think about that strategically because, ultimately, you know, we got to get these treatments out there helping people now.

Dr. Insel: If I can add one piece to that, in looking at the - some of the reviews done like the AHRQ review, the comments made

were that in this field there's not sufficient rigor in many of the studies done and the lack of standard outcome measures, the absence of common data elements. There were a whole series of things that probably could go into play, where the IACC could help to raise the standards in the field with maybe a set of recommendations to the research community.

That may be another element as we think about what the - how to provide better evidence or how to make better use of the evidence that people are already collecting.

So it's not quite the same as saying that we need more RCTs. It's saying we need better science, as well.

Dr. Batra: Tom, this is Anshu. And kind of along the lines of what Geri said about somehow delivering treatments to the real world, what I would also like to see is an emphasis on developing some reliable physiologic measures for diagnosis, that's not qualitative but -- and then eventually tools that we can then use to monitor, you know,

strengths and weaknesses and progress based on treatment interventions more from a long-term standpoint.

Dr. Insel: Okay. So there are a number of issues around outcome measures. Just to mention - and I'm going to just put all this on the table and then we can start to filter it - there was a couple of people, who have commented about getting a better understanding of what the impact the *DSM-5* will be, besides the development of this new label of a social communication disorder - whether even the autism, the ASD section, will have an impact. So another issue to think about within the research framework.

And then, Lyn, you had some suggestions around an issue that had to do with the comorbidities question, right?

Ms. Redwood: Yes. I did, Tom, and, you know, during our public comment almost every time we have parents, who talk about, you know, their children being sick.

I think at the last meeting there was a

person, who made sort of an eloquent request for some type of protocol or even hospital similar to St. Jude's to, you know, provide care for children with autism that would be a model that could be used throughout the country.

There was another parent, who spoke about self-injurious behaviors and how devastating those were and that we really don't have good therapies for those.

And I just think this is an area where the IACC could do something now to help improve the health of children, and it's something that we continue to hear over and over again and I think it's a huge opportunity for us.

And it's something that goes completely across the life span, whether it's sensory issues and pain or GI issues and pain or immune system dysfunction, and physicians are somewhat hesitant to treat those issues because they don't have good guidelines.

So that was the area where I thought we

could really do something now that would be really useful to the community.

And there was actually - when I looked back over the Strategic Plan, I think it was in question for under treatment. There was an initiative in there to actually hold a workshop that would advance the understanding of clinical subtypes and treatment personalization, and that was supposed to be accomplished by 2011, and to my knowledge we've never had such a workshop or it hasn't been funded.

So I was thinking that that would be a perfect opportunity, in that workshop format, to bring in experts to address some of these comorbidities and to flesh out what are effective treatments and then to publish some guidelines that will help to guide the missions in caring for individuals with autism.

Ms. Crandy: This is Jan Crandy. I'd like to follow up on a comment on that. Could we also talk about making a protocol medical

work-up for when a child gets diagnosed? Because I know a lot of kids don't get that medical work-up, that we could have a guideline on that.

Dr. Dawson: You know, I think - I should point out that the American Association - anyway, I'm on the panel - but of Neurology - American College of Neurology? Association? What is it called?

Dr. Daniels: I think it's American Academy of Neurology.

Dr. Dawson: Yes, American Academy of Neurology. Sorry about that. But anyway, they are in the process, and actually the American Academy of Pediatrics has a very nice kind of brief summary of a medical work-up for a child with autism.

I was just looking at it the other day. But the American Academy of Neurology is also developing new guidelines on that. And there are some, you know, nice papers on that. But I would be happy circulate what the American Academy of Pediatrics has put out. It's really

quite comprehensive.

Dr. Daniels: That would be great, Geri. If you could send it to OARC we could get it out to everybody.

Dr. Dawson: Yes, I'll do that.

Ms. Crandy: And maybe this Committee could endorse that then.

Ms. Redwood: Just a concern I had with regard to that though I just wanted to mention too is that especially with a lot of the self-injurious behaviors and the children that are nonverbal, I mean, I hear reports from parents all the time that they've had some type of underlying medical condition, whether it was an ear infection or something that was completely overlooked because they were nonverbal and that once they were treated appropriately then a lot of that self-injurious behavior went away.

And, you know, I have concerns about using such things, especially electroconvulsive therapy for self-injurious behaviors, without having some guidelines for

doing a full medical work-up prior to doing something like that.

Mr. Robertson: Can I make a comment? This is Scott Robertson. What I wondered is, if such a workshop were held could it also include discussion of interactions that autistic individuals - children and adults - have with the medical system and healthcare system in terms of understanding medical issues and how sensory and, say, different understandings of pain and things like that fit into that?

Like to give you an example, I co-presented with some colleagues at a national conference on pain, actually a few months ago, and we did a session on autism on how autistic adults interacting with the healthcare system may have trouble kind of explaining in terms of sensory issues and how the experience of pain being felt differently.

And this may not be something that comes intrinsically - you know, easily for it to be understood by healthcare providers, who may

not be as always familiar, you know, with some of these differences around sensory pain, et cetera, by autistic people.

And, you know, part of the problem there is there's not really good literature on these things. Some of the things like the pain and the sensory things impacting, you know, health things and impacting kind of quality of life, I mean, there's not really good peer reviewed literature on a lot of those areas.

Dr. Dawson: So this is Geri. I just wanted to reinforce that notion that as part of the focus on medical comorbidities that we do have a section - whether it's, you know, a written document or a discussion or part of the Strategic Plan that we have a section that targets the adult population, because in fact I've been reading a lot about this recently.

I just read - there have been some very nice reviews, by the way, that's come out and I was just reading one yesterday published in JADD and this one was on how - the kinds of transition services that adolescents get as

they move into adulthood, where they're transitioning from pediatrics into adult care.

And just as an example, they said that only 14 percent of youths, as adolescents, even had a conversation as they left pediatrics about where they would go or how their insurance, you know, might change or how they would find a provider.

And so -- and then there's been some very nice surveys recently that talk about the lack of providers and the need for physician training. So adult healthcare, I think, is just a huge gap.

Mr. Robertson: Geri, I just wanted to just quickly just add something else to that. This is Scott Robertson again. ASAN has a grant from the Special Health Foundation.

We're creating some policy briefs on people with development disabilities, including autistic individuals and their interaction with healthcare system and the transition from, say, pediatrics to adult healthcare and how, you know, it's not just a

problem for autistic people. It's a real problem actually with intellectual development disabilities broadly in the transition supports.

And then a related thing that I wanted to mention on the resources, that we had a grant, a multi-year grant that we've had over the last few years from NIMH to develop - this was in partnership with AASPIRE, the Academic Autistic Spectrum Partnership In Research Education, to develop the toolkit and resources to help autistic adults with their interaction with the healthcare system from a communications also kind of standpoint.

So that may also be helpful, the toolkit may also be helpful for the - you know, for discussions at, say, the workshop and some other things related to interaction with the healthcare system.

Dr. Dawson: Yes, that sounds fantastic, Scott.

Mr. Robertson: Yeah, we're trying our best to come up with good things that are

helpful for real practical issues that have been raised and are found now - and AASPIRE also - if you go to AASPIRE's website and I can send it over email - I think it's AASPIRE.org - they're also investigating a lot of other things related to health and well-being experiences of autistic adults and other things around like victimization, et cetera.

Dr. Insel: Can we frame that as a research issue? Because our task here will be to define the science gap or the needs that needs to be a focus for research projects going forward.

Dr. Dawson: Well, certainly in terms of, I think, dissemination science, in terms of how we actually disseminate information in an effective way out to the communities, so that they're using best practices.

But also I think there's a number of really targeted research questions. So, you know, understanding, for example, why it is that adults with autism have a mortality rate that's, you know, approximately six times

higher than the general population, and whether there might be good strategies that could be used in terms of prevention of SUDEP, which apparently is one of the contributors to mortality, or even programs that have to do with prevention of poor health outcomes, including obesity and heart disease and other poor health outcomes that now have been documented in adults with autism.

So those are just some - or the pain, the whole issue of pain and perception of pain and how that influences, you know, medical care. So I'm sure there's a lot of very important research questions.

Ms. Singer: I would also - hello?

Dr. Daniels: Who's speaking?

Ms. Singer: Hello, can you hear me?

Dr. Dawson: Yes, we can hear you, Alison.

Ms. Singer: I would also add to that issues of improving safety of healthcare delivery.

I think I definitely agree with points

that have been made regarding the - constantly heard during the public speaking sessions with regard to safety of some of those unstudied interventions.

And to Noah's point, I think we also have to look at issues of safety that may be unique to individuals with ASD.

Dr. Insel: So this sounds like one whole series of items related to Lyn's original idea about bringing forward an agenda around comorbidity medical care, autism within a broader healthcare framework.

Again, I wanted to use this first few minutes just to put items on the table, and we can circle back to any of these. Other general areas to think about or to talk about?

Dr. Boyle: This is Coleen. Could I ask for a bit of a clarification because in listening to the conversation it feels like some of what we're talking about - and I know we're in the brainstorming phase here - crosses with the Services and Policies Subcommittee.

And I know they have a research base to them as well. So do we have a sense of, you know, where the line in the sand is drawn between those?

Dr. Insel: Well, I think it's going to be difficult also to draw a single line. They are going to have a pretty big agenda as well.

They're going to be meeting this week and a lot of focus initially for them will be in developing a letter that will deal with issues of coverage in the context of the Affordable Care Act and essential benefits and some of the things that are playing out in real time. So there's a little bit of urgency for them.

But, no question, there will be many issues that are very similar to what we're talking about here. I think they're going to also have to grapple with questions of healthcare, beyond just the specialty care for people with ASD, but how do we ensure that anyone with an ASD diagnosis gets optimal healthcare, broadly. That's a very big

services issue.

Dr. Boyle: Okay. So I guess I'm the - I'm just trying to get my head around this. So I'm thinking of things like guidelines.

Dr. Insel: Yes, so you're right. I think the - you know, the question - and actually I think, if I can speak for Lyn - I think the way she originally framed it was to say the study of comorbidities may help us to understand - that is, the science here may help us to dissect the subtypes.

And that's a different question than coming up with guidelines or coming up with the optimal services or the dissemination of science.

Dr. Boyle: Right. Right. And the translation of those.

Dr. Insel: Right. Lyn, is that a fair assumption?

Ms. Redwood: Yes. I'm sorry. I had it on mute. Can you hear me?

Dr. Boyle: Yes.

Dr. Insel: Yes. And I should say, since

the public is in listen-only mode, so they can't speak up but they are interested in what we're talking about. And it would be good and I'll try to do this myself - this is Tom - to identify yourself when you're speaking so that people know who's engaged.

So we've got several items down here, but I'd like to just invite you to think about other areas of science, other research topics, things that as a Subcommittee that we may want to shine a light on that have not shown up in the research plan or have not been part of the scientific discussion so much for autism.

Dr. Koroshetz: This is Walter again. I just go back to what Tom said in the beginning, which came out at the last meeting. To my view, a lot of progress is held back by the lack of these common data elements, and so my question is, is that something that we could tackle that would really advance the field? So just interested in comments there.

Dr. Dawson: You know, I do think there has been some progress in that area, and I was

just attending a meeting in New York with other non-profits, such as the Michael J. Fox Foundation and VIA Foundation and some of these other ones and this came up, this issue of data standards.

And, you know, I was surprised to see that autism was actually a little farther ahead in terms of, you know, the work that's been done with NDAR.

Now, there's still a lot of work to be done but it's not like we're starting, I think, from ground zero.

Dr. Insel: What's been done on the side of standardized outcome measures for clinical trials, whether they're psycho-social or biomedical? Do we have like a set of very clear best practices for demonstrating change in ASD?

Dr. Dawson: Well, so, we convened, as you know, about a year and a half ago, a group of people who were comprised of experts in autism, who have run - and we focused on pharmacological trials so that, you know,

although we in our - we did a literature review and we included behavioral trials in this.

But anyway we did a comprehensive - it was a - excuse me, individuals from academia and also from industry, so we had representatives from Pfizer and Roche, and then Autism Speaks staff and then we also met with the FDA.

So it was a pretty multidimensional group. But we did a complete review of outcome measures in the area of social communication, repetitive behaviors, and anxiety. And we developed sort of an algorithm for rating these based on, you know, whether they were sensitive to change, their empirical validity, their burden and so forth.

And there's three papers one is just about ready to be submitted - that have come out of that process, that then go through what we have and, you know, what is recommended.

So, you know, we did come up in each of those categories with measures that are the

best but, you know, they aren't perfect by any means. I think this is also a huge area that needs to be addressed. And, you know, I think it's going to be really important, particularly in the media, the pharmacology kinds of trials.

Ms. Crandy: Geri, this is Jan Crandy. Was there any talk about adaptive measures like the Vineland and different things like that to show changes in -

Dr. Dawson: Well, we decided to focus on four symptoms. And so in the beginning it was social communication and then we had collapse, repetitive behaviors, and anxiety. And then that - it was clear that those needed to be separated. Or, really, we started out with repetitive behaviors and then the issue of anxiety arose and then we decided that we needed two separate groups.

So we didn't take on everything. We were particularly concerned that as new drugs are being developed that are designed to address core symptoms of autism that one of the

barriers to progress, particularly in terms of getting FDA approval and around clinical end points, is that if there was a lack of consensus.

So, for example, in the arbaclofen trial, which is a Seaside trial that is testing a compound that was supposed to affect, you know, social behavior, they actually had to - with the FDA they would only agree to having irritability as an outcome because that's the only thing that there had been precedent for.

So anyway we thought it was very important that we start thinking about the core symptoms and how, you know, what do we have now that could measure those in a quantitative way that are sensitive to change and reliable and so forth.

So anyway those - and I could probably share at least one of those pretty soon, but they're still being refined.

But we certainly could have the folks that headed those up, or even I, you know, but

we could have the leaders of those groups come in and present to the IACC. That would be maybe interesting.

Dr. Insel: Geri, this is Tom. Would it be worth having the FDA?

Dr. Dawson: Absolutely, and they -

Dr. Insel: At a meeting like that?

Dr. Dawson: Yeah, really closely involved in that. In fact, the same meeting I was at last week Janet Woodcock was there, and this came up again and she - you know, they've really appreciated this work, and one of the things that the FDA is doing now is working with different groups to qualify end points.

There's a qualification process. So they've actually reached out to us to talk about how we can work together to qualify some of these measures as end points so that you don't have as much questions, you know, when a group goes to the FDA to get a trial approved. So they're very - and then just another related issue, as long as we're on the topic, you know, is this issue of whether autism

might be considered in some of these breakthrough designations.

That's another important topic related to this. And that - what that means is that because there's such an urgent unmet need that one could consider allowing a company like Seaside Therapeutics, for example, to bring a drug to market sooner in the process, as long as there's no safety or very little safety concern.

And so there - they've never done this for a developmental disability before but they're - again, Janet Woodcock expressed great interest in considering this. So there's some I think very interesting things going on in this area of outcome measures in clinical trials as it relates to pharmacological interventions.

Mr. Robertson: Geri, this is Scott Robertson. I had a comment related to, like, the main traits around autism. Is there any way that the - possibly the suggestion that the Strategic Plan could have something, and I

don't know how research questions would be geared around this, but focusing on the fact that while there's a lot of discussion and research literature, et cetera, around social communication and they're considered, you know, core elements of autism, there's broad recognition of the executive functioning and sensory and motor, but difficulties and differences but not really good developed literature on those areas and that hasn't really changed in recent years on - although we have had a little progress and my understanding is that the *DSM-5* criteria is now going to incorporate, you know, a mention at least of sensory in there.

Is there any potential for the plan possibly, you know, to address this in terms of, you know, meshing that we need much better solid literature on these areas, especially if, for instance, this fits back to the translational kind of aspect of the individuals, for instance, interacting with the healthcare system?

If we don't really have good, you know, really a sense of research on, you know, on the core elements of, say, like, pain experience and sensory, et cetera, it makes it harder to then, you know, have interactions or discussion when healthcare providers want to see, you know, what the research base is on these things when it doesn't really exist that well.

Dr. Dawson: I think it's just a really excellent point and you're right that if we've - people start to do research in this area and if there aren't good end points or measures of these important domains like sensory that's going to be a real barrier.

So I think in general this notion of just better measures that quantify the different aspects of autism that can be used in a research context that that's a really important area. I know I could go on and on but -

Dr. Koroshetz: So is that something that the IACC could do a workshop on that would

have an action that comes out of it - that would be helpful to the field?

Dr. Insel: Yes, Geri, this is Tom. I guess the question is what hasn't been covered already in the workshops that you did a year or two ago and whether it's time to look at this again.

The reason I'm thinking about it is in terms of - we have limited time here as an IACC. We're not - you know, our charter ends in 2014 and this - if you think about what we can do, that might really have an impact.

If we could simply come up with a way of improving clinical trials that could be really helpful because you don't want to be in a position of having a lot of trials that don't add up to anything.

We want to be able to standardize these measures and have a way of measuring things, like Scott was just saying, that we really care about. I'm not sure that some of the current trials actually accomplish that. Was this - is there a need that we could fill in

that short term in the next 6 months or so?

Dr. Dawson: You know, it seems to me that it dovetails very nicely to where we started out the conversation around evidence-based treatments and the need to build the evidence for treatment whether they're existing or new ones and that a component of that task - you know, identifying what are the barriers that - you know, is it just literally running more RCTs?

No, it's actually developing better measures. There may be a need for clinical trial networks - you know, patient registries, whatever, you know, addressing the barriers to conducting good clinical trial research whether it's behavioral or medical I think is very important and the outcome measures is just one piece of that and there are, I think, some very innovative things that are going on.

There's a lot of interest in using technology, you know, whether it's smart phones or other kinds of technology as outcome measures and also there's a very big interest

in the idea of conducting clinical trials in the context of where people get medical care and how you use information that's collected in electronic medical records in real time and real settings rather than having clinical trials always be conducted outside the context of where clinical care occurs, and there's been a lot of talk about that, I think.

Ms. Redwood: Geri, my only concern with that, and Walter too, is that it seems so broad and not as specific to autism. I mean, in terms of clinical trials I would think that there would be other agencies, other institutes that - working on, you know, the best way to conduct clinical trials and outcome measures.

I'm just having a little bit of a difficult time seeing that as something new and innovative that's specifically -

Dr. Koroshetz: No. The outcome measures are just purely autism specific that you need to nail down. So, for instance, you know, it was mentioned that the FDA has a policy

whereby they qualify certain outcome measures.

With that - and if you could do that in autism that will just be tremendous because then the drug companies they see a path forward. All I have to do use this outcome method. FDA approved it, it was qualified and I'm going to get my drug approved.

I mean, that's just one example. But for any therapy once you get that level of, you know, reliance about an outcome measure everything becomes so much easier, if it's true.

I mean, if it's a bad outcome measure it's not going to be good but, you know, a good outcome measure, once it goes through all these hoops and is approved at that level that would be spectacular and it's autism specific.

Dr. Insel: This is Tom. I would emphasize too Geri's point a minute ago about this really feeds into the issue of providing the evidence base that payers need beyond FDA and the companies.

Even when you look at behavioral

conventions, the biggest concern as you go back through these meta analyses and the Cochrane reports and the AHRQ reports and the one that the American Academy of Pediatrics have done recently, it's really done to say how strong is the evidence for behavioral approaches in autism.

The biggest concern they see is the lack of standardization in the - both in the way the trials are done but even more so in the outcome measures.

So there's a real confusion about what it is that you could say was, as you would put it, a qualified marker of change.

So this has huge implications and the absence of really standardized rigorous processes for clinical trials means that payers can claim that there's no evidence base.

Dr. Dawson: You know, I wonder whether we could look at this, Lyn, and I'm thinking in response to your comment. So if we think about this as there is a desire perhaps on

this group to focus on building the evidence base around treatments that will help people with autism and that one of the - and there's a need to prioritize areas of research relative to treatment so one of the priorities, clearly, is to address medical comorbidities.

Another priority has to do with, you know, adult treatment and we could - we could prioritize where the types of treatments that we need more research but then another part of this would be to discuss what are the needs that will allow for rigorous, you know, trials to be designed, so things like good outcome measures.

So some of the things that we need to address are more general but we also need to address specific topic areas, like medical comorbidity.

Dr. Koroshetz: Just to add, the other thing is that somebody brought up electronic medical record, so the problem with the electronic medical record is the language is

not codified.

So if you could ever get to the point where there was a generally-accepted, you know, outcome measure in autism that you could make so that every pediatrician or every caregiver in autism is using the same system, then you could extract that from electronic health records and it would be an incredibly valuable number - a source of information.

So if you could get that - so I would say, like, for stroke we got pretty close to that with what's called the NIH stroke scale score, where we had to do a trial. No one had an outcome measure that was good. Somebody designed one. They validated it. It got used in trials and now it's basically used in practice and so you can collect large databases of information.

The American Stroke Association has, you know, 150,000 stroke patients all with the same outcome measure. So you can really look at some interesting things when you get to that level of common data collection.

Dr. Batra: This is Anshu. This goes back to my prior comment that, you know, I think - I think with autism it's so heterogeneous that, you know, I don't think - we can't identify one single outcome measure and that's why, you know, what I need as a pediatrician is a tool, something I can use to - a reliable tool to diagnose and then use that tool to then, you know, monitor changes in the brain whether it's behavioral changes or physiologic change. And, you know, I'd like to see focus on that because it's so heterogeneous.

Dr. Boyle: This is Coleen. How do the *DSM-5* severity levels perhaps relate to, you know, trying to get a better sense of, you know, I guess what we're all talking about - outcome for autism - and is there a way to use those severity levels and maybe operationalize them, such as doing something, you know, developing a scale around that?

Dr. Dawson: I don't see how you can do that with autism. I mean, I really - you know, with children you have to - you know, early on

you use developmental scales and you assess the individual developmental domains.

And as the children get older then you start monitoring and assessing their cognitive functions along with that. So -

Dr. Boyle: Yes. But with those - I mean, those of you who are more familiar with the severity levels for the *DSM-5* is there a way to operationalize those or is this going to be something that is left sort of in the clinical purview?

Dr. Dawson: That would be a good question for Sue and it has been posed to her and I've been - I'm wracking my brain to remember what she said. I wanted to bring that up with her.

But it's a good thought and I can't remember whether she was positive or negative in her response.

But, you know, it has, I think, crossed people's mind that since it is a ratings scale and, you know, there are - I mean, one of - I'll just tell you in the social communication

domain the measure that rose to the top is a social withdrawal subscale of the Aberrant Behavior Checklist and it's a checklist that goes from preschool through adult and it could be for anyone and it has - it's a pretty good measure of, you know, social withdrawal.

So I mean, it is possible to develop these kinds of, you know, cross-development types of measures. But it takes a lot of - you know, they do take development.

Mr. Robertson: Geri, I had a question related to this notion on scales or outcomes is that I - I guess maybe more of a comment but I worry a little bit and this kind relates a little bit back to what had been discussed at the previous full IACC meeting is that one of the pitfalls sometimes is that sometimes these outcome measures, these scales, can measure things that are kind of more easily quantifiable or can just be kind of jotted down as a list of those easily readily observable things and not be getting us a big picture of, you know, real - especially, say,

for adults but this would also apply for youth as well - you know, real pragmatic kind of things that are meaningful for autistic people and our families.

So, for instance, for adults that might be things like, you know, does the person have gainful employment - if the person wanted to go for higher education were they able to do so.

You know, are they able to live and connect in the community with other people social connections-wise. So they may have developed adaptations for social difficulties but maybe they desire to have more friendships and don't have that available.

So I just hope that if there's - if there's a scale developed or other kind of outcome measures, you know, using these settings that it would make sure to measure, you know, real pragmatic practical things that are real meaningful rather than just, say, a list of things like, say, eye contact or reciprocal communication that may not, you

know, be as practical in terms of the real meaningful things in terms of big picture outcomes.

Dr. Dawson: Yes, and you know, there are two things that are emphasized, Scott. One is that, and the FDA really emphasizes this, that the measures really need to have meaning from a functional context - you know, how does it affect people's everyday lives?

And then the second thing that's emphasized is that you really need to ask people with autism themselves, you know, what - how they would characterize improvement - that it's really important to talk to people that you're trying to help and understand it from that point of view. So I -

Mr. Robertson: Yes, and that's partly - why I mentioned it partly is knowing many autistic adults. A lot of them will say they just want to have a job like full time - you know, full-time employment.

That's a real meaningful, you know, measurable kind of thing. You know, do they

have employment if they want to have it.

Dr. Insel: This is an area - this is Tom - where there's quite a bit of innovation and so I hope that if we go down this route of talking about outcome measures we're not just talking about paper and pencil checklists and scales because I think, especially for autism, we should be able to do far better than that and get at a bunch of functional measures, including some that you would do in a lab and some you might not - you might do in the real world.

But it seems to me that this is an area that just hasn't been developed in the sense that you've got a lot of good cognitive scientists and developmental psychologists, who are doing interesting research.

But most of that has never translated over to the clinical trials arena, where people are still using checklists. And I think one thing the IACC could do is to bring these groups together and to come up with a set of guidelines with the FDA's encouragement of

what it might look like and would improve the quality of outcomes in either psychosocial or biomedical trials.

So I've got a list here. It's - and we've been at this for a little less than an hour and but I thought I'd just kind of make sure everybody knows what's on the menu and then we can circle back on any part of this.

So one item that we haven't talked about is how we will address the next year or this year's update to the Strategic Plan. So we will have to spend a little bit of time talking about that.

We talked a bit about from the previous meeting and just slightly today about *DSM-5* issues - both what it means for a new definition of ASD as well as the social communications disorder.

We've talked about comorbidity and the unmet medical needs, particularly in the adult population, and Lyn has talked about the need to think about kind of a research framework around unmet medical needs and comorbidity for

autism.

We talked about the - just the quality of clinical trials, the use of common data elements, outcome measures including everything from sensory processing to functional measures.

Geri brought up the need to have a research repository of research evidence that can help to inform payers whether it's insurance - private insurance or Medicaid - about what is the evidence base so that we actually have a way of affecting evidence-based practices and clarify what's worth paying for.

And Anshu brought up this really interesting idea of developing a toolkit for either diagnosis or for monitoring response in clinical practice, something that doesn't exist currently.

So that's a list of about six items. If we think about how you want to work as a group before we circle back to any of these are there - is there anything else that we should

consider within our purview as this Subcommittee, something you'd like to accomplish let's say over the next year or 15 months?

Dr. Dawson: Tom, one of the things that I hear from the community that is a high priority and I just want to - I don't know how we should address this in terms of this Subcommittee but the, you know, the role of environmental risk factors and, you know, its innovative strategies for studying environmental risk factors, understanding - you know, epigenetics is certainly getting a lot of traction in autism, and then in general how you interpret and what is the meaning for our community of the environmental risk factors that have been identified.

So we get a lot of questions around, well, you know, what should we recommend to women about folic acid and, you know, what should we recommend to women about taking medications during pregnancy.

And not to say that we can take on those

things but these are things that are very much on the mind of our community is how the environment plays a role in terms of risk factors and I just - and I know it's also an area that Lyn has pointed out a number of times that we still haven't, you know, made that much progress in.

So maybe it's just a matter of when we go back and perhaps try to prioritize that we can keep that in mind that it's still an area that we need to get better understanding of.

Dr. Birnbaum: This is Linda Birnbaum. I totally agree.

Dr. Insel: So that's number seven. Any other issues that we should put on the list?

Ms. Singer: No, but can we talk about combining some of the issues because I think that - this is Alison Singer. I think that one of the things that we have never done with regard to the Strategic Plan is we have never identified priorities.

When you look at the Strategic Plan each of the directives appears to be equally

important as all of the others and I think it would be worthwhile in this iteration of the plan to try to go through and talk about the issues that Jan has raised.

Should we reprioritize certain areas of the plan based on what has been done, what hasn't been done, what has been done successfully, and what has not been done successfully?

Ms. Redwood: Alison, this is Lyn and I agree with that 100 percent but I think to be able to do that is going to take a good, at least, day or two to go through each of these objectives and try to understand what information have we been able to obtain over the last 5 years and whether or not that objective has been met, as Tom said earlier - whether or not we really want to continue resources.

Is that the wrong question to ask to begin with and then once we do that I think what we have left we can then prioritize. I think it'd be difficult to do now without

actually going through the plan to figure out what we've accomplished.

Ms. Singer: I agree. To me, that's where we should focus. I mean, you and I and Geri, this is now the fifth plan that we've written and we've never gone through and then prioritized or examined the areas where the plan has been effective in making change in terms of the research priorities.

We've never gone through and looked at what was accomplished. We're always adding objectives but I don't know that we've actually looked and said this was accomplished, this was successful, this was unsuccessful. So I agree with you, Lyn.

Ms. Redwood: Yes. We've got to do that.

Ms. Crandy: Let's make that number eight.

Ms. Singer: I mean, I think we can do that as part of our congressionally-mandated required work on the Strategic Plan this year is to go through and evaluate and prioritize.

Dr. Insel: Yes, this is Tom. Just to

clarify, this is number one. This is - we are mandated to do this so we have to do an update of the plan and we heard this, I think, Alison, and you and Lyn brought this up at our last full meeting that if we're talking about an update maybe that most critical thing to do would be to set some priorities. Out of the 78 objectives where are we and where do we want to go going forward?

Remember, we have the Portfolio Analysis that tells us kind of what's been funded but we don't have any actual mechanism to say what has been learned, what's been accomplished, and as Lyn suggests, what maybe was important 3 years ago but is less important today. And so we should just shift in a new direction.

Ms. Singer: I also think that we have to look at evaluating the plan through the same lens with which we wrote the plan, which was we took a very consumer-focused approach when we wrote the plan.

We looked at it from the standpoint of how real people with autism and their family

what questions they might ask with regard to research.

And I think when we evaluate the plan we have to look at the value or lack of value to real people, which is not necessarily counting the number of publications that have come from the research.

It's really looking at the research and saying where have we been able to create real value that has improved the lives of people with autism and their families.

I don't know what measure that is but I think that's something that's really worthwhile discussing.

Ms. Redwood: Alison, if you go back to the vision statement, we actually have in there that the Strategic Plan will accelerate and inspire research that will profoundly improve the health and wellbeing of every person on the autism spectrum across the life span. So I think that's sort of the metrics we evaluate our accomplishments.

Dr. Insel: If we do that what would be

the best process for this?

Ms. Redwood: If you look at each of these research objectives, Tom, and you determine, you know, number one, was it accomplished and if it was accomplished what did we learn, and then you take it a level further and ask did what we learn really help to improve the health and wellbeing of an individual with autism.

That's sort of the focus that I hear Alison saying that we wrote the plan with and that that's how we should evaluate it.

Dr. Insel: Let me just think through that a little bit more with you. I mean, is the process to bring a group of experts together to then pose that question to them?

Do we bring a group of consumers together or a group of both or what's that - I'm just trying to understand how the Subcommittee wants to structure this to get it done and is this what we want to do for 2013 as our update or would this be sufficient.

Ms. Redwood: Tom, I think it's fine

after having been at this for 5 years that we really dig in and see what we've accomplished. So yes, I do think that's what we should do for the updates.

Dr. Dawson: Does that - would that be alongside of the idea of prioritization or would the prioritization perhaps come out of the, you know, evaluation of what we've accomplished?

Ms. Singer: I think when we look and see what we've accomplished we can - or we can prioritize. We would be - it would be silly to prioritize something and then determine later that it's been accomplished.

Dr. Dawson: Right.

Ms. Singer: So I think - one thing to get at this would be in the past when we were writing the plans we would bring groups of experts together to work on figuring out where the gaps were and where the needs were, and now I think we could bring the same groups of people together to say what have we accomplished over the last 5 years and what

needs to be the priorities for the next 5 years.

Dr. Batra: And Alison, to piggyback on the - this is Anshu - I mean, I think it's important not only to have the research experts but also, I think, consumers.

I think you've got to have, you know, parents - families who - you know, practitioners who are in the trenches who are affected by this and, you know, may - you know, will really be able to shed some light into what really what's critical in terms of need and what has really helped them. So -

Ms. Singer: Absolutely. That was just an oversight. I did not mean to say that stakeholders and other constituents should not be part of it. Absolutely.

Ms. Redwood: I'm also wondering, one of the things that I asked for previously was if we could look at cumulative funding in terms of each of these objectives because we wrote these objectives to be measurable and time-bound so we could actually go back and more

easily evaluate them and, you know, whether that's going to require bringing in some outside staff or expertise to do that.

But I would like to see cumulative funding and then a list of the projects that have been funded, what the results were of those and then we could take that information once we pull it all together and present it to, say, this sort of focus group of experts in the field, along with consumers.

Dr. Batra: So Lyn, this is Anshu. It's sort of an accountability report is what you're suggesting.

Ms. Redwood: Yes, I guess along those lines, Anshu.

Dr. Batra: High time for that. Absolutely. Where has our funding been going, what have we gotten out of it and how do we need to or where do we need to now, you know, shift or emphasize? Absolutely. Accountability.

Dr. Daniels: This is Susan. I'd like to address a little bit of what you were talking

about, about cumulative funding.

One of the challenges that we've had in the OARC we initially wanted to do cumulative funding but one of the problems is that these objectives have changed around every year and so things have been added to the same objectives or they've changed in their order and their composition and so it's really hard from one year to the next to measure because there have been changes.

So they - it's something that would be pretty difficult to do but if the Committee wants to try to attempt to do it we could provide you with all the data from all of the years and you could try to put it together. But for us, we've looked at it and it's pretty tough to do, given the changes.

There are certain ones that may have stayed the same all 5 years but some of them or most of them have had some kind of change.

Ms. Redwood: Susan, I started doing that for this part of the update to question three and there were new initiatives that were

added.

And so when I put this in a chart format and I had each year like 2009, 2010, 2011, it would just be new added. So if you didn't have something during that time and it had a new time frame and it was an objective written say in 2009 that wasn't in the 2008 plan it was easy to look at that and tell it was a new objective - that we could still determine whether or not we had accomplished that objective.

I mean, there's - you know, like the one I mentioned a few minutes ago, which was to convene a workshop that was to be completed in 2011. It would be really easy to look at that objective and determine whether or not we've met it.

So I agree, some of them will be more complicated but some of them will be really pretty easy to do. I started doing it myself. It's time consuming but it's not impossible.

Dr. Daniels: Well, the Portfolio Analysis already does some of that and so the

things like workshops, which I think there were three of, those were pretty easy and those were accounted for in the Portfolio Analysis.

But many of the more complex ones, especially ones where the text was changed and things were added and the recommended budget changed from year to year, it will be a little bit challenging.

But we have all the data and are perfectly willing to provide it to the Committee to look through. It's also a huge amount of data. If you want, like, all the projects and so forth we have it all available and would be happy to provide it.

Dr. Dawson: I guess theoretically one could have - I'm just brainstorming here - some Work Groups by topic area.

So within each topic area you have X number of objectives and that what one would do is to - for a specific objective look at what funding by NIH or, you know, I don't know whether we want to get down to the science in

the Autism Speaks - it gets more, and the Autism Science Foundation, you know, do we get all of the funding that has been done in that area or just NIH or Department of Ed.

But in any case, you could determine whether funding had been directed to address that objective and then, you know, the next step would be well, what was found if studies had actually been completed.

I think one of the things - we have done outcome analyses of the Autism Speaks grant and one of the things to keep in mind is that, you know, it takes projects time to get done.

So you fund a grant and, you know, a 3- to 5-year grant publication may come out, you know, in the 5th year or 6th and so, you know, sometimes things take time to get to fruition.

So really looking at, you know, what the results were, I think, is a pretty big task. Not to say it's not important. I mean, I think accountability is critical. I'm just trying to look at the scope of the task.

Dr. Daniels: This is Susan again. So all

the projects have been counted up and so that's something that we could easily provide to the Committee and we have provided in the form of the reports.

But if you wanted it digested in a different way we could provide it in a different format. But in terms of outcomes that would be something the Committee would need to figure out how they want to do.

Dr. Dawson: And I'm also wondering how is this - how would a more systematic process like that where one, you know, looks through what is the exact amount of funding and what was found and so forth.

Would that be a better process than, say, convening a group of both, you know, IACC members and experts to look at a group of objectives and to assess the degree to which we have accomplished them or, you know, so for example, you know, if there were questions about we need to identify biomarkers for stratification, if you got a group of people together and really talked about what do we

know in the field now that 5 years has passed or however many for the IACC, you know, where do we stand on that question now.

A little bit like, you know, what we did with the update - where do we stand and what do we need. So I'm trying to understand how this process would be different than that.

Ms. Redwood: Well, Geri, I sort of thought that that would happen - but that would be sort of a secondary phase after we sort of went through and called out the objectives we have now, and then the ones that were sort of outstanding are the ones that didn't appear as though they had been fulfilled.

Then we would bring in experts and sort of ask what is known in the field - what are the needs, and families as well, and that would be sort of the second phase, which would then go into the prioritization of the plan.

Ms. Singer: I also - I think that during the process of doing the review, the annual review, Geri, you're right. A lot of these

questions came up.

But a lot of these additional issues were tabled and we said well, we'll hold that off for when we do the update. And that - so falling into that category is really the prioritization.

And I think Lyn is right. There's some steps that need to be taken before we can do a good job with the prioritization.

But each year when we do the annual review we table the prioritization and what I'm saying now - in my opinion, now is the time to put the prioritization on the front burner.

Dr. Dawson: Right, and I guess I'm just saying in terms of the accountability piece there's at least two ways to do it.

One is a very systematic way, where you really try to track down, for example, with NIH or any other funding agency funded an area of research - what did they find and, you know, what are the answers and try to look to publication, to how many publication. You

know, so there could be a very laborious process.

Or you can imagine that a process, where you looked at each objective and you pretty much try to synthesize, you know, what we know and whether we've addressed that objective based on the literature that's out there combined with what's currently being funded and give it sort of a temperature check.

You can imagine very little progress, you know, some progress, you know, all the way to we've accomplished that objective. That's more based on kind of an expert review rather than, you know, a laborious systematic process.

Ms. Singer: Right. And I think what Susan was saying is that OARC, through the portfolio analysis, does a lot of what you're describing as the first option.

And so my feeling would be that we should take a more qualitative temperature-taking type of analysis, as you're describing in option two. We have that -

Dr. Dawson: Yes, that's my sense too.

Dr. Koroshetz: If I can throw out one model we used against NINDS and stroke, we put together what was called the Stroke Progress Review Group and they were divided into 16 different Subgroups, each of which had 10 people in each Group and they, every 5 years, reviewed progress in their area and was published on the web and in journals.

It was a way of keeping track of areas. It was qualitative, not quantitative. But I think if you're going to - I think this is a monumental task, which may be well worth doing.

But I - but I would go towards more of an expert panel, broken down into particular areas for it to be useful.

Ms. Redwood: Could we not do both? I just - I feel like we've spent millions and millions and millions of dollars and we need to be accountable for that, and I think going back through and looking at where - what we've spent money on and what information we derived

from that is really important.

And I have some concerns about bringing in experts in these areas because, you know, my spider sense is that maybe the experts say, oh my gosh, we've just accomplished everything and we've made all these wonderful breakthroughs but in the big realm of things that really may not be the case and that's where I think it's important to bring in the consumers, as well because I know that a lot of the consumers in the community don't really see where those great big breakthroughs have really translated into something that has helped their child.

Dr. Koroshetz: I have no objection to that. I just think that you have to break it down question by question and it's probably for each question it's a fairly significant effort and requires, as you mentioned, a multidisciplinary team of both investigators and patients.

So I'm not saying it's not worth doing. I'm just saying that if you want to - if it's

going to be valuable, it has to be a major undertaking. You can't do - you can't do it short, quick. There's no quick way of doing this.

Ms. Redwood: Tom, is there an Office of Research Portfolio Analysis at NIH?

Dr. Insel: There is but they don't do this. They provide, really, the tools to look at the entire portfolio of like - and which we call RCDC, which is just a research coding effort.

What you're asking is something a bit different and we've had this conversation before. I think it's a really important one and that is we have - in doing a Portfolio Analysis, we've been saying we've funded this many grants for this many dollars in this many places.

What you're asking is so what. You know, what - so what have we gotten out of that and what is useful and what do we know having done that, so that we won't have to do more of that.

We can actually now do something else. And there isn't really a group that does that. That's - I mean, program at each institute does that to some extent, so we try to ensure there isn't a lot of redundancy but it is a different process.

I like Anshu's, you know, name to this as an accountability report because that's - it's really asking what's been the return on the investment, not so much what's the investment.

We can give you that in our portfolio analysis. There isn't anybody that I can think of, who that does that well except folks in program and they don't do it from the perspective of a consumer group. So we would have to establish - we'd have to bring folks in, I think, to help us with this.

It would - I think it'd be useful for us to just for a moment imagine what the final product would look like, how that would be informative.

And so if you took any one of our seven

objectives or seven big questions, what would we be talking about for each one of them that - as a deliverable for this effort?

What would we get from that and we've been talking about prioritizing and, certainly, when you have 78 objectives you got to have some way to prioritize.

But how would you see that in a - in a final document? I'm having a little trouble sort of picturing exactly what this is relative to what we just went through, which is what do you - what do we know, what do we need.

Ms. Redwood: Tom, I see it as being very different from that, in that we would go through each of these objectives and determine whether or not they had been fulfilled and then we could even use this same format for our update and then below it, say, for, let's see, 2009 on a short-term objective we were supposed to look at three randomized controlled clinical trials that addressed co-occurring medical conditions associated with

ASD by 2010 and we had a budget there over 3 years.

If that was accomplished then we can take it off, look at what we've learned from that and decide whether or not we need - what's the next question to ask or is there a completely new question that we need to ask.

So that information will then feed into the update or an entirely new Strategic Plan. But I just hate for us to keep going on with this Plan, funding it when we've not really done an assessment of how we're doing and what have we accomplished and what do we still need to accomplish, and that all feeds into a new plan of priorities.

Ms. Singer: I think what - I think what Tom is asking for is a framework. The way we came up with a framework for the original plan.

I think what you're looking for now is what is the framework of the deliverable that would be the results of this effort and maybe what we can - one framework we can consider is

since the original document is a series of seven questions, the framework for this piece could be how far have we come in answering each of the questions.

Do we know more - are we better able to answer the questions now than we were 5 years ago and why.

Dr. Dawson: So I wonder - I wonder about that if it's going to be satisfying in terms of knowledge generation, which is - you know, with the answering the question versus, I think, what Lyn was saying was, you know, improving people's lives.

So one question I have, when we think about this accountability it's one thing to say, you know, we have an objective that we would understand on genetic grid factors or something and one could say well, over the last 5 years we've actually uncovered multiple genes and we understand, you know, the genetic architecture of autism so much better than we did, yes, we've made progress. But the question is has this had any impact on

people's lives.

And so I think that's going to be, you know, it's going to be a more - it's a very important task but I think we're going to have to put our thinking caps on of how we would assess that.

You know, to me it seems like the only way to come close to that is to use a qualitative expert and community participation process, right, where you get a group of people, who are the right people in the room, that know what has been accomplished that know the field and that area as well as people where it could impact their lives and come up with a consensus statement.

So, for example, you could say well, you know, now very soon the American Academy of Pediatrics has - is about ready to endorse the, you know, use of micro array or as part of the diagnostic work-up, which is going to impact health insurance coverage and in fact 50 percent of patients get their micro array testing paid for by insurance.

So you could start to say, as part of this qualitative analysis of how some of this information is becoming translated into, you know, the real world and to the clinic and going through people's lives.

We have to have a group of people on that panel that represent, you know, both the knowledge generation piece which is, you know, the scientists, all the way to just consumers and then to come up with some kind of an assessment that's qualitative that might then you end up with a, you know, great progress, so-so progress or almost no progress made in this area.

Dr. Koroshetz: Do you feel that there's enough areas where there's been major progress? You know, we feel here with a lot of different diseases and we've been doing research for 30 years.

I don't think we've really changed lives yet. But in autism do you think that there's already been a major improvement in people's lives?

Dr. Dawson: Well, I think that it's all relative and depends on how you measure it. But let's just take something like, you know, Lyn was talking about medical comorbidities and absolutely that's a huge area and we need a lot more research.

But I know that when I first joined Autism Speaks there was controversy about whether children with autism or adults for that matter have GI problems, right?

Do they even have any more GI problems than the general population - that was the big question - and most people believed they did not. It's just something the parents kind of thought they had more but they didn't.

Well, so we've gone all the way from that to in - you know, in the fall in the journal "Pediatrics" were the first physician - empirically-based physician guidelines on the assessment and treatment of GI conditions for autism.

So you would think that, you know, there still are people that are going to use those

guidelines. But, you know, that I would say is pretty - you know, it's not where we want to be but there's been some progress.

Dr. Insel: Geri?

Dr. Dawson: How many - how many physicians are using the screening tools that were developed, for example.

Dr. Carey: This is Matt Carey. Can I throw in, I guess, three comments? One is - I mean, when Geri's describing, you know, a group of experts and community members and everything else, I mean, isn't that us?

Doesn't that describe the IACC itself? So I mean, you know, why are we looking for something outside?

The other one is kind of two sides of the same question. We talk about progress towards goals and the goals are written as we will fund this, not, you know, we will get a result from that, and there is some sort of progress you have right there at the red light, green light, yellow light thing that's already set up to kind of monitor that.

I think the aspect - the extra dimension of, you know, what are the results back to us that, you know, to the - you know, as the community, that's the big question.

But I think part of this, you know, we are - you know, there is kind of a measure going on. But it's - and, again, based on that - based on the language we've got, which is fairly closed-ended and it doesn't have that result-based thing of, you know, question of - you know, it's research. You can't say we will fund and answer this question.

You know, we're going to fund it. But I mean, we do need to know did we do a good job of that and did we answer these or are we on track to answer some of these questions.

So anyway just throwing - especially the first one out. I mean, really, are we spending a lot of time really describing ourselves as a Committee. I mean, we've got the - we've got, you know, community members.

We've got, you know, experts. You know, it's another task and I don't know if, you

know, for us to do but it sounds like we're describing ourselves.

Dr. Koroshetz: Just from my point of view, you know, when we did this for stroke I think we had 150 people working on it.

It depends on how, you know, if you really want to do it seriously it's a - you know, you have to really look at everything and have a Group for each question and so it gets - it gets fairly big.

Dr. Batra: Walter, this is Anshu. Can you just give me a small example of that in the stroke arena, which you just mentioned?

Dr. Koroshetz: Yes. I actually just sent an email around, which has the website. It's a little bit - it's basically started in, like, 2001 and a Group got together and just kind of broke the - all stroke research field down into about 16 Groups and then every 5 years they would just analyze all the progress that's been made in the area and then also like we did is basically say where are the new areas that have come up are.

And it was - it was the same themes over and over again. The Groups kind of changed a little bit but there was a core that was there the whole time.

Ms. Crandy: Well, but I think the comorbidity piece is - it's not - they're diagnosing autism but then they have to look for those other conditions - that not every kid will have those and so they don't generally do those medical studies on our kids, unless the parent complains that I think my kid has stomach problems.

Ms. Singer: Walter, what was the deliverable of that - of that Group?

Dr. Koroshetz: That's a good question. So the deliverable was to basically inform the institute and the scientific community about what the progress has been in terms of the investments at NIH and primarily the American Stroke Association have been making.

Now, that being said, what we finally did after 15 years is because it was so hard to dissolve and do something with, we forced

them to come to a prioritization process whereby the 16 Groups came up with total of nine major recommendations.

So but that was the basis on which we could do that. Without having had all that groundwork done we wouldn't have been able to get to a logical prioritization process.

Dr. Insel: Geri, this is Tom. At Autism Speaks you go through an accountability exercise, don't you, every year?

Dr. Dawson: Well, so we use a system of just - it's called outcome analysis and I was just looking up - I just got a report from the Faster Cures Association yesterday on innovative ways for assessing - you know, doing outcome analyses. So I'm going to look that up and hopefully send it around to you.

But ours really was - it was based on a web-based inquiry tool, where we go back to the investigators themselves to understand what was accomplished with the funding that we gave them all the way from, you know, of course, publication and dissemination, you

know, in terms of the citations of that publication but also people funded and did they stay in the field. So we're interested in bringing new talent and keeping them in the field.

But then we actually had them describe the impact - you know, did you develop a new treatment, you know, and empirically validate it. And they had a way of both describing the impact and then we have an impact rating in terms of, you know, how much significance we think this really had.

So, you know, it's not perfect and I'm - you know, I do think that a lot of the nonprofits are struggling with this in general and there are starting to be more creative ways of doing it. But that's how we've been doing it.

Dr. Insel: It is a challenge because the nature of science is that it often goes very slowly relative to the needs of families and you don't want to end up condemning an area that may have enormous long-term outcomes

because it just is taking longer than you would like it to.

So it's - you know, this is - this is not a trivial question about how best to do this.

Dr. Koroshetz: Yes, on the other hand, I would say that sometimes you keep doing this after, you know, 15 years and you say gosh, we haven't really gotten to second base yet.

So, you know, let's just really make a big effort. So it is - I think it is worthwhile, I mean, to track and see where the progress is and where it's stagnant because it helps you, you know, basically prioritize eventually on where to make a big push.

Dr. Boyle: Yes, that's what I was going to say. I mean, I really think the - helping with the prioritization is really important.

Dr. Insel: And you'll remember the - in the Strategic Plan in that first section, where we talked about the values, accountability is a key part of it.

And yet in 5 years, other than the

Portfolio Analysis that does account and has the color code for whether we've done the funding or not, there's no - there's never been an assessment of impact.

Dr. Boyle: We could try. This is Coleen. We could try and just pilot one of the questions and see how it works. You know, have a small group of us work together, come up with a process.

Dr. Koroshetz: Yes, I think that would be - that would be very instructive and -

Ms. Redwood: Coleen, I tried to do that with the update. I do think it's doable and I think we need to make a commitment to do it.

Dr. Boyle: So Lyn, you cut out on me. I'm sorry.

Ms. Redwood: I was just saying I think we just need to make a commitment to do it. I see piloting it but I - you know, maybe all of us tonight could just sort of look through it and see and maybe divide it up the way Walter has described it or, you know, into groups.

But I think we need to make a commitment

to do it. I would hate for us to meet and come back and say oh, it's too hard or it's too tedious.

I think we could do it and I think to Tom's question about we wouldn't want to, you know, throw out something because it was taking too long to get answers, you know, and so when you talk about investing in a long-term strategy and a short-term strategy, so you diversify your portfolio, I would think you would do the same thing with research, where you had long-term projects but then you also had more short-term high-risk high-reward projects.

Ms. Singer: So I think that the value of the pilot is not to determine whether or not to go forward with all the questions but rather to really get at some of these issues of process - what are the best - what are the best methods to use in order to answer the question.

Dr. Boyle: Yes, that's what I was thinking, yes. And maybe choosing this

question. Maybe not the first one.

I was just thinking one or maybe even the first one because the first one has, you know, the - has less of the genetics aspect of it and is a little bit, I think, easier to actually maybe work out the process on.

Dr. Insel: Coleen, am I hearing that you're volunteering to help us do this?

Dr. Boyle: Well, I'd be happy to help.

Dr. Batra: I'll volunteer. I'll help.

Dr. Insel: Great. I like the idea, very quickly - and I don't think this takes endless hours - I think rather quickly, you know, a Group could take a look at question one and feedback to the rest of us how that works and what needs to be done and what would be a reasonable process to get this done.

Who would need to be in the mix? How would we get the information that we need? What kind of time frame it would take?

Would we have to have face-to-face meetings or could we set up webinars to get this done? Those kinds of issues would be

really helpful to know knowing that, again, we have to deliver the next update in 9 months, something like that.

Dr. Boyle: So and then, I guess, you know, my thoughts hearing the various suggestions I don't feel like it needs a full meeting. I think, you know, we could set up maybe a 2- or 3-hour conference block, whoever wants to work in the Group.

Maybe do some homework beforehand and, again, I'd have to kind of go through question one, kind of get a sense of it and then we can report back to you. All I'm trying to get a sense of is, you know, what the process will be and what the deliverables would be from it.

Dr. Insel: Yes, that's terrific. So I think I heard Alison volunteer. Who else?

Dr. Batra: I'll help. Anshu.

Dr. Insel: Is that Anshu? Okay. Anybody else?

Ms. Redwood: I'll help, Tom. This is Lyn.

Dr. Insel: Great.

Dr. Carey: This is Matt Carey. If there's room, I'll help.

Dr. Boyle: Always room.

Dr. Insel: Always room at the inn.

Dr. Dawson: If you feel that I - that I would be helpful I'm very happy to be on.

Dr. Boyle: Thanks, Geri.

Dr. Insel: Who was that?

Dr. Dawson: Geri. I'm happy to participate if you think it would be helpful.

Dr. Boyle: We need some folks to be the sounding board too so -

Dr. Batra: On another note - this is Anshu - I wanted to ask about something Geri had mentioned about sometimes these studies can take a long - you know, many years. We may not have results or outcomes in a timely fashion.

Any thoughts on how we can help speed that up in terms of the - whether it's the process, whether it's, you know, design of studies, whether - whatever it is.

I'm throwing it out there because that's

a big issue in terms of getting results and then getting it out to the - to the public.

Dr. Insel: This is Tom. We talk about this all the time at NIMH and I think where we've come around to over the years is moving from worrying about how to get research into practice and now much more focused on how do you get practice into research.

So bringing in especially the Kaisers and the Group Healths and the very large practice networks and using electronic health records and using what's now called the Learning Health System, using an approach that actually does research within a practice setting, so that every patient becomes, in some ways, a partner in this effort.

It's hard to do without the electronic health records or without a bounded healthcare system. It's very hard to do.

But just as an example, we have something called the Mental Health Research Network. It has 11 million patients in it and it allows us to very quickly answer certain

kinds of questions that can then be almost immediately put into practice.

So it's not perfect for every kind of question that comes up but it's one of the ways, in which you can accelerate this process.

Mr. Robertson: Tom, can I make just a quick comment related to that? This is Scott Robertson.

Is a part of that which you're describing also taking reports with, like, community-based participatory research where you involve the community members - you know, the stakeholder groups as active kind of partners in the research process and you're making sure that things are kind of practical at the beginning?

Is that partly what you mean also with the, you know, bringing, you know, the - bringing practice into research, not just research into practice?

Dr. Insel: Yes, that's another side of it. That's a little different than what I was

talking about but it's another way of thinking about in that case one of the most relevant questions to be answered.

But often what happens even with community participatory-based research or community-based participatory research, which is another major movement in clinical research, I mean, is that you're still often bringing communities to academic health centers where you're trying to get the science done. I'm not sure that at the end of the day that's as efficient.

It's just going into where the healthcare is given and making that the - making that your laboratory.

Your laboratory has 10 million people in it, who can very quickly answer questions that are relevant that - and then get implemented as part of the actual project.

So it might be - if it's of interest we can bring some of the people who have pioneered this who can talk about where it works, where it doesn't work.

It does seem to me that in autism where most families - at least for kids with autism are plugged into pediatrics practices of one sort or another there may be an opportunity to do this.

But you have to look at the numbers to make sure. Certainly, the Lewin Group Study, which was a bounded group of Kaiser healthcare - Kaiser-insured patients - there were 33,000 kids with autism in that project.

So if you set it up in the right way you can imagine getting a lot of information out from people, who are already in the system and who would contribute with the idea that their healthcare providers are collecting the data with the subjects and that goes right into practice.

So it's worth thinking about. Maybe it would be an interesting topic to bring to an IACC meeting if people want to hear more about it.

Dr. Dawson: So Tom, I would absolutely love to have us, you know, have that as a

topic at one of our IACC meetings and I think it really relates back very nicely to the first topic around developing the database, you know, for evidence-base for treatments.

And in fact I was at a meeting a week ago and I heard someone - her name is Laura Esserman who's the director of breast cancer -

Dr. Insel: I-Spy 2. She does I-Spy 2.

Dr. Dawson: Yes, she does I-Spy 2 and -

Dr. Insel: That's a great example, yes.

Dr. Dawson: - she is - I was just blown away by her talk and how they're - and I guess what I was mentioning earlier about this idea of conducting research in the place where it happened. It would be great to have her come talk.

Ms. Singer: Geri, what was her name? Laura what?

Dr. Dawson: Laura Esserman, E-S-S-E-R-M-A-N and this panel was - the panel was called "Leveraging Innovation and Technology to Accelerate the Development of Treatments" and so she -

Ms. Singer: Love the title.

Dr. Dawson: Yes. So it was - it was all lots of different ideas about how you use technology to accelerate, you know, treatments and research.

Dr. Insel: What Laura does is a little different. I mean, there the idea is to create a clinical trial, in which it's totally adaptive.

So depending on a - whatever biomarker you have, if you go down lane one versus lane two versus lane three and then if you don't respond very quickly you shift lanes so that they're always optimizing the treatment within a trial so that somebody gets the very best treatment for them.

And if it's a big enough trial you then get answers for all of the different options of different kinds of treatments.

So I-Spy 2 is a great example of doing that for breast cancer. We fund that through the biomarkers consortium and it's been a - it's been a - kind of a model that we've been

interested in developing for other disorders.

The problem is that in autism we don't have biomarkers to drive that kind of an effort. So we have nothing to adapt with.

Dr. Dawson: So, you know - I know that she's known for I-Spy 2 but this - her talk was really more about broader - she's working very hard on this idea of just how you use the electronic medical records and you use, you know, research that's happening in hospitals or clinics, you know, as your way of conducting clinical trials, rather than outside of the clinical care setting.

Dr. Insel: Right.

Dr. Dawson: It really wasn't focused on the I-Spy 2 project.

Dr. Insel: Yes. We have a whole program that we've developed at NIH in the common fund. It's called the healthcare collaboratory or healthcare systems collaboratory effort and it works with these large healthcare systems' electronic health records to do practical trials of various sorts.

And just as a, you know, an example of the kind of science you can do is the big question in the realm of hypertension is it better to take your medicines in the morning or at night, and we can quickly randomize 100,000 people, who are all taking medicine.

We just make sure some - half take it in the morning and half take it at night and within a month or a few months you'd have an answer to a question that actually could have enormous healthcare consequences.

So that's - there's seven of those trials. There isn't anything else directly relevant to autism because nothing came in for autism.

But there are a couple that are not too far off and the group that Greg Simons runs at Group Health in Seattle may be the closest match to what people were interested in in autism and that maybe having him come to talk about how do you do these kinds of large scale efforts. They don't cost very much.

They involve sometimes tens of thousands

or hundreds of thousands of people and yet they can answer questions very quickly and some of the questions are - really do make a difference in healthcare. So that might be a - he gives a spectacular talk. It might be fun to hear from somebody like him.

Dr. Dawson: You know, the other person too would be Paul Law because I think (inaudible) the first clinical trial on the IAN Network, right, where all of the patients are recruited through the IAN Network and sent their - omega 3 and fatty acids - and I thought that was very innovative too.

These are all just ideas for accelerating research. I mean, maybe that's the topic, right.

Dr. Insel: So maybe - why don't we think about doing a panel for the IACC for a full Committee meeting about the kind of innovations that are out there right now? I think that would be really interesting.

Well, we're almost at 4 o'clock. I think the meeting is scheduled to go a bit longer

but I want to just make sure that we've done our homework and the most important thing we had to do was to talk about the updates of the plan and I think you've given us a way forward - Coleen, thank you - to at least pilot a way of considering 2013 as the year of accountability and we use this year, this update, to really look at what we've accomplished for each of the seven questions.

We need to still define that process for doing that and what the deliverable will look like.

But I'm hearing from the Subcommittee that that's the way forward in the short run and we could plan to spend just a very small amount of time in the next couple of weeks getting this Group together under Coleen to feedback to us how best to actually move this forward. Would that -

Dr. Boyle: That sounds okay to me and I was going to hope I could twist Walter's arm since he has been extremely helpful in terms of the experiences around stroke.

Dr. Koroshetz: Well, stop twisting. I give in. I give up.

Dr. Boyle: Okay. Thanks, Walter.

Dr. Koroshetz: Sure. Happy.

Dr. Insel: And then I'm hearing that at least one thing we can do in the short-term is to plan for a panel for the full IACC meeting around innovations and maybe especially related to clinical trials.

The other topics that came up around comorbidity, around *DSM-5*, the quality of clinical trials - how we inform payers and get the evidence base we need, the tool kit, and environmental risk factors. Those are all areas that have been raised here.

How would you like to handle any of those or how do you want to take those forward, or should we just bite off the Strategic Plan and this panel as a first step?

Ms. Redwood: On which panel?

Dr. Insel: This would be the idea of having a panel at the IACC meeting on innovations and clinical trials like we were

just talking about with Laura Esserman.

Ms. Redwood: Okay. Could we also - I mean, the other thing she read off I think those would also be amenable to panels at the IACC meeting too or have people come in to specifically talk on this topic, to be able to -

Dr. Insel: Yes. I think the comorbidity ones, Lyn, that you've brought up several times is a general interest and it seems like in almost every meeting this comes up in some form.

So I do feel like we should do something substantial there. I don't know if it would be sufficient to do that as a panel at the IACC meeting or maybe that would be a way to start.

But I think all of us have heard loud and clear the need both in terms of adults - there's enormous unmet medical need but also within certain populations of children on the spectrum where they don't seem to be getting the healthcare they need because people assume that all symptoms can be explained by having

autism.

So I'd like to think about how we address that in the short term.

Mr. Robertson: Tom, also a comment related to the innovations area - is there a possibility that maybe you and other people, who will represent the NIH agencies, maybe could put together any other kind of interesting things like you mentioned in terms of that, you know, the innovative research kind of efforts in terms of bringing together large organizations.

Are there other efforts like that within HHS and maybe other agencies that we should be tapping and looking at and, you know, that we haven't really thought about and discussions that could be - you know, we just mention at the IACC meeting as things to consider for the - you know, that are out there that maybe people haven't thought of as relevant possibly before.

Dr. Insel: So can you unpack that a little bit more? What are you - what agency -

Mr. Robertson: Well, what I mean is you were - you were mentioning, for instance, that the research effort in terms of bringing into practice the large companies to be involved in connection as far as research efforts.

And I wondered if there were other kind of things like that going on within HHS that, you know, could be relevant to our work that, you know, that people don't think about as much as people don't - there hasn't been a connection to autism before is what I mean.

Dr. Insel: Yes. No, I think that's a great question. I'll have to give that some thought because I'm not - I'm not sure -

Mr. Robertson: Because I'm just - I'm just thinking that there might be other things out there like that, that if we looked broadly across HHS and maybe - HHS and other parts of the government, you know, maybe there are other things out there too that, you know, already going on that, you know, we could kind of draw from to - you know, to incorporate in our work.

Dr. Insel: Yes. I think definitely worth considering and nothing comes to mind but I'd be interested if there are innovations or experiments or things going on elsewhere within the department that should be looked at.

There's certainly a huge amount happening around the Affordable Care Act and this may be a good time to mention and maybe this would be a, you know, great thing to bring to an IACC meeting, the whole innovation effort at CMS, where there's something called CMMI, which is the innovative - I guess it's called the Center for Medicaid/Medicare Innovations Institute or something like that which has been spending a lot of money or will be spending a lot of money on new projects to test out in the community, new approaches to healthcare.

This is a huge, huge investment that CMS is making and lots of pretty spectacular ideas are going to be tried out. Unfortunately, there wasn't a single application for autism.

Dr. Batra: Wow. That's - this is Anshu - that's pretty baffling to me. Can you just clarify what exactly this - the CMMI is in terms of how it would be applied in the real world?

Dr. Insel: This is kind of one of those things that had never happened before. CMS has traditionally just been in the business of putting money out the door to match what states spend on Medicaid or to provide Medicare services.

What happened in this current administration is somebody asked the question well, isn't there a better way to do this and how do we know that what we're spending money on is being used efficiently and wouldn't it be good to take just maybe one or two or three percent of our budget and do some experiments and trying to see if we could do things even more efficiently.

So that was the impetus for creating this innovation center within CMS and they have had a number of calls for applications.

Their budget is actually enormous and so they're putting a lot of money into projects that are much more real-world than what NIH normally does although many of the things they're doing we're doing collaboratively with them.

They've had several calls for applications. The most recent one is from state - you know, state systems, state Medicaid and mostly state Medicaid directors to try out new projects or new approaches to care.

And as I said, I think they got lots of great ideas. Some were focused on diabetes or collaborative care. They got many in the realm of substance abuse and mental health. But there was not a single application for autism. And I don't know what that means but it's worrisome.

Dr. Batra: It is worrisome because I mean, California for one is just bursting at the seams in terms of its fiscal irresponsibility and I just - I can't believe

that the Medicaid system - that the regional centers in California haven't reached out to look at their system and see how they can become more efficient. It just - it baffles me.

Dr. Insel: Yes. I was so surprised by this that I went to them and said what gives. You know, why isn't there - why hasn't there been any interest. They didn't have any answer at all. They just - they were -

Dr. Batra: I'm more interested in the dissemination of information issue. You know, maybe they need to reach out to the state directors of these regional centers and, you know. I mean, I would suspect -

Dr. Insel: Well, those are the people who applied. So, I mean, they obviously knew about the program. I'm not sure why autism didn't surface as an area.

But anyway, the door may still be open. I'm sure they'll be doing other calls over the next several months and so it's worth hearing about that.

But we could bring somebody from CMMI to talk about what the program is. It's incredibly important for autism so it's -

Dr. Batra: Because it's such an underserved population. You know, the Medicaid population in this country are probably the, you know, most underserved and so I'm so amazed that the autism community hasn't reached out.

Dr. Dawson: Tom, could you send us a link for information on that program, or Susan?

Dr. Insel: Sure can.

Dr. Dawson: That would be great.

Dr. Insel: Yes. We'll put that out there and I - the - I don't know what the current calls are, just what RFAs they have out. But it's definitely worth looking at what they have supported.

These are very large-scale. These are multi - tens of millions of dollars for each project. So these are big and but very relevant to how healthcare is delivered.

Kind of goes back to Scott's question about how do - how do we make sure we're linking carefully to practice and to communities.

Dr. Koroshetz: Yes, I was actually up there on Monday talking to them and besides - the other - the other area that they are looking into is the accountable care type of bundled payment systems, whereby it gets away from fee for service and you try and put together, you know, the best possible treatment program for a patient that would improve quality and reduce cost.

So they are looking - they are definitely looking for innovative ideas and I think it depends a lot on who comes in. They're not - you know, it's really has to - there has to be a lot of motivation - groundswell of motivation to apply and get these things running.

Dr. Insel: So in our last few minutes I'm kind of looking for a to-do list here for our Subcommittee. We've got a few things and

I'll circulate some of the things we just talked about.

Is there anything else that people want to take on in the short term? I'm not looking for work but I want to make sure that we move forward in areas where you think we have the most traction.

Dr. Dawson: So Tom, I'd like to at least develop a strategy for how we want to address the *DSM-5* and social communication disorder issue, whether that's going to be making recommendations more in terms of, you know, a letter from the IACC or if it's going to be the need for research.

But I really - I think I'm - this is an area of great concern in terms of the impact that that change in diagnosis will have and not only on the prevalence estimates but also on access to care because, for example, the insurance reform effort that Autism Speaks has taken on are really based on a child or an adult, you know, having the diagnosis of autism or autism spectrum disorder.

And now what they - you know, with the social communication disorder we lump - we've kind of cut off the very tail end of the autism spectrum and, you know, what's going to happen to a child who now gets a diagnosis of social communication disorder.

And I think there's some research now that can help us understand and make a more informed set of recommendations around this. So I'd love to have at least some kind of a strategy around that issue.

Dr. Insel: Other thoughts about this?

Ms. Redwood: Geri, since you're most familiar with it could you - would you mind spearheading that initiative?

Dr. Dawson: Sure. I would be happy to do that. But I would love to hear from the Group what your thoughts are on the best way, you know, forward.

Is it a Working Group and meet separately and come back with recommendations or, you know, just coming up jointly with a strategy?

I would imagine that Coleen might want to be on this one too.

Dr. Boyle: Yes. Well, I am bringing the issue around to the severity indicator for *DSM-5*.

You know, we've been - there's been increasing interest in terms of capturing severity so we would love to get a sense of how well that new aspect of *DSM-5* really reflects functioning and severity and the conversation we had earlier.

Dr. Dawson: Right. Well, and the other thing that - so the field trial if you - if you really drill down on the data from them and then there's some other data that's in press that I can't, you know, talk about in detail but I can tell you that they're very consistent with the field trials, suggests that quite a few children, who previously had a diagnosis of PDD-NOS now will have a diagnosis of social communication disorder.

Unless you include social communication disorder as part of the spectrum, you know,

you will affect the prevalence estimates because, you know, our prevalence estimates have included those kids. So, you know, I think it's - I think these are pretty significant issues, especially when you've been doing surveillance over time and also, you know, if these children were the ones that had PDD previously and we know that children with PDD-NOS do respond well to behavioral intervention, then one might want to recommend that they receive the same kind of interventions at least until we have a better understanding of whether they should have different intervention.

Dr. Insel: This is an area where it's hard not to get nervous, given the way that states are trying to cut services.

Dr. Dawson: Yes, I should - I should say.

Dr. Insel: You know, it would be really great to build something in before the change before May or whenever that is and then to monitor this in real time and find out, you

know, in a particular state system what actually happens in terms of access to care and coverage.

Dr. Dawson: I think that's a fabulous idea. I think, you know, we have talked about at Autism Speaks having a place on our website where families can report, you know, not getting access.

But I think that it has some systematic data, you know, about how clinicians are using this and also if the child has social communication disorder what are clinicians doing in terms of their recommendations for treatment.

Does this child now just get speech therapy or are they being referred for early intervention? I think these are some really important questions.

Dr. Boyle: Is this something that could be captured in one way through IAN?

Dr. Dawson: Possibly. I mean, that might be a great - you know, maybe this is another one of those like some of our other projects

like wandering, where we want to bring together funding from a lot of different organizations and do an IAN study.

Dr. Insel: So what about if you and a couple other people who might be interested in this were to just think through some options and bring those to the IACC so that we could make a recommendation?

It may be that it's something that will be done through one of these electronic systems or social media or something like that.

But it does seem like we have this unique moment because this is going to happen starting this summer, presumably after May, when they release all the new diagnostic manuals at a mere cost of $80 a copy for the basic text and some, what is it, $270 or $300 and some for the whole package.

So it will happen in 2013 and we need to ask how are we going to monitor the change in practice accordingly and what kinds of problems does this create, which nobody's

really thought through well enough.

So could you - I wonder if you and Coleen and a couple of other people would at least put your heads together and come back to us with some ideas about what IACC might do or what IACC could recommend gets done by others so that we're on top of this.

Dr. Dawson: I'd be happy to. Who else would like to join that Group?

Ms. Crandy: This is Jan Crandy. I don't know if I can. If you allow me to - I'm not on the Subcommittee but I would like to participate on that.

In Nevada we have a BDR right now that's going to be in front of our legislation that we're adding communication disorders to our slot program to make sure those kids get funding.

Dr. Insel: Yes. So that's really interesting. That's exactly what kind of question that's going to be on -

Ms. Singer: What's the program? What's the slot program, Jan?

Ms. Crandy: Our state has a program that funds evidence-based treatment that provides assistance to parents for kids on the spectrum.

So we just wanted to make sure that when kids start getting diagnosed with communication disorders they can still - they can get funded through that program too along with the other kids that have a autism spectrum disorder diagnosis.

Dr. Insel: But Jan, it raises the question of whether all 50 states are going to have to make this decision and I just think given the pressure on state Medicaid budgets and when you look at Medicaid waiver questions this is going to be really a significant issue.

It's not so much a research issue. It's a problem being created through the *DSM* that will have to play out in the services arena. So it crosses over.

I'm not sure how much this Subgroup will have to deal with it but certainly the IACC

ought to be thinking about it.

Dr. Boyle: Yes, I was thinking, you know, should we ask our education colleagues or - the folks from CMS to join us on this discussion or -

Dr. Insel: Yes, I think it'd be great to get maybe someone from CMS like John or -

Dr. Boyle: Yes.

Dr. Insel: - and see if somebody from education could also pitch in. That would be great. And then could we ask you to just give us some feedback for the full meeting, which is - Susan, when is the full meeting?

Dr. Daniels: The full meeting is on April 9th -

Dr. Insel: Right. So -

Dr. Daniels: - and it's fine for - this would essentially be sort of a Planning Group but it's fine for other members that are not on the Subcommittee to participate.

Dr. Insel: Great. Yes. So anybody who's interested just speak now and Geri will take your name down.

Dr. Dawson: I wanted to just make a quick comment about the fact that there was a briefing that was held. I don't know whether others were on it but it was with the *DSM-5*.

Well, it was the APA, DEO and the *DSM-5* care with David Kupfer and the APA president and a number of folks who've really spearheaded the *DSM-5* and they held a briefing for the Consumer and Family Advocacy Group and it was really informative.

They did say that it was coming out in May and that when we had an opportunity to ask questions and when I brought up some of the issues that I just raised, what David said was that they really were very interested in monitoring and understanding the impact of the changes and that they were very open to revising based on feedback or - of course, he would say this but, you know, he seemed sincere that they understand that there's a lot of data that needs to be collected on this.

Dr. Boyle: Do they have any systematic

way of collecting that, Geri?

Dr. Dawson: No, not really. In fact, we're funding two studies and he applauded, you know, that. But I think that this kind of IACC-driven, you know, effort will be well received.

Dr. Boyle: Okay.

Dr. Insel: Yes, I think somebody needs to run the feedback and we have to remember that though they talk about this as a dynamic process it's a book and it's not that easy to publish a new version.

So it's not - it's not a 21st century approach to something like this where you have a web-based version that can be modified based on new information that comes in.

So I - you know, I think it's going to be important to monitor, collect the data, give them feedback and how it actually changes what they're doing is not as clear.

And they're sensitive to these issues but they were always driven with a model of having a textbook that they would sell and not

- so it's not being done in the sense of a sort of public service or like the World Health Organization is doing the ICD electronically.

There's no cost to anybody to go on and look at the new version of ICD and it can be modified as necessary. This is a different process and it's going to be a little harder, I think, to make changes after May.

But all the more important that we monitor or someone monitors closely what the impacts are and provides that information to the public.

Mr. Robertson: Tom, this is Scott Robertson. I'd like to be involved in this partly because I've had some experience in terms of what ASAN had with the - with our suggestions we had when APA was going through this process over the last 2 years for the development of *DSM-5* criteria and the trainings that we're hopeful - we're planning to be doing in the next few years to help with educating people about the trainings but also

on the services side.

And maybe this also, again, as you said, shades more into the services arena and the role for the Services and Policy [Sub] Committee.

It's the impact on the service system side. Here in Pennsylvania, we actually happened to be coincidentally going through, like, a future planning process for our developmental disability services and that's something that I intend to mention at our Work Groups here at the state level in the next several months is going to be happening with that planning process because we have autism-specific waiver-based service systems for us to develop and funding for families of autistic people, et cetera, et cetera.

And, for instance, how is social communication disorder is going to impact – that is that some of those folks will no longer be able to maybe access some of those things where they would have with an autism spectrum diagnosis.

Dr. Insel: Great. Okay. So -

Dr. Boyle: This is Coleen. I would just suggest one more person to add and that was Laura Kavanagh from HRSA because they have the national surveys that ask about autism so, you know, clearly it would be a good way to at least from a national perspective monitor some of this.

Dr. Dawson: And you know who else is very, very interested in this is John Robison. I remember he brought it up at the meeting.

Dr. Boyle: Particularly around adults, yes.

Dr. Insel: Okay. So that will - Geri, you'll drive that particular train and it sounds like you've got a good group to help advise you and then we'll expect some feedback in April to get a sense of what the Group thinks are the best options for us.

And thanks to Walter for sending around the CMMI link, so you all should have that by now, if you want to learn more about that particular - the innovation center at CMS.

We've got just a couple minutes left. Any final comments from the Group? There's still a bunch of hanging chads here.

We haven't talked about the toolkit that Anshu brought up, the idea of how do we make sure that we inform payers of evidence-based practices.

Environmental risk factors hasn't come back up and I think on the clinical trials quality we'll try to identify some of that for this next meeting if we're able to do something like that.

Comorbidity, which we discussed quite a bit in this meeting, where are we with that? Can we again - Susan, is it possible to at least plan for a panel at the IACC meeting or is it too late to do that?

Dr. Daniels: Well, we have a lot of different ideas for the April meeting and we can't do everything in April that we - if we prioritize - if that's a higher priority than some of the other items that were proposed for April then we can - we can move things around.

But we also should consider putting some things in the July meeting and some things in the October meeting.

Dr. Insel: Okay. Well, I think what we've heard today that took, you know, much of the first hour is the interest in this particular topic and we heard it play out in a number of ways in terms of adult populations and coming up with guidelines, and it sounds like in this area there are some things to cite already.

Some of the work from the American Academy of Pediatrics would be good to get promoted and to make sure that that's out there where people see it. So it does seem like there's an opportunity to do more here.

Ms. Redwood: Tom, the other - the other issue was biomarkers that we have in the Strategic Plan, actually to ask the questions whether or not they're part of the disease process or maybe even responsible for some of the disability because that's another sort of separate question to ask with regards to

comorbidities.

And if there is a pattern of these comorbidities that we see that either can be used to assess severity or to develop biomarkers I think that's another question that needs to be asked too. There's a lot of work that needs to be done with regard to the comorbidity issue.

Dr. Insel: Right. So is that something we want to develop for the July meeting and think about how we could put some part of the full IACC - because I think there's a lot of interest on this in the services side as well.

Could we plan for having a panel in July? That would take a good chunk of the meeting to really dig into this.

Dr. Daniels: From the OARC's perspective - this is Susan - that would be fine.

Dr. Insel: The meeting is getting a little rowdy there. Either that or there's an asteroid approaching.

Lyn, are you okay with doing this in July?

Ms. Redwood: Yes, that's fine, Tom. I wasn't certain who you were posing the question to. Or, you know, we also have this opportunity in the Strategic Plan for doing workshops.

I just don't know if it might be something that would even be worthwhile doing an entire workshop. But definitely a first step is having a panel to sort of bring information to.

Dr. Insel: Okay. Well, maybe what we could do is bring this forward in April, get some additional ideas of what people would want to hear about. I know this - there's a lot of interest from members of the Committee, who are not on this call.

So I wouldn't want to lock this in. But let's plan to take a chunk of time in the July meeting to really drill deeper into this topic.

We're just about out of time. Anything else that the Group wants to put forward before we adjourn?

Dr. Boyle: So when is our next Subcommittee call? Just trying to wrap my head around what we need to - when we need to get back to you all by in terms of the process for the accountability review.

Dr. Insel: That's a Susan question.

Dr. Daniels: So yes, you don't have a Subcommittee call planned yet.

Dr. Boyle: Okay.

Dr. Daniels: But you could - I don't know how quickly you think you would have an answer. If you feel that you would have an answer by April 9th you could provide that at the April 9th meeting.

But if you need a little more time we could plan a Subcommittee meeting for later in April.

Dr. Boyle: We'll try to have something by April 9th. That seems doable. Okay.

Dr. Insel: Okay. Any other issues before we adjourn?

Thanks to everybody for joining us and, Susan, I appreciate the considerable effort to

make this happen in spite of a snowquester. Hopefully, we'll have better weather in April when we meet as a full Committee.

Dr. Koroshetz: Hey, there's no snow on the streets.

Dr. Insel: I know. In the course of our phone call we've gone from blizzard to no snow. So it's been a very, very helpful phone call in that respect.

Dr. Koroshetz: I think President Obama is going to make fun of us all for shutting down today.

Dr. Insel: Well, we were - but we were at work, in fact. Thanks so much, everybody.

(Whereupon, at 4:33 p.m., the Subcommittee adjourned.)