U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

NATIONAL INSTITUTE OF MENTAL HEALTH

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INTERAGENCY AUTISM COORDINATING COMMITTEE

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SCIENTIFIC WORKSHOP

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WEDNESDAY,
SEPTEMBER 30, 2009

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The workshop convened in Salon E of the Bethesda North Marriott Hotel & Conference Center, 5701 Marinelli Road, Bethesda, Maryland, at 9:00 a.m., Della Hann, IACC Executive Secretary, presiding.

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PROCEEDINGS

8:45 a.m.

DR. HANN: Good morning.

I'm Della Hann. I serve as the Executive Secretary, which doesn't mean a lot, for the Interagency Autism Coordinating Committee.

I want to welcome everyone to the first in a series of science workshops, a series that will probably occur yearly.

The Interagency Autism Coordinating Committee is a group that came together as a result of the Combating Autism Act of 2006. So it is in legislation, and the Coordinating Committee is comprised of both public members and federal members.

One of its major charges in the legislation is to produce and to yearly update a strategic plan for autism research. That is why we are here today, in terms of convening a science workshop to assist the Committee in determining how best to update the strategic

plan that it completed in January.

So the way that we have organized today, the next two days, is essentially we took each of the different chapters, major chapters, of the plan, and we have convened panels to help us think through, essentially, what the gaps, opportunities, and priorities might look like in terms of updating the plan.

Each of the panels is comprised of members of the scientific community, the clinical community, as well as the autism family/personal community.

The Committee felt that it was very important to make sure that all of those different perspectives were brought to bear, because that is what this plan is about in terms of not only advancing the science, but making certain that the science is addressing the needs and concerns of the various communities.

I want to remind everyone that the presentations today and all of the discussions

are being videotaped and will be archived. There are people watching us now, hopefully, who are tuning in.

So I do ask, when you do need to make a comment, to make sure that your microphone is on, so that it can be captured and so that people can hear you.

Today what we are going to do for each of the panels is the panels will do their presentations. They have 30 minutes in which to make their presentations of their combined efforts.

I want to say, also, that I want to thank all of our panelists tremendously. You all have been working very hard over the last few weeks, and we desperately appreciate the efforts that you have done to help bring us here today.

It has actually been pretty remarkable, each of the panels, in terms of the collegiality and the degree to which a number of important issues have been brought to bear.

We really look forward to hearing the presentations.

Each of the panels, in addition to the members who were brought together, also have two IACC members who are serving as liaison. The role of the liaisons today will be to help moderate the discussions when their panels are doing their presentations.

So the panel will present. Usually, each panel is being represented by one or two members. We are going to ask the panelists to come up here to actually do their presentations.

The moderators, that is, the IACC liaisons, can either come up here or stay seated. It makes no difference.

Following the 30-minute presentation, we will then have a period of conversation and discussion amongst all the panelists, which will then be followed by a period of time allowing for the members of the public and the attendees to make comments and also engage in

discussion with that particular panel.

Now, thanks to the hotel, as well as some of our staffing, we have been able to secure this lovely little moderator button here to help people know when they are running through their time. So everyone will be able to see, essentially. When you are at your five-minute warning level, the yellow light will come on. Then, when you are out of time, the red light will come on.

We really want to encourage people as much as possible to please stay within the parameters of the times. We have a really packed agenda, trying to move through and ensure good amounts of time for discussion.

In addition, I wanted to also introduce and thank members of my staff who have done incredible work over the last few weeks in terms of assisting us and making sure that we are all here today with the material that you have before you, as well as a lot of material that was prepared in advance.

I know they are not going to like this, but I am going to ask them to stand, so that everybody gets to see who they are.

Dr. Susan Daniels, Dr. Azik Schwechter, Ms. Lina Perez, Ms. Erin Bryant, Dr. Sarah Rhodes, Dr. Monica Mallampalli, and Ms. Nicole Jones.

(Applause.)

So, anyway, these are the folks who have really helped us get here today. They are also the people you can turn to if you've got a question in terms of logistics or slides, or whatever. Those are the folks that you need to try to find in terms of helping you through that.

The last thing I would like to mention before I turn this over to Dr. Insel is that several of us will be leaving for a short period of time this morning. There is an event that is occurring on main campus at NIH. We are very privileged that the President of the United States is visiting NIH this morning

to celebrate NIH-supported research through the American Recovery and Reinvestment Act. So some of us are actually going to be there. So that's fun.

But we will be back. Never fear, we will be back. It will only be a brief period of time that we are gone.

So, with that, I will now turn this over to Dr. Thomas Insel, who is Director for the National Institute of Mental Health, and Chair of the Interagency Autism Coordinating Committee.

DR. INSEL: Well, good morning, everyone.

I am going to stay down here because I want to share some slides with you, and it will just be easier, I think, and maybe a little more convenient and conversational if I do it from here.

Della, thanks so much for getting us started.

I want to start by thanking all of you

who have participated in these panels. This has been an incredibly busy month or six weeks. This, because of a variety of scheduling problems, ended up getting stacked up pretty much at the end of our fiscal year.

We wanted to get this whole process done by the end of September, and we just about made it. We're maybe a day late by tomorrow.

As Della mentioned, the reason for all of that is that we are essentially trying to help the IACC to do this legislated revision of the plan, the updating of the plan that occurs each year.

Now I wanted to make sure that you understand that the plan isn't that old. Well, it was basically submitted to the Secretary on, I think, the 20th of January of this year. So, as a five-year strategic plan, we are not even one year into it.

So it was not our expectation that you would scrap it and rewrite it, and I hope that is not going to be your recommendation because

we are just getting started on implementing many parts of the plan.

I thought, to give you some sense of that, because this has been an extraordinary nine months, eight months, since the plan was released, that I would take you through what we call the ARRA, the American Recovery and Reinvestment Act, which provided a real special opportunity to jumpstart this.

I remember when the plan was submitted. I think it was someone from this Committee who said, from the IACC, who said, well, this is great that we have this roadmap, but really is there going to be any gas in the car? ARRA provided exactly that.

So, if we can just take maybe 10 minutes, let me walk you through what this American Recovery and Reinvestment Act, that's ARRA, did for jumpstarting the plan.

The slides, hopefully, those who are joining us remotely will be able to watch them as well.

ARRA was passed, as I mentioned, with the arrival of the new Administration, and there were really three things that they were setting out to do.

One was to stimulate the economy.

The second was to create and preserve jobs. This was, after all, essentially, a jobs act. And they recognized here this unprecedented opportunity to do this by advancing biomedical research at the same time.

Now the key to this Act was that everything needed to happen very quickly. You may remember the term that was being used at the time was "shovel-ready". We were calling projects "beaker-ready".

The reason we were thinking about that was because what the Administration wanted was to get people back to work or to, as it says, preserve jobs for people who were about to lose them.

So the money was to be spent in two

years. That meant that, for this to happen, since our fiscal year ends today, that the money, essentially, needed to be out the doors by today, which was quite a challenge for us because this was not something we had planned on, and it was much more money than we had expected. It was over $10 billion that came to NIH for this very rapid implementation.

So we thought about this really in two ways from the get-go.

The first was that we could put some of the stimulus funds out the door very quickly by using existing mechanisms. That is, grants that were deemed to be meritorious by peer review, but we didn't have the funds to pay them. So we expanded our paylines.

We also were able to provide administrative supplements. For the last five years, NIH has had flat budgets for the most part, and we were actually below inflation.

The way we have coped with that is we have been generally cutting every grant budget

by about 10 percent, sometimes 15 percent. That is pretty tough, especially as the years go on and there's no inflationary increase. So there were many people who were funded with outstanding projects who were at this point in need of supplements.

So some of the funds could be provided to these grants that had already been through peer review, were out there running, and were running on empty. So that was done quite quickly. About, in our case, for my Institute, perhaps 20 percent of the money went out the door very quickly to do just that.

At the same time, we thought of this as an opportunity to create some new both Challenge and what we call Grand Opportunity grants. I will tell you more about those in a moment. But these were projects that didn't exist that we thought could be signatures for the Recovery Act, and something that we could look back on much as we did in the 1930s with

new projects that were developed as the nation recovered from the Depression.

There were several of those. There were really three that we focused on. There were Challenge grants. These were up to a million dollar grants over two years, so $500,000 a year for two years.

The Grand Opportunity Awards, or GO grants, that go for more than two years -- I'm sorry -- go for more than a million dollars over two years.

Then there was a special RFA that was developed for autism. This, I must say, we really had the strategic plan to thank for this. This would not have happened, I think, without it, but the opportunity to make the case that a group of people had come together, identified important gaps and urgent opportunities in one area of science. Therefore, it was worth building a Request for Applications and putting some money aside, in this case about $60 million, specifically for

autism. This is the only disease-specific effort in the entire Recovery Act program at NIH. So we were quite fortunate in that regard.

But it would be misleading to think that the only autism investments were within that RFA. As you can see here, some of the Challenge grant topics, like linking to NDAR and providing studies of how to access services better, or looking at comparative effectiveness, and actually one effort, which was called specifically addressing the challenge of the IACC, coming up with projects that would specifically look at the areas that were recognized as gaps in the short-term objectives in the strategic plan. So the Challenge grants were really NIH-wide.

The Grand Opportunity projects that I mentioned there were from NIMH, but they are highly-relevant to autism.

And the RFA, which was focused on the heterogeneity of ASD, as I mentioned, was $60

million set aside from five Institutes.

I will say a little bit more about the specific RFA because this is the one that has gotten probably the most attention. It is not just on the heterogeneity because it does involve in the language Request for Applications that look at the short-term objectives of the plan.

We got 590 proposals, roughly $500 million in proposals that came in. There was a very rigorous peer review for this. It was, actually, kind of a two-stage process with what we call an editorial board that looked at the first cut, and then a group of about, I believe, 90 people who came in in the middle of June, 20 percent of them being what we call public members, or usually they are people who are either affected with ASD or have family members affected.

Together, within one day, they went through the proposals, looking at both the editorial board comments and created their own

agenda for what they thought was most important to fund.

These went to the NIMH Council in mid-July. They have now, as of today, or as of yesterday, been funded.

The actual awards exceeded $60 million. Because of such a robust response and the quality of the grants that came through, the Institutes felt that we just needed to stretch the original commitment. So the actual final figure will be something like $69 million. Because this is all happening over the last few days, we are still getting the final numbers, but it will certainly be over $65 million.

As you look at what is in the list of things funded, happily, virtually every large part of the strategic plan was addressed in some form. I have just pulled out a few examples of the kinds of projects that were funded through either this RFA for autism heterogeneity or through one of the Challenge

grants, and you get a sense of what is in place, from rapid-screening instruments to biomarkers, deep sequencing, and epigenomics to look at environmental impact on the genome, new treatments that have been looked at, and a fair number of projects that focus on adult services or urban settings, telehealth, and even autism in the second half of life, as a broad area.

You can actually see much more about this yourself by doing to this part of the NIH website called "RePORTER". This has a list of everything that has been funded. It is available to any of you at any time.

If you go in and you put the search term of "autism", you will get something like 193 grants that will come up. You can actually request that these be limited to just the ARRA awards, Recovery Act awards, so you will have a chance to see what was supported through that effort.

The actual numbers, as we look at them,

are probably, well, they are still a little bit fluid, but I can give you a sense here of what to expect.

First of all, we can say by today, which is the last day of our fiscal year, that, indeed, all of this is out the door in the way that we had hoped. The RFA, along with the Challenge and GO grants, have projects that match with every objective of the strategic plan, which was very much what we wanted. That is where it has been so valuable to have this roadmap.

We have also used some of the funds to jumpstart NDAR, which has gone from something like 300 GUIDs -- these are Global Unique Identifiers; these are 300 subjects in NDAR -- a year ago, to about 12,000 as of today. We expect that number to double under the Recovery Act over the next two years.

The NDAR has now been expanded to about 15,000 elements. So part of the Recovery Act has been helpful in building this database.

Finally, if you just look at the dollars themselves, I think when you add all of this together -- and again, these are not final because we are still working on some of the details of the budgets that have gone out, some of which are literally going out this morning or yesterday -- it looks like it will be well over the $60 million that were in the RFA for autism. It probably is going to be closer to something over 85 over two years. So that is, roughly, 42, something like that, per year. That is on top of our base funding.

I should make the point that, as far as we can tell, there has been no substitution here. So we don't believe that our base commitment to autism research has changed or gone down at all. It may have gone up. We won't have those numbers for another couple of months, again, because the fiscal year is still working its way through the coding process and all of that. So we will have that fairly soon, but not finalized for another

couple of months.

So that is a quick rundown. I wanted you to see what we are looking at, just to give you an idea that there's been an awful lot of activity guided by the strategic plan. I have to say, with a little bit of apprehension, that one reason I wanted to show you this is that, if you are about to tell us that we should throw away the strategic plan that we did in January and start over, you are too late because we are not going to get another $10 billion for these kinds of efforts. At least, we don't expect to. We will have to hear what the President says this morning.

But I think the best evidence we have so far is that the budgets are going to stay relatively flat at NIH. So we will be back to the kinds of budgets that we have been working with and trying to figure out how we can make some incremental gains and commitments to ASD research.

So this was a very special opportunity. We hope we have used it well, because all of you are involved in thinking about tweaking this plan and making sure that we get it to the best place we can have it for the 1.1 version of the strategic plan.

I wanted you to know that there's a lot going on since the thing was actually put up in January. There is probably an opportunity, as we go through the next couple of days, to hear about some of the individual projects that are already funded.

So I am going to stop there.

Susan, can we take one minute or two minutes for questions, and see if there are any questions before I turn this over to Susan? And we can start the day's work.

Any questions? Lee?

MR. GROSSMAN: Hi. Way down here on the end.

Just so that we have a little bit of guidance as we go through the next two days,

so we're looking at 1.1 now in the strategic plan. With the funding that is available through the ARRA funds and what you think will be available next year, with the recommendations that come out of today, how will that fit into, let's say, the 2.0 of the strategic plan?

DR. INSEL: When you say, "2.0", you're thinking of when?

MR. GROSSMAN: Today forward.

DR. INSEL: So, at this point, we are still working with the 1.1 version, the January 20th version of the strategic plan.

What we are hoping for from all of you is something that looks like the 1.1 version. The great thing about having the strategic plan was we were prepared for this windfall. We are not expecting another windfall. Ninety-five percent of the ARRA money has now been obligated, as of this morning.

So what we have just done was based on the 1.1 version. 1.1 will, hopefully, have

some chance for us to improve and maybe to recognize priorities a little bit differently.

What we had originally hoped for, knowing that the recommendations that were in the plan would take two, three, four years to implement, we had hoped at this point not to be told that we needed to rewrite the plan, but to get a sense from you on two things really:

Has there been some breakthrough since January that would inform this plan in a different way and may change the priorities or may provide a suggestion of something new that we didn't know about a year ago, when we were working on this?

And the second was, as you probably heard in your panel discussions, there were some issues that we just didn't deal with last year. It was partly because we were racing toward this January 20th deadline. We thought it was really important to have a plan to deliver to a new Secretary of HHS.

So there were several issues that were deferred. Those should have been presented to you as panel members to consider whether they needed to be reworked and rethought of for this version of the plan. We know that from the get-go. We just ran out of time.

So those are the issues that I hope will come forward over the next couple of days. If you do decide that you want to scrap what was written in January and do something very different with different strategic objectives, all I can tell you is, at least at NIH, we don't expect there to be another opportunity like we have had in the last eight to nine months. I think that window has closed.

There will be ways of tweaking budgets and moving money sort of incrementally, as we have been doing for the last few years. But this was really unprecedented and probably unique.

Any other questions or issues before we move on?

(No response.)

Okay. Susan, I am going to turn this over to you, and we can start with our work.

DR. DANIELS: Great. Thank you, Tom.

Welcome to everyone. It is wonderful to see you all here. I am glad everyone made it safely.

We really look forward to the discussion that is going to go on today and all these presentations.

So, at this time, I would like Panel I liaisons and presenters to go up to the podium. If the liaisons could introduce themselves and introduce the presenters and the people on their panel, then we will hear the first presentation on Question 1 of the strategic plan: When should I be concerned? That is, about diagnosis.

DR. JOHNSON: Thank you for your patience with us while we work out logistics here.

My name is Jennifer Johnson. I am co-

liaison for the first panel. I am with the Administration on Developmental Disabilities in the Administration for Children and Families, HHS.

Our panel focused on the first question: When should I be concerned?

Did you want to do introductions of the presenters and the panelists?

DR. JANVIER: Yes.

DR. JOHNSON: Okay, great.

So I am going to turn it over to my co-facilitator.

DR. JANVIER: I am Yvette Janvier. I am a public member of the IACC. I'm a developmental pediatrician.

I think, looking around the room, we seem to have the ladies group here today. Just to mention all of our members, Geraldine Dawson, Rebecca Landa, Deborah Fein, Catherine Lord, Paula Durbin-Westby, Nancy Wiseman participated in all of our pre-meeting discussions.

So today, presenting, we have Geraldine Dawson, who is the Chief Science Officer of Autism Speaks, professor at the University of North Carolina, Columbia, and the University of Washington. She is the former Director of the University of Washington Autism Center.

Dr. Deborah Fein is a professor at the University of Connecticut, and Paula Durbin-Westby is an autistic on the Board of Directors of the Autistic Self-Advocacy Network.

MS. DURBIN-WESTBY: Hi. I'm Paula Durbin-Westby.

Our first panel addresses diagnosis and assessment: when should I be concerned? The questions we have: what are the early warning signs? Are there typical characteristics that are part of an ASD diagnosis? How much variation is there in symptoms and severity associated with ASD?

The first thing our panel addressed was revising the aspirational goal. The original

was children with or at risk for ASD will be identified by 24 months and receive appropriate interventions.

We broadened it to include older children, adolescents, adults, and we took out the 24 months because that age can change, depending on research. We also included reliable methods rather than just any method.

So we came up with: "Children at risk for ASD will be identified through reliable methods during the pre-clinical stage before ASD behavioral characteristics are present, and people who have ASD will be detected at the point when ASD characteristics are observable across the lifespan."

Next slide.

The gaps we found were that, originally, we had focused mostly on children, the original strategic plan. So the broad gap is the need for early diagnosis in children is the main emphasis in the current plan. This should be broadened to include identification

across the lifespan and in diverse groups, such as females and minorities.

Next.

We came up with, I think, 13 short-term objectives. I am going to be doing about half of them, and then I will turn it over to Geri Dawson.

"Determine the sensitivity and specificity of broad-band developmental screening versus autism-specific screening tools in both high-risk and population-based samples."

The rationale for this is that many pediatricians are using broad-band developmental screening tools for all children in their practice. Thus, it would be helpful to know if such screeners could effectively serve as a first-level screener for ASD.

Although some evidence suggests that general developmental assessments do not detect many children who screen positive on autism-specific assessments, other studies

have provided conflicting results.

No. 2 is: "Develop and validate effective screening tools for infants at risk for ASD below age 18 months."

Our rationale is recent studies indicate that both biological, e.g., head growth, and behavioral, such as orientating to name and discouragement of visual attention, signs and symptoms of autism, are present during the infant period. Even if such screens detected only a portion of children with ASD, and later screening to catch the remainder remained necessary, children detected before 18 months would be able to benefit from the earliest-possible intervention.

Three, "Determine the generalizability of early risk or trait markers and developmental trajectories identified in infant siblings and other high-risk samples to general population samples."

Much of the research focused on development of these markers, and

developmental pathways for ASD has been conducted with infant sibling or high-risk samples. However, the extent to which the findings related to screening, risk, and development can be generalized to population-based samples remains unknown.

Thus, it is important that studies that examine ASD screening tools and other risk markers be conducted on population-based as well as high-risk samples.

Next slide.

"Develop and validate screening and diagnostic measures for detection of people with subtle characteristics of ASD."

Existing studies on the sensitivity and specificity of early ASD screening tools indicate that children, adolescents, and adults with subtle forms of ASD, including those diagnosed with Asperger's Syndrome, are often missed.

Little is known about the early signs and symptoms or characteristics of ASD during

the infant and toddler period. The lack of early identification of these children delays the participation and early intervention programs which could potentially greatly influence outcome.

The lack of identification of adolescents and adults precludes their getting the assistance that could optimize their functioning.

Five: "Develop methods for screening and diagnosis of co-occurring medical conditions in ASD and understand the relationship between these conditions, ASD characteristics, and short- and long-term outcome."

It is well-recognized that ASD is associated with risk for a wide range of co-occurring medical and psychiatric conditions that greatly impact level of functioning, quality of life, response to interventions, and outcome. Such conditions may include metabolic disease, epilepsy, GI problems,

sleep disturbances, ADHD, and anxiety, among others.

These conditions are often present during early developmental periods, but little is known about best methods for screening and diagnosis of such conditions, their prevalence across different developmental periods, their relationship to the core symptoms or characteristics of ASD, and their relationship with long-term outcome. Recognizing and treating such conditions can have a significant impact on quality of life.

Six: "Develop effective ASD screening and diagnostic tools for use with adolescents and adults."

As awareness of ASD increases, it is more common that individuals with ASD are being diagnosed as adolescents and adults. However, we are still lacking in appropriate diagnostic methods for adults, in particular.

One challenge is that current methods rely on parent report of early symptoms. This

is problematic since the parent may not be available; the adult with suspected ASD might not want to involve his or her parent in the evaluation, and recall of symptom expression after such a long period is likely to be unreliable. The development of more feasible and reliable screening and diagnostic tools for ASD in adulthood is, thus, imperative.

Next slide.

"Understand and identify methods to address barriers to early screening and detection of ASD among ethnic minority populations."

Virtually all ASD screening and diagnostic tools have been developed on samples that are largely white and middle to upper class. Currently, little is known about the level of autism awareness, the pattern of autism services utilization, and barriers to timely and appropriate diagnosis and treatment among ethnic minority communities.

For example, a recent study of more than 2500 children who met research criteria for ASD found that white children were significantly more likely to receive an ASD diagnosis in the community than black and Hispanic children. Other data suggests that minority children may be screened and diagnosed later than white children.

Screening and diagnosis are essential to qualify for appropriate educational and medical services.

Many factors are likely to contribute to this disparity in diagnosis, including differences in parental awareness, help seeking advocacy and support, and clinician behavior.

Eight: "Understand factors that impede or promote the use of ASD diagnostic and screening tools in community settings, such as pediatricians in general practice."

Although ASD screening tools exist and the AAP has made a clear recommendation that

all children should be screened for ASD at 18 and 24 months of age, many pediatricians are not using such tools.

If the research on the development of ASD screening and diagnostic tools is to have real impact on the lives of individuals with ASD and their families, it is important that practitioners use such tools.

To address this issue, we need to better understand the factors, including those related to financial, ethical, logistical, and training issues that promote and impede use of existing screening and diagnostic tools for ASD.

And my last one is No. 9: "Develop and test the efficacy of programs to train practitioners in the use of ASD screening tools and in effective, respectful, and positive communication with families, following a positive screen or diagnosis."

Although screening tools exist -- this is starting to look like -- I'm not doing the

rationale for that because I copied in the one for the one before.

Anyway, develop and test efficacy.

And I will turn it over to Geri.

DR. DAWSON: Okay. No. 10 under the short-term objectives is "To investigate the extent to which early diagnostic evaluation leads to appropriate early interventions."

So we, obviously, know that screening is only useful if it does lead to appropriate services. So we need to understand the extent to which this occurs and also the barriers that may exist that prevent this from happening.

Next is: "To identify and consider the ways of addressing the wide range of ethical and clinical issues related to diagnosis, assessment, and communication of genetic, environmental, and clinical risk for autism, as well as the social and clinical effects of the diagnosis on the child and the family."

So, as tools for identifying infants and

other individuals at risk for ASD are developed, a wide range of clinical and ethical issues need to be addressed. These include what kind of counseling needs to be available for the family, what are the appropriate methods for communicating risk, what are the recommendations for doing risk assessments, and monitoring when a child is identified at risk, and so forth.

The next has to do with a research opportunity. This is a recommendation for supplementary funding for the National Children's Study to enhance the current design, so that the relationship between genetic and environmental risk markers and ASD diagnosis can be studied in a population-based sample.

So this is a unique opportunity where 100,000 individuals are going to be followed longitudinally from conception through diagnosis and actually into adulthood. As you know, most of our studies that have looked at

early risk markers are conducted with high-risk samples; the infant sibling samples, in particular.

So this is a really unique opportunity to study risk factors in the context of a large population-based sample. We would anticipate about 600 of these individuals would develop autism. However, there are limitations in the current design. This includes the follow-up after screening positive for a diagnosis of a child with autism as well as limitations in the kind of data that are collected that have to do with risk factors; in particular, the collection of medical records.

The second research opportunity would be to create a coordinated database of both phenotypic and biological information on the existing high-risk samples. So we do know that, as part of the ACE networks and also, I'm sure, as part of the ARRA funding, that there are many high-risk infant samples that

are being collected currently. However, these will take several years to come to fruition.

There exists a sample of about 2,000 existing infant sibling samples that already have diagnostic information. What we are recommending is that there be a database collected and DNA collected on these samples, so that we can use this as a way of testing potential candidate genetic risk markers, as well as to test hypotheses that then may inform the studies that are ongoing with high-risk samples.

Moving on, then, to the long-term objectives, one is to identify pre-clinical markers of risk for autism. So we know that advances in molecular neuroscience have allowed us in other diseases to identify risk for certain diseases before the actual symptoms are manifest.

So, for example, Alzheimer's, Parkinson's disease, we now have pre-clinical markers. This allows us to identify these

individuals at a period where treatment could begin before symptoms are present.

So, in autism, we know that there's early atypical head growth that emerges before the onset of overt symptoms, suggesting there's already progressive changes in the brain at this period.

So the long-term goal would be to identify these infants at this pre-clinical stage, so that we can offer opportunity for intervention at this period.

So we would recommend research that uses genetic imaging, behavioral and biochemical tools to validate these possible pre-clinical markers.

The next long-term goal is to understand the predictive relationship between early signs and symptoms of ASD risk and developmental trajectory, including what the early signs look like in relationship to variations in developmental course, including autism regression.

So, at this point, we are learning a lot about these early risk markers. We still know very little about how these risk markers predict variations in trajectory.

In particular, we need to do this in population-based samples. Currently, we are only looking at this in a high-risk sample. It would be informative to look at this in a population-based sample as well.

Then, finally, another long-term objective is to determine the prevalence of and factors associated with changes in the core features of ASD. In particular, there's some research studies that suggest that a proportion of children actually lose their diagnosis, and we know very little about the factors that are related to loss of diagnosis, both intervention factors as well as biological factors.

We also have some evidence that individuals who lose their diagnosis, nevertheless, have a number of clinical

symptoms. So it is very common for these children to have ADHD, anxiety, depression, tics. So we need to understand these associated conditions that persist as residual problems, so that we can make sure to be sensitive to those and to develop appropriate treatments.

So, just really in summary, this will take just a couple of minutes to give you just a brief summary of what we have proposed then.

One is to revise the aspirational goal to reflect efforts toward reliable detection of ASD at younger ages and also through the lifespan. So, when we think about an aspirational goal, we really did encourage the IACC plan to have something that is a stretch goal. We think this is a good stretch goal for us all to aspire to.

Second is to develop and validate screening tools for a wider range of populations, including not only younger children, but adolescents and adults, and also

people that have more subtle characteristics, such as individuals with Asperger's Syndrome.

The next is the importance of evaluating broad-band developmental screening measures because these are what pediatricians are using, and we really need to know if these are going to be effective, or do we need to make sure that pediatricians are using autism-specific screeners?

Next is to develop methods for screening and diagnosis of comorbid medical conditions. We know these exist. They have a huge impact on quality of life. The physicians are often missing these. We don't have good methods for screening and assessment of these conditions.

We also want to make sure that we can define the barriers that exist in using the screening measures in ethnic minority populations at community settings and by pediatricians, and to make sure that we develop and test training programs for professionals to actually use the screening

and diagnostic measures.

Then, finally, we need to address a wide range of ethical issues that are related to screening diagnosis. Particularly, as we identify more genetic and other biological and environmental risk factors, there are a number of ethical issues that we need to address.

Let's see here. Is that it? Okay, thank you very much.

DR. DANIELS: Thank you very much.

So, Panel 1, you can be seated back at the table. That will probably be more conducive to the discussion.

Panel 1 members will be available now for discussion with the entire group of panelists who have been invited to the workshop to talk about the ideas that they have presented, these proposed new objectives and different ideas that they have presented for Question 1.

So please start. Does anyone have questions for Panel 1? This is the time for

panelist discussion and IACC members at the table.

We will have 45 minutes. Actually, you are running a little bit early, so you will have a little bit more time even to have this discussion. Then we will be opening up to the public for a 45-minute discussion following this.

MS. BLACKWELL: I would just like to say thank you, Panel 1, for your great work. I think Panel 5 would certainly agree with your trend toward focusing across the lifespan because that also came out in our discussions.

I just wanted to flag for you that there is one particular short-term goal. Panel 5 clarified that Chapter 6, we are proposing, will actually be focused on adults. So I think you have at least one proposed short-term objective: develop effective ASD screening and diagnostic tools for use with adolescents and adults, that we have also very close to duplicated in Chapter 6. So it may

be that that ends up in Chapter 6.

So thank you so much. It is excellent to see that we were operating down the same path.

DR. DANIELS: There were many areas that the panels overlapped in. So I think that will come out, hopefully, in this discussion.

So any of you on other panels who had burning issues with diagnosis, please ask questions to Panel 1 and feel free to discuss.

DR. SAMSTAD: Am I supposed to push this? Okay.

Is it okay if I ask a question? I was curious about No. 11, which looks good, but, you know, in the adult population -- that's the genetics one -- in the adult population, a lot of the patients that I see have never had genetic testing.

I am noticing that the item really just focuses -- it just says, "child and family". I am wondering if we can maybe broaden that a little bit to include adult genetic testing as

well.

I had a couple of other questions. Maybe I missed it in here.

I noticed there's a lot of focus on comorbid medical conditions, but I have a lot of challenges as a clinician with comorbid psychiatric conditions as well and how to screen and diagnose for those. So I was wondering if perhaps that is something to include.

I guess those are my main two comments.

DR. FEIN: I think we were intending the psychiatric to be included with the medical. So I think we could just make that explicit, say, "medical and psychiatric".

MS. DURBIN-WESTBY: This is Paula Durbin-Westby.

On No. 11, I sort of wanted it to be a little bit different, but we would have spent our entire conference call on it. And I agree that it focuses a bit too much on children and family and the effects of diagnosis on the

child and family.

I wanted a study to address ethical, legal, and social issues of both early diagnosis and subsequent early intervention, and including topics like the effect of pharmacological agents on autistic people; the effect of early intervention, behavioral or other interventions, on autism developmental trajectory, including unintended consequences; impact of research results on individuals, families, and our society; researcher bias at every stage in the research process, which our stated No. 11 doesn't cover; bias associated with funding sources, priorities and values of people on the autism spectrum, and families and society, and perceptions of autism portrayed by researchers, clinicians, media, and advocacy organizations.

And also, with the focus of the unfortunately-named "Combating Autism Act" and the focus on a cure, like in the crosscutting themes section there's a statement that we may

someday achieve the goal of prevention. And our question, many parents and people on the spectrum that I am here today representing, want to know who "we" is because the goal for us often serves as supports appropriate treatments, interventions that are safe, communication to families about what the risks if you include your child or your adolescent or yourself in a study.

So I did want to broaden it, and we will see what happens.

MR. GROSSMAN: Hi. This is Lee Grossman.

First of all, I just want to say, wow, that was an excellent start to the day. I cannot thank you enough for your approach to this first question.

I was actually quite shocked and pleased by what I heard because it moved the science to a more practical and clinical realm. That was what I had hoped we would be hearing throughout the day. I want to thank you for

that.

What we struggle with -- I am a member of the IACC -- and what we struggle with on the IACC for the strategic plan is that it is primarily research-oriented. So my question to you is, in your deliberations, how did you bridge that gap between what is in the strategic plan, which is, again, of this research focus, to the clinical realm?

DR. DAWSON: Well, I think one way of thinking about this is the field of dissemination science. We can identify an early risk marker, identify a good screening tool, but if people aren't using those, then it really isn't going to have an impact on people's lives.

There is a science that is involved in understanding what are the factors that are either promoting or impeding the use of those tools. What are the effective training programs that would make sure that people use the tools in the community? And even what are

the variety of ways in which one can disseminate information to the community?

So, if you look at other fields, if we look at AIDS or other mental health conditions, they have a much more rich and developed dissemination science portfolio. So I think there is a way of having it still be research, but it is research about how to get the tools and the findings out into the community to impact people's lives.

DR. DICICCO-BLOOM: Thank you for your deep presentation. I wanted to ask about points No. 12 and 13 regarding supplementary funding, suggesting, basically, to take advantage of the populations, the large-scale, ongoing, deep phenotype populations, and trying to collect biological materials. This, of course, is an issue that overlaps, as you will hear this afternoon from Panel 2, and I think it runs throughout.

So this seems to me to be a very important unmet opportunity. We really will

need deep phenotyping, both cognitive, functional, and structural. Then to relate this to genetics, to biological specimens, to fibroblasts, this is really important.

I was wondering, I know we are not supposed to be talking about implementation procedures here, just talking about supplementing funding. But I was wondering what your deliberations, what you were thinking, since many of you do participate in these actual programs, whether it is the National Children's Study or the Baby Sibs or CADDRE.

How are you envisioning encouraging investigators in these studies to actually create the resources to put away materials?

DR. DAWSON: So, in terms of the National Children's Study, there now has been formed -- actually, Autism Speaks is overseeing this -- an expert advisory panel that is advising the National Children's Study about how to take advantage of this

opportunity.

So there's two subcommittees that have been formed. One is on screening and diagnosis, which Craig Newschaffer and Marshalyn Yeargin-Allsopp are heading up. Then another one on environmental risk factors, which Irva Hertz-Picciotto is overseeing.

They have identified some specific design weaknesses that really make it so that we can't take advantage of this amazing opportunity fully. One has to do with just adding the ASD diagnosis after screening positive.

Then the second has to do with the collection of medical records. So, right now, all of the data on, say, mother's use of medications or whether she had an infection during pregnancy, and so forth, is only collected through a questionnaire. But by gathering the medical records, there's a number of scientific questions that could be

addressed.

We are also developing projections of how much this would cost, but in the context of a study that has cost billions, it certainly seems to be a very good investment.

So that panel is putting together this proposal. It will be presented to the Federal Advisory Committee for the National Children's Study this fall.

In terms of Baby Sibs Research Consortium, this is already a collaborating group of 22 investigators who are conducting research on high-risk samples. We already have supported the development of a database of all the phenotypic information.

What is being suggested here is that there also be DNA collected on the sample, since we already have 2,000 infant sibs who have a diagnosis and who have a coordinated database. By going back and collecting DNA, this would allow us to have a sample ready at hand where we could begin to look at things

like early genetic risk markers for risk for autism in a fairly large high-risk sample.

DR. FEIN: If I could just add one short thing to that, I think collaborating the National Children's Study to include more detailed assessment of the children and follow-up of the children will also allow us to address some other specific short- and long-term objectives in the Panel 1.

For example, if we are going to screen kids at two, and then they won't be followed up at three, what kind of communication to the family? What are the ethical issues involved in communicating risk to the family?

So I know Dr. Newschaffer, in particular, is interested in the ethics of communicating risk. So there will be a chance to really get information from that study, if it is expanded, to meet some of the other research objectives that we presented here.

DR. SWEDO: Hi. Sue Swedo.

I just wanted to follow on on that

question because it is one of the things we struggle with all the time in the IACC strategic plan. That is that the short-term goal is to pursue supplemental funding, but the National Children's Longitudinal Study, by definition, is going to be many years into the future before we have some of the answers, even for things like early diagnosis.

How does that, then, relate into your long-term objectives of improving diagnosis?

DR. FEIN: I think it relates to both the short- and long-term. I think some of the data will not be that many years. I mean, the ultimate outcome for the children will be many years away, but I think the screening is, I think, if I am remembering correctly, is going to start in about a year.

So, actually, to do some screening and assessment of environmental risk factors, and then to get a diagnosis at age three, is not really that far in the future, compared to like a regular RO1 five-year grant.

DR. SWEDO: Right. I guess it is more that many of the sites for the National Children's Longitudinal Study aren't even onboard yet. So they won't begin recruiting moms to those studies, much less being able to study the children. And it is a very limited population at the present time.

DR. DAWSON: Right. I think the idea here is to be kind of proactive in our approach because we know the study is ongoing. It is unprecedented. It is a huge investment by NIH. It probably is, honestly, our only opportunity to study these kinds of risk factors in a population-based sample.

So, even though, yes, it is going to take time to unfold, in order to get in on the groundwork to make these design changes, we have to be doing it now. So maybe the investment is to make sure that the piloting or whatever has to happen to add those additional supplements, so that this can be used to study autism, that should be occurring

now.

Even if it takes five or eight years to manifest results, it still seems to me just an incredible opportunity that this community probably doesn't want to miss.

DR. SWEDO: I actually agree completely. I think it just comes out of the frustration that we all have with sort of achieving the short-term goal and having people expect to really see a product at that point in time; whereas, trying to temper that enthusiasm with some knowledge of what the actual timetable will be.

DR. DANIELS: Alison Singer, did you still have a question?

MS. SINGER: Yes. At the last IMFAR meeting, Cathy Lord, who I know is on your panel, but apparently isn't here today -- oh, there she is. Oh, hi.

Cathy, you outlined at the IMFAR some impending changes to the DSM V with regard to diagnosis. I was wondering if your panel had

talked about how we might update our strategic plan to incorporate those changes that look like they are coming down the pike.

DR. LORD: No. I think that many people are aware of those, but because they are not final and because we are pretty focused on trying to adapt the existing goals, we didn't talk about that. But that might be something to talk about. I don't know.

I guess, speaking for someone who is on the panel, but one of many members, I think most of the goals do inherently assume that there is an autism spectrum as opposed to very separate, different disorders within autism. Or if there are -- actually, there may be separate disorders -- but, ultimately, what we are talking about, when we talk about ASD, is a variety of different behavioral symptoms that somehow hang together, which may be related to a whole range of different etiological factors.

So I think that the focus for our group

was on identifying any of those and not trying to pull apart separate ones. I don't know, but I should see what my group thinks.

MS. DURBIN-WESTBY: This is Paula Durbin-Westby.

Since I don't think there is any research that shows that there is actually different forms of autism, so looking at characteristics and variability of those characteristics and skills within an individual person, and that way, being able to address heterogeneity, I think that is a good way to go.

DR. DANIELS: Dr. Perner?

DR. PERNER: Two areas of interest here: the first one relates to short-term objective No. 4 with this talk about the early screening and diagnostic measures for individuals with subtle symptoms. I think we need to consider here whether we might be able to come up with potentially some benefits from research of people who may not formally qualify for a

diagnosis.

Somewhere in the sand, usually, you have to draw a line for who actually has a condition and who doesn't. Think of all the people who may be in the periphery. Again, this also relates to the idea of an individual transitioning from one diagnostic category to another, and remaining residual symptoms, to the extent that somebody may be diagnosed after he or she has learned a number of coping skills.

Secondly, I want to commend the emphasis on the idea of development of what I would think of as a respective database of individuals, actually containing individual-level data of some of the studies.

I think the impact of heterogeneity on autism research is considerable. Hopefully, in this respect, we will discover a number of autism subtypes for the development of research. It becomes very important, then, in retrospect, to go back and be able to adjust

for certain factors.

We know, for example, that some individuals may need the polar opposite treatment of others. So, in retrospect, if we can go back and adjust for the subtype of individuals, that would be extremely helpful.

DR. DANIELS: Jeff Sell?

MR. SELL: Just could somebody from the panel elaborate on an area that is really of grave concern to a lot of the community and the Autism Society specifically. It is with respect to No. 7, the understanding and identifying methods to address barriers with respect to early screening and detection of ASD among ethnic minority populations.

We are constantly seeing the same populations at our conferences, at scientific events, and what have you. I just wonder, what, if any, thought was given in terms of identifying the gaps and looking for potential opportunities within the context of the strategic plan of IACC, to see if we could

beef that up a little bit.

DR. FEIN: Well, I think there are really many issues folded in here. So one is trying to encourage participation of families from minority backgrounds in conferences, participating in studies, et cetera.

I completely agree with you; I think we were focused a little more on the actual provision of community service. So screening, diagnosis, and early intervention.

There is some data to suggest that, for many different, complex reasons, I think the children from minority backgrounds are picked up later. They are given services that are, in general, less intense.

I think there are several people who are doing studies in the community and pediatric offices to try to identify the barriers to the earlier screening for this population, in particular.

I think it is very complex and has all kinds of social factors and cultural factors.

DR. DANIELS: Was there a question down there from Craig Newschaffer? I can't see which microphone is on.

DR. HANSEN: So I guess the question that I wondered if you addressed, and I would love to have a lot more thinking about this, is, which are the areas or the barriers to getting screening to be done effectively in pediatric practices, I guess related in this context of healthcare reform?

Talking to a lot of pediatricians about not having time, not having training, I think those are huge issues that I would love to have dissemination science address as well as have this issue come up in terms of thinking about healthcare reform.

DR. FEIN: I couldn't agree more. I think we didn't address that specifically because it was outside our purview. But one of my colleagues who is a developmental pediatrician is doing a study where she is interviewing in-depth community pediatricians

to see what the barriers are. They are a lot of the things that we already know, plus, some additional ones that I think are not in the literature.

Reimbursement is No. 1. If there were reliable reimbursement for screening, diagnostic, a communication session, as Paula pointed out, with respectful and effective communication of what the child's development suggests and interventions, then it would be pretty easy to get pediatricians onboard, I think.

DR. DAWSON: I think the other point here, too, is that, if we think about trying to develop training programs or dissemination programs to reach pediatricians and other clinicians in the community, that if we don't first understand the factors that would either promote or impede their use of these, then I think we won't optimally design those training programs.

DR. DANIELS: Craig Newschaffer.

DR. NEWSCHAFFER: Thank you.

I will pose this as a question to the work group. I think maybe the question is sort of more one for the IACC. It flows from my experience on my work group. It has to do with the issue of prioritization, and whether or not you had time to consider that.

The dilemma being that we have a number of objectives in the existing plan that, despite the infusion of funds and projects that are underway, are still very worthy objectives. When the task is to identify gaps in other opportunities, you are sort of picking between the existing objectives or maybe amplifying or coming up with subareas that could be encompassed by existing objectives.

So I know that we sort of felt this a little bit in our group, and we didn't have much time to discuss prioritization. I mean you could pick on one of these. You could talk about developing effective screening

tools for infants below 18 months. Laudable goal, fabulous. But you could also look at that we still have work to do on evaluation and understanding about efficacy to effectiveness of screening tools for older kids. There's a prioritization issue there.

So the question is, did you have a chance to consider that? I think I probably know what the answer is. Then it bounces back to a larger question to the IACC, in my mind, about how that is going to be done.

MS. DURBIN-WESTBY: Hi. This is Paula.

I don't know if this will exactly answer your question, but we did look for things that were subareas. I treated my panelists during the first call to my detailed analysis of the 117 studies that were funded under our question.

I noted that there was -- I forget which one now, but it was one of the ones that said studies in adult, different groups, and it gave a wide range. I thought, good, this is

where I will see the studies that were funded for adults. There were 19 studies, and 18 were studies of children.

So my point is that, by identifying these little, smaller areas, I think, speaking for the group, that we were hoping to get some of these things that are not being addressed or that weren't in 2008. I know that was just one year.

So anybody else?

DR. DAWSON: Yes. I think there are a number of factors that one would want to consider in terms of prioritization. One would be to see how these new suggestions map onto the new ARRA funding, because I think some of these things have been addressed or studies are ongoing now. It may be that that would then take care of that for now or it may be that, by adding a little bit of supplemental funding to some existing study, that you could leverage it. That would, I think, of course, be a high priority.

But the other two factors to consider, besides opportunities for leveraging, are, what are the areas in which we know very, very little? And we know that this is an urgent area, such as adult diagnosis or understanding more diagnosis throughout the lifespan, such an unmet area. We know that this is going to be so crucial.

Then I think the other thing is to look at these in terms of kind of immediate impact on the quality of life of individuals with autism. So assessment of comorbid medical conditions I think is something where, if one could do that well, we could have an immediate impact on quality of life.

So those are just some ideas about how one might think about prioritization.

DR. JANVIER: I had a comment on that, too. I guess I would look at it very differently, being in the trenches and doing projects and teaching pediatricians in their offices on screening tools.

We do have screening tools with variable sensitivity and specificity, but implementing them is a tremendous challenge. My colleagues in states like Massachusetts, where there is mandated screening based on a lawsuit, they are actually, without any difficulty, now implementing certain screening tools; whereas, in many other states, honestly, they have no motivation to do that.

I kind of look at pediatricians and the practice of pediatrics as kind of a mom-and-pop grocery store. I mean it is not truly a system of healthcare. These may be a group of one; it may be a group of 10, or maybe something in between.

But they are trying to get through their day and pay their rent and overhead and their staff. Honestly, the last thing they want to do is find a family where they have to spend another hour to deal with a lot of time and stress on them, stress on their staff, and then try to refer them to a system that

doesn't exist, where they don't have a place to address the issue.

So it is really very challenging. The studies that I have seen on implementation, it can take 17 years to implement change. So the AAPs come out with great guidelines. We have tools that are recommended. But without a major impetus -- I mean I thought of don't give the pediatricians any funding for whatever it may be without evidence that they have done certain screening tools.

I mean, unfortunately, we don't have a system of healthcare like that. Again, these are individual folks that are out there on their own. Rarely do we have an effective system where we can make this happen.

DR. DANIELS: Cathy Rice?

DR. RICE: Hi. Thank you for your work. I have a couple of questions and comments.

First is following up on the comment that was made about considering how to integrate the issue of the line between a

diagnosis and disorder and features of autism. I think when we are considering screening and diagnostic tools, that is really essential for us not to just identify the features, but to help us clarify the field in terms of what really constitutes an actual diagnosis, as in a disorder, versus the features.

That type of clarity and having tools that help us sort out that would help immensely in terms of the challenges we face and the bigger questions about prevalence of autism, and is it changing. It really has a lot to do with how we draw that line.

So I would just reiterate that as an important thing to think about how to integrate into the objectives.

A second comment was we talked a little bit about the ethical and clinical barriers for early screening, and this may be incorporated into objectives 2 and 11. But one thing I think that is particularly important to consider is, for children under

18 and 24 months, particularly objective No. 2.

Not only do we have the tools to evaluate those children and identify the features, I think an important aspect to include there is also the acceptance, especially when we are talking about doing a general population screen versus an at-risk sample, and are the families able to hear that information if there's risk? Then does that actually help or impede their following up on the information.

For instance, some studies on very early screening, looking at kids at age 14 months, have found that families were turned off from seeking help at 14 months, but they were able to accept it at 18 months.

So I think in terms of when we are talking about the ethical and the clinical and the barriers, those types of things, that we particularly call out the special challenges of when we are going very young in a general

population, when these are families who are coming to their pediatrician without any indication of concern and are getting told that there may be risk here.

So I think that that is an important aspect to make sure we specifically include.

Any comments to that one?

(No response.)

Then I just have a third question, which is I noticed that the original objective No. 1.5, which calls out response to intervention for improving tools there, I didn't see any kind of objective that specifically looks at how to evaluate response to intervention, and just was wondering what the panel thought about that objective and whether it was necessary to include it or not.

DR. LORD: Actually, we did talk about it and then we ended up thinking that that should probably come from the intervention group. But it isn't that we didn't think it was important. So we should just probably

make sure it goes somewhere.

So the notion of, how do you quantify or how do you best represent various outcomes of intervention? It is not just improvements in IQ.

So that does seem like a really important thing that we need to make sure comes. I don't know if you guys have it in yours, but it should be someplace, you're absolutely right.

MS. DURBIN-WESTBY: This is Paula.

Cathy, I think that that is a good point to bring up about the acceptance. At really young ages, people are probably going to not have had any thought about it. But, even at older ages, I think -- I just wrote, "Language, language, language" because a friend of mine came in and threw a really glossy, thick folder on my desk and said, "Maybe you can do something with this. It doesn't do anything for me." It was from a major clinic.

The first sentence was, "Parents are devastated when they receive an autism diagnosis." That, as the first sentence, it just completely turned her off. She worked with her child, but she didn't go back to that particular center. She just was very put off by it.

So I think the language that gets used to talk about autism, starting from the diagnosis and the very first "Here's your diagnosis and your pamphlet", needs to be very positive toward the family experience and the experience of the individual.

DR. DANIELS: Craig Newschaffer?

DR. NEWSCHAFFER: Thank you. Forgive me if I am obsessing on this point, but just to follow up: the original plan has a specific objective about developing measures for tracking intervention responsiveness. I am very concerned that the interpretation of this process is that, if we don't mention things that are already in there, that that means

there's some diminished enthusiasm or lack of endorsement for continuing along that path.

I think we need to be very clear, or at least for our group, that we are identifying gaps and maybe refining certain opportunities, but that if it is not mentioned, it doesn't mean that there's a lack of enthusiasm for it or we think it is no longer on the table.

DR. DANIELS: Lyn Redwood?

MS. REDWOOD: I first want to thank the Committee for all their hard work. This is just wonderful information.

As a public member of IACC, I went through, I think there were 290 responses, and I want to thank the staff for compiling all of them in this wonderful notebook. I just wanted to mention some of the items that came out of the public comments that I am not certain whether or not they were considered, if this is the appropriate place for them, but I just wanted to mention them.

One of them was to develop clinical

guidelines to screen for risk factors, including family history. I am just wondering if we are at the point yet where we could start looking at either risk factors in the parents, whether it is autoimmune disorders or things where we could identify risk factors even prenatally and start following these infants more closely. So I thought that was an important factor to consider.

Another one that was listed, too, was with regard to biomarkers. I am sure this comes up in almost all of the different questions in the plan. But I am wondering if with No. 5, when we are looking at screening for co-occurring medical conditions, whether or not we could add something in there, too, to also try to collect biomarkers for those co-occurring medical conditions as well.

And the third one has to do with epidemiology and surveillance. I am not certain if this is the appropriate place for this to go in, but, again, this was one of the

comments that was received from the Request for Information.

The recommendation was to continue to monitor the prevalence of ASD and investigate differences in prevalence among specific subpopulations.

For example, we know, for some reason, New Jersey has a very high rate of autism. So I think there's things that we could learn from going in and looking at these subpopulations with regard to rates of autism.

So I just wanted to sort of bring attention to those three recommendations because I didn't see them specifically within your recommendations from the Committee.

MS. WISEMAN: Specific to the guidelines, clinical risk factors, we absolutely addressed that. That was one of my important issues, is that we look at the underlying immune and gastrointestinal and metabolic issues, the underlying factors and some of the biomarkers. So we definitely did

talk about that. I believe we incorporated it into one of the objectives.

MS. REDWOOD: I just didn't see biomarkers listed. I think it was No. 5. Is it in there? Maybe I just missed it.

MS. WISEMAN: Yes, I believe it was in there. If it isn't there, it should be in there because that was definitely a big issue.

DR. DAWSON: And also, in terms of the objective that has to do with the screening, develop methods for screening and assessment of comorbid medical and psychiatric conditions, I think our intention was that biomarkers might be one of those methods, right?

So it was really looking broadly at, what are the best ways of screening? Is it through a questionnaire? Is it through a biomarker? Is it through family history? Is it all of those things?

So we know very little at this point about what are the best methods for making

sure that we pick up those conditions. So one could imagine a study where you approach this on a lot of different levels, both behaviorally, biomarkers, family history, and then look to see which one of those is an effective screener for these conditions.

DR. FEIN: But I think we might want to just insert "or family factors" into the No. 2 because we really were focused on the children themselves. Biomarkers and behavioral markers, but I think we didn't really think about including family markers in there. That would be easy to add.

And I wanted to mention one other thing. We did go through all of the RFA/RFI information. I think, by the time we did that, we had already developed the first list, and we decided that almost everything that had been suggested in the public forum was already addressed in our goals with one exception, I think. And we did talk about including it as a goal and somehow it is not in there. The

panel can just decide if maybe it should be put back in, because this seemed to us to be the one thing suggested by the public that wasn't really included.

That was to develop better tools to assess skill levels and functioning levels in children with ASD, cognitive skills, social skills, adaptive functioning. Because studies now are generally just using standardized measures, and we don't really know if they function in the same way in this population as they do in other populations. So that would be a research area to look at.

DR. DAWSON: Yes, and just to elaborate on that, a related issue there is the assessment of non-verbal individuals; that we still have very poor tools for individuals who can't express themselves verbally because most of the assessment tools really do rely on either understanding or expressing language. So that was something that was not incorporated. We sort of left it off, and

then last night were thinking it should be added back in.

MS. REDWOOD: What about the prevalence study in high-risk populations, like Somalis? Is that represented somewhere else in the plan? That was one of the recommendations.

DR. FEIN: I don't think we were thinking of epidemiology as part of ours, but maybe the IACC people could talk to that.

DR. DAWSON: I think we were thinking of epidemiology from the point of view of, what are the appropriate tools for identifying caseness? So the Catherine Rice question earlier about, how do we make sure that we can identify what is a case and what is not a case?

But I think, in terms of looking at different populations from an epidemiological point of view, to learn from that, that might go more under, why did this happen or what are the causes?

So those epidemiology studies can be

used for a lot of different reasons. It sounds like the ones that you are talking about might fit more under causes.

DR. DANIELS: Cathy Rice?

DR. RICE: Lyn, in answer to your question, my read on the current plan is that it is under objective 3.9, that it is kind of buried in there, but not really called out anywhere in particular.

MS. REDWOOD: Thanks, Cathy. It was just that it was in our packet under this particular question. So that is why I raised the issue. Thank you.

DR. DANIELS: Yes, please go ahead.

DR. HANSEN: I wonder if I could ask a question that is a little broader question. It was brought up by Craig Newschaffer about, how does one prioritize all these things?

I was impressed that in this part one you really broke out a whole lot of things from what was there in the original. So now you've really created a whole lot more

specific areas of targets and focus.

In the initial plan, there was a certain amount of money allocated to each area. As we now all go through each of our sections, do we need to argue more passionately for one particular thing or for our section, to say there's a limited amount of money to go around?

Yet, as I understand it, it is not our job to give any kind of priority to anything. Is that right? We don't get to decide the money. We don't decide the priorities. Somebody else does.

How do we influence the somebody else to say, if you were going to do these things, we would suggest you do these things first and you save these for later? Because having 100 things looks good on paper, but it doesn't mean anything until you see how they get prioritized.

Is there an answer to that at this point?

DR. DANIELS: I will address that. We actually did ask all of the panels to consider prioritization. However, it is up to the IACC to determine the final prioritization within the plan.

So we would encourage the panels to share their ideas about priorities, and most of the IACC members are here today to hear what you have to say and will consider that in their deliberations in the next few months.

DR. HANSEN: So we should mention prioritization if we can?

DR. DANIELS: Yes.

DR. HANSEN: Okay.

DR. DAWSON: So I think that, and I'm just speaking for myself now because the panel really did not spend a long time talking about prioritization, but there were some themes that really cut across a lot of the recommendations that this panel made.

I think one Yvette just alluded to was the idea of devoting some money on

dissemination and implementation science is important. So that plays out in those objectives in several different ways, whether it is ethnic minority populations, training programs for physicians, whether it is understanding the barriers to use of these in a community setting. So those are all kind of under the area of implementation/dissemination science.

I think the other was kind of broadening our idea of diagnosis and screening away from just young children 18 to 24 months to include the lifespan, the comorbid medical conditions, and more subtle kinds of characteristics.

And the third issue I think is important to consider is just leveraging and opportunities. You know, it is always a priority, I believe, if there is a study like the National Children's Study or others where a little bit of funding goes a long ways, then those always, I think, get a little bit higher priority in that sense.

So those are the three factors I think one could consider.

MS. BLACKWELL: Thanks, Geri.

I would just like to echo again that I think our panel, Panel 5, really did touch on some of these directly, the first being dissemination of research into communities. So, when we get to Panel 5, I hope you will be pleased with the way or just we could talk about our approach for that.

Also, we certainly did get to the lifespan issues in Chapter 6. So it is great to know that we are all on the same page or pages. So thanks.

DR. DANIELS: Down here?

DR. STATE: Matt.

DR. DANIELS: Matt, sorry.

DR. STATE: No problem.

I guess I had a process question as well. I mean it seems to me that this issue of priorities is really also a question of context, right? We just heard that $85

million is going to be spent over the next two years; obviously, some of that addressing issues that are very important to all of us.

So we have got a horse-and-cart problem a little bit in this discussion about, you know, trying to figure out what has already been committed, what has really been the focus of that money, and then where can we best make use, as Geri pointed out, the issue of leveraging.

So my process question is sort of, when does that integration happen? When does it happen that there's a comparison of what the overall objectives of this group are in the light of the funding that is happening over the next two years?

DR. DANIELS: I can address that one as well. So the IACC will be meeting on October 23rd, the full Committee, and the Planning Committee is hoping to have a conference call in the next couple of weeks to begin discussing the outcomes here.

We hope that ARRA funding information will be available by that time. Since some of the grants just literally got funded today or yesterday, we didn't have that information available in time for all of this activity, but the IACC will have that for its deliberations.

Alison?

MS. SINGER: Geri, can I just ask you to expand on what you just described as a priority, specifically, your priority No. 2, which you described as broadening diagnosis away from just children?

Would you also include in there the need to broaden, as Cathy was saying earlier, to look at symptoms that lead in one direction to disability and maybe other symptoms that lead at times to differences, but different types of disability? Would you encourage us to look at those differences as well?

DR. DAWSON: Absolutely. I think that that is going to be a very important theme. I

guess the whole idea here is that we have focused a lot of research and attention on developing these early screening and diagnostic measures, which is fabulous. Now we are actually talking about dissemination.

So now I think we need to step back and get into issues such as you are talking about. What are ways of looking at more subtle kinds of problems that may not even lead to a full diagnosis? What are the strengths and weaknesses, special skills, and so forth?

But, also, again, the adult lifespan and the idea that autism isn't for some individuals only a behavioral disability, but also includes some of these medical conditions that we have tended not to address.

So it is a broadening of the way we think about assessment. I think that it is just time for us to do that.

MS. DURBIN-WESTBY: This is Paula.

If you reach research strength and skills as well as disabilities and also

differences, it will probably lead somewhat away from the stated goal of preventing autism because you're going to find that there is a pattern of real positive skills and abilities that many of us have, including people that the outward appearance of them looks like they might be very, very disabled, so that they don't have any positive qualities or skills.

I think that needs to be an important research area. I hope that it will be.

DR. SHORE: Yes, and I will second that, what Paula said. As a matter of fact, one of the members of group No. 4, Sharisa Kochmeister, who was supposed to be here, but, unfortunately, she is ill and she isn't able to.

She's a brilliant woman. She's non-verbal. As Paula had mentioned, just by looking at her, she would present as most people would consider as low-functioning, which is also a word we need to work with because it doesn't really accurately describe

things. But she can contribute amazing material to our panel.

MS. DURBIN-WESTBY: If I can get my words out, what Stephen mentioned about using low-functioning and high-functioning, I was in on the other calls. I know people struggle with it because people don't like high-functioning and low-functioning, but it is hard to talk about it without doing something like that, which is why we started using variability to show that there is a different spread of skills and disabilities.

But, also, I looked at, dating back to 1999, the Anti-Stigma Mental Health Initiative, and they specifically have in there as one of their examples low-functioning, and that it is a stigmatizing thing.

Sharisa said on one of the calls that she said that she found it insulting. Also, I think it can be just inaccurate. So I think that people need to move away from that and

start thinking about it differently.

One of the ways that that can happen is to include adults or teens or children on the autism spectrum in all levels of research, including input, evaluation, deciding how the project should run, because we have knowledge of what it is like to live with autism.

MS. BLACKWELL: Paula, the way our panel approached this was to discuss all people with autism across the ASD spectrum. So that is pretty much the language that we used in our objectives.

DR. DANIELS: Lee?

MR. GROSSMAN: Yes, Paula, as a member of Panel 3, we were the ones tasked with the prevention issue. So we will be discussing that more during our presentation later.

I think there was a fairly good consensus on what our definition of prevention will be, but we will be discussing that later.

DR. DANIELS: Ed?

DR. COOK: Yes, I want to follow up

because, actually, this is a very important question, and variability and heterogeneity is the issue, but it doesn't solve for us the challenge that we have of how to be respectful, but also acknowledge the differences.

So I'm asking for help, and I was hoping you had the language that would solve this for me personally, as the brother of someone who would have been called low-functioning.

But it came up because the issue was too much emphasis on intervention at the higher end of whatever variable dimension you want to talk about. So how do we talk about that and be respectful and still get the work done to help people with their distress? I'm not even that comfortable with disability, but that is really what we want to prevent, is distress and disability.

So I look forward to further dialog on this because it is a very important issue, I think.

DR. DANIELS: Bob?

DR. HENDREN: You make a number of references to thinking about diagnosis in adults with autism. You talk about it as though maybe first diagnosis or first recognizing. Yet, I think implied, but maybe not specifically stated, is the way diagnosis changes with treatment over time, and the way then somebody can assume, because the symptoms look different, that they don't still have need of intervention or they don't still have autism in the same kind of way.

Maybe it is improved or better, but I think about adolescents or young adults that have learned through good treatment to maintain joint attention, to have good eye contact. Their language has a certain fluctuation in the way that they speak.

Then a school or a program will say, well, this person doesn't have autism; they don't have these classic symptoms. So they don't need to be in this particular program

any longer or they don't fit here anymore. Or maybe they have affective instability along with that. So someone says, well, they have bipolar and they need to go to the mental health sector.

I wonder if there is a way of emphasizing looking at trying to see how the diagnosis might change over time, and how we might mistakenly shift our diagnosis, if we don't look at a full range of understanding where they are.

DR. DANIELS: Geri?

DR. DAWSON: So I think, just in terms of sort of struggling with this issue of the many, many forms of autism, perhaps what we're all striving for is either you could call it promotion of the most positive outcome for every individual, which means reduction of suffering and promotion of independence and choice, and a life that is happy, where people can fulfill their own dreams. The pathway is very different.

So, if you talk about prevention, you want to prevent a situation where a person doesn't have the ability to be independent and to communicate and to seek pleasure, and so forth, and to be void of severe medical problems.

So I think we can all kind of perhaps think about that kind of language. Then I think we get away from some of the notions of prevention that may have negative connotations for many individuals.

DR. DANIELS: I think we are coming to the close of our 45 minutes. Is there any other burning question that anyone has that they would like to ask before we close? Peter?

DR. GERHARDT: Yes, Peter Gerhardt.

I would just add very, very quickly that I think one of the challenges with the issue of diagnosis across the spectrum relative to these short-term and long-term goals is when we talk about high-functioning, low-

functioning, across the spectrum, the issue really relates to adaptive behavior and adaptive competencies. That is nowhere in really the discussion.

We talk about social skills, rebel behavior, and problem behavior, but we don't talk about adaptive competencies. We oftentimes refer to the high-functioning and low-functioning is inaccurate because someone who might be labeled low-functioning really has some academic competencies, some cognitive abilities, but I know quite a few adults with IQs above 140 who have no adaptive competencies and are very low-functioning in life.

So not only does this challenge one way across the spectrum, it cuts the other way. So I do think the more we can do to look at what are the adaptive issues, the adaptive behavior challenges, the better we are going to be as we look forward on this issue.

DR. DANIELS: Well, thank you very much

for a wonderful discussion and all the hard work of Panel 1.

At this time, we would like to open the floor for questions and comments from the public. If you would please come to either microphone and alternate between microphones?

PARTICIPANT: Hi. Thank you. This has been fabulous. It is really great as a parent.

I have a son who is 15 years old, non-verbal, low-functioning. He had a first diagnosis at 11 months by an MRI. Because of that diagnosis, then he was delayed in being diagnosed on the autism spectrum because I think doctors are scared to put another diagnosis on top of a first diagnosis to parents. For that, it took him all through elementary school to be put in the right program.

So you had on the thing that early diagnosis for children on this spectrum, white children, other minorities and stuff, but you

don't mention the special needs population that is being missed, that they are not being diagnosed early enough to get the right early intervention. So that was my thought.

DR. FEIN: Yes, if I could just respond to that, I think that is a great point. I mean we were thinking of the opposite, I think. We were really focused on kids with an early ASD diagnosis and then what else is missed. But if another diagnosis comes first, how often is the ASD missed? I think that could easily be worked into the objectives.

PARTICIPANT: Right. Because I brought it up. I was living in Boston at the time. Children's Hospital at that point in Boston was the No. 1 children's hospital in the United States. I brought it up to a doctor there when my son was 15, 18 months old. I said he has very autistic-like tendencies, and they're like, "Yes, well, yes", but it never went farther than that until we moved to Maryland. So I think that it has to be

brought up.

My son does not have Down's Syndrome, but I know a lot of people who their children with Down's Syndrome are also on the autism spectrum. I was very amazed to realize it is such a large population with Down's Syndrome where they also have a diagnosis of then autism. So I think it is something that has to be brought up, that doctors have to remember the special needs population, they can also have dual diagnoses.

Thank you. Thank you very much.

DR. DANIELS: Thank you.

DR. JESIEN: Good morning. My name is George Jesien, and I'm with the Association of University Centers on Disabilities.

We have been doing a series of Act Early Summits that bring state teams together around early identification over the last couple of years. One of the themes that has come across in all of those meetings has been, one, the lack of personnel; two, the lack of

appropriately-trained personnel.

I just wanted to applaud the objective that you had in this first panel around professional training. The real utility of science in terms of new findings and discovering new knowledge is really in its translation to the field and its application and acknowledgment by families and professionals. The investment in research really does need to be combined with the translation of that knowledge to practitioners and family members.

While I am here, I would like to just add a couple of suggestions to that recommendation. The first is, given the complexity of autism and its medical, behavioral, communication, and the mental health aspects, that you insert the word "interdisciplinary", that autism is not just the province of the medical profession, but occupational therapists, speech and language therapists, social workers, educators,

behavioral interventionists. This is really an opportunity, I think, to make sure that we have a broad spectrum of professionals that are involved in providing the supports and services.

The second -- and I think you can do this by including a phrase in the RFAs that go out and in the supports for training -- is that you include that people on the spectrum and family members need to be part of those training programs.

It seems to me that, if we include people on the spectrum and family members, from the basis of the formation of the professionals that will serve as our next cohort, we are going to be much further ahead than trying to insert people on the spectrum in discussions. I would advise that that happen very early in their professional development, as they are going through school and graduate programs.

Then the third, given the current status

of health disparities in this country, I would also state that we need a real priority on recruiting from ethnically- and culturally-different groups and need to get those people into our training programs, so that our professional field can begin to reflect the populations that we should be serving.

So thank you very much.

DR. DANIELS: Thank you.

Are there more questions from members of the public who are in attendance?

DR. FEIN: I would just like to add quickly about that last point, I think we could and should easily incorporate that in No. 9, just to broaden practitioners so it is not just talking about pediatricians.

MR. JOHNSON: Hi. My name is Chase Johnson. I am the ASAN intern.

I just, as a child or a young man being diagnosed with Asperger's in the early nineties, kind of when it was becoming sort of like a booming, popular thing, I ran into my

own issues in terms of when I went to high school, in terms of accommodations. I performed pretty well academically. However, when it came time for me to take the SATs, they would not give me accommodations because of my academic performance, and I didn't do so well on those.

I guess I think autism should be viewed as something a lot more, if you will, fluid because, when I was younger, I had things like echolalia, which really isn't all that often associated with Asperger's. Correct me if I'm wrong. It could be, but as far as I understood, it really wasn't all that often.

I don't know. It was very interesting and very frustrating at times just trying to get like the correct help as necessary for my own issues in high school in terms of those accommodations.

So I am just going to repeat it, like it should be viewed as something a lot more fluid and changing. I think it is sort of like an

evolving process, if you will, a little bit for me at least; I don't know about everyone else. I'm just speaking for how it has affected me personally.

It has just been, I don't want to call it an uphill battle per se, but it is just it sort of has like its ups and downs, and what have you.

I'm sorry, I'm just rambling at this point, but I just wanted to add in like a few points.

Especially that fluid term is how I think it should be viewed nowadays or as it pertains to this workshop.

DR. FEIN: I just wanted to point out that one of the terms that we tried to include in the objectives had to do with, when someone receives a diagnosis, does this actually lead to appropriate intervention?

We also made a point of saying appropriate services, accommodations, and interventions, recognizing that the whole

issue of diagnosis needs to lead to accommodations, recognizing the frustration that people experience when they don't have those accommodations and can't really actualize themselves because of that.

DR. DANIELS: Are there any more questions or comments from anyone in attendance?

DR. SAMSTAD: Can I follow up on the first public comment? I wanted to say that she raises a good point, which is this idea that, if somebody has one diagnosis, that autism may not be considered. I think that is true in the adult population as well. I think there are a lot of folks in general mental health clinics who maybe have bipolar disorder or schizophrenia, or whatever, and clinicians aren't necessarily looking for a diagnosis of autism in that population.

So I was very happy to see the screening tool item included in here. My hope is that that can be a tool that not only would be

appropriate in primary care settings, but also in general mental health clinics for helping to identify folks that need additional services.

Thanks.

DR. KING: I would like to follow up on George Jesien's comment about workforce development and raise the question early because I think it will apply to a number of the groups today, which is that, in addition to expanding the treatment workforce, which is a critical need, that many of the research priorities that are being put forward today won't happen unless appropriate grants come in with a cadre of investigators that are up to the task of being able to affect this important work.

I wonder if at some point that needs to be called out, sort of a workforce development for the investigators to go into the areas that we have not yet traveled, thinking about Geri's comment about the intervention science,

for example, and our need to reach out into other fields to bring that to bear on autism, and even further upstream, whether there are specific investigators that we need to develop or support to be able to affect some of the priorities that we are putting forth.

DR. DANIELS: Ann?

MS. GIBBONS: Yes. My name is Ann Gibbons.

I just wanted to make a general comment. I want to encourage Chase to speak up whenever possible because you said you were rambling. Actually, you did a very eloquent job.

Our panel struggled a good deal with talking around and for other people. The main reason I am in this room today is I am here to speak for my son, not for myself. So, please, whenever possible, ramble and contribute to the conversation because we really want to hear what you have to say.

DR. DANIELS: Others? Are there further

comments?

Please come to the microphone.

PARTICIPANT: Thank you.

I just wanted to support the comment made by this gentleman about work groups, to bring in researchers in the field that are working with and who are doing assessment and intervention with autism, but might need further training, to participate in research.

I am an occupational therapist, also a researcher. I was going to bring this up at treatment, but it seems like we are moving in that direction.

There are hundreds, probably thousands, of occupational therapists working with children with autism who need direction in what works, when it works, how frequently it works. We are spending a lot of dollars on it. I think we deserve to study it. That's all.

DR. DANIELS: Thank you.

Other comments? Chase?

MR. JOHNSON: Chiming off of that a little bit, I really liked whoever brought up the idea of interdisciplinary sort of as being like approached for a view. And I also liked the occupational therapy discussion that we just had there.

For me, occupational therapy was helpful in terms of (a) learning how to write legibly, as, again, just because I have terrible writing, and (b) it was interesting.

Like I was sort of a test subject for like I don't know whether it is still being used because I didn't need much more occupational therapy after this test. But, basically, the test, how it went, it was sort of like, I think it may have lasted like, it was spread out over like a few months over the course of maybe like 40-some hours, where I would have headphones on, and they play just like a tempo, if you will.

I would have to clap to this exact tempo at this exact beat in order to increase

concentration and just sort of awareness of how to concentrate in terms of like studying, and just sort of to increase the ability just -- I am trying to think of the best way to put this -- I guess to function in the classroom really in terms of like keeping up at the mental rate of whatever is going on around me, because of like how I think maybe at like a different wave length or a different rate, how we approach a given issue may be different.

So just sort of learning how to adapt, this adaptive behavior, is also a really, really interesting subject to bring up as well.

It is just I have a lot of friends with Asperger's, and we just sort of like make cheap little Asperger's jokes toward each other. So one of the things that we all kind of have believed, that if you really want to sort of help the condition, I think -- and I was discussing this sort of briefly -- there is really no better way to help. I can't

really say this for all forums or all themes within the spectrum, but at least for Asperger's, there really is no better thing to help it than the school of hard knocks really.

So I learned through a lot of very difficult experiences, whether it be academically or socially. So that helped sort of mentally curb behavior in my mind, and just sort of like, whoa, it is just sort of like that lesson of life, when you put your hand in like fire sort of lesson. Then like it finally clicks mentally.

Like some people it takes longer. For me, it took a very long time, but a lot of things did click and change over time. It curbed certain behaviors, especially like the whole looking in the eye, variation in voice, monotone sort of thing.

Just a lot of very interesting intervention with the adaptive behavior, I found to be pretty helpful.

So I am just going to stop rambling

again. But thank you.

DR. DANIELS: Peter?

DR. GERHARDT: I just wanted to very briefly applaud this interest in not only diagnosis of older individuals, but talking about workforce development for researchers, because I would hope that that would stimulate workforce development for people who actually want to work to support adults across the spectrum.

Because, as we know, Department of Human Services data indicate that, for a program supporting adults with developmental disabilities in general, there's an annual 50 percent turnover rate and a 10 percent vacancy rate, which makes it very difficult to provide appropriate, let alone adequate, services for individuals.

So this emphasis on older learners and the capabilities there, I truly hope excites the interest in later intervention that some of our early intervention work has sparked in

terms of early intervention. So that we actually can develop a workforce that is there to support people to lives of dignity, competence, and quality, which is, I think, what this is all really about.

So I am very excited by the discussion so far.

DR. SHORE: Peter, thanks. That just follows my comments about Chase's input, and what Chase has so eloquently described. That just demonstrates for us that we really need to listen to people's experiences on the autism spectrum, listen to their schools of hard knocks. So that we can take these experiences and help people further on down the line, as we look at -- and this will be one of our questions when we get to Panel 4 -- how do we balance our portfolio of interventions between novel, targeted interventions and testing of currently modestly-helpful interventions?

There is a lot out there, but where is

the boundary between looking at snake oil and really looking at stuff that seems to help an awful lot of people, but we don't quite have the evidence-based research on it yet.

DR. DANIELS: Thank you.

David?

DR. MANDELL: So I like this discussion a lot. I was trying to think about it is hard not to jump straight to Panel 4, right? It is hard not to start immediately talking about intervention.

But I did want to suggest that maybe this has a lot of implications for Panel 1 as well. Especially when we talk about workforce development and training, developmental screening is not an autism issue.

If we make it an autism issue, in some ways we have kind of artificially narrowed the field; that there are a tremendous number of people out there who do screening, both formal and informal. Some of them are really good at identifying kids with developmental needs,

including autism, and some not so much.

So there's a giant natural experiment going on out there that we can take advantage of to see what kind of screening practices and what kind of people seem to be doing a good job in communities, and also thinking about those professional organizations that are responsible for inculcating those skills, not just in pediatricians, but in child care workers and in other professional guilds, and think about what we can do.

Just like we are thinking about the Child Health Study and how we can add on something to that, how do we add onto the current infrastructure for training professionals who are working with kids with autism and adults with autism, whether they know it or not, and providing them with the tools to do this?

So it is kind of the same discussion that we are having about intervention, but we need to be applying those same principles to

our early detection.

DR. DANIELS: Thank you.

Other comments? Lee?

MR. GROSSMAN: Well, I'm not sure how we've done this, but Panel 1 seems to have expanded the dialog well beyond intervention into employment and residential and everything else, which is absolutely working for me. I am hoping that we all head in that direction.

But I kind of want to throw this out to the group then because, as we talk about these processes, about what we need to do, how we have to develop the workplace setting, et cetera, it really hasn't been part of our discussion heretofore, but it seems as though the systems that are currently in place -- and maybe this is me opining a little bit -- just aren't adequate to adjust and to deal with the complexities of not only autism, but disabilities in general.

They are disjointed typically. There are some rather archaic policies, such as to

qualify for some programs, you have to be at poverty level. There's just a whole host of issues that we have with the current systems that are in place at all levels, community, state, and federal levels.

So I guess I am throwing this out to the group to think that if that is beyond the purview of the IACC to begin to honestly and practically and with great attention, start dealing with these systemic issues as part of our strategic plan.

MS. BLACKWELL: Lee, this is Ellen.

I just wanted to add that Lee and I are actually Co-chairs of the Services Subcommittee of the IACC. I hope that Lee is really pleased with the work we did in Panel 5 because we did, in fact, address this issue head-on in terms of coordinating the systems approach.

So I am so glad, as you said, that Panel 1 just kicked off in this way.

DR. DAWSON: It seems to me that anytime

that you are involved in collecting data for the purpose of either understanding things like what are the systems that are out there, what are the barriers to the implementation, and so forth, as well as if we try to implement something, does it work, right, collecting data on effectiveness of various schemes for change in the community, then that is research.

So I do think that it can be helpful not to draw a strict line between services and research, but rather let that line kind of move. Because I think anytime you are collecting data, that is research. You wouldn't want to engage in services without collecting some kind of information on its effectiveness.

DR. DANIELS: Ed?

DR. COOK: Yes. I'm getting more general questions even. That is that, in terms of the agencies represented here, I mean I previously had questions about, for

development of medications or study of them, why the FDA wasn't involved. But a lot of the discussion here is making me wonder if SAMHSA is or shouldn't be involved in this process.

DR. DANIELS: SAMHSA is a member of the IACC.

DR. COOK: Are they represented here?

DR. DANIELS: Is Larke here? No.

DR. COOK: Oh, okay, great.

DR. LORD: Somebody -- and now I can't remember who it was -- just brought up that, I mean, obviously, the new plans for healthcare in the U.S. are in flux, but it seems like that is something that we need the IACC to represent us, represent anyone who cares about autism in the future, especially as things are changing so much.

Because that is something, as a researcher and as somebody who runs a clinic, it is very hard to speak for without sounding like we want this for ourselves, but you guys can do it. I would love to have that as a

back part of all of the agenda, thinking about how are these objectives going to fit into whatever is going to happen, and can you guys be our representatives to make sure that this is a good thing, not a bad thing, for us?

Anyway, it seems like that is another, again, avenue of change that is going to likely happen.

DR. DANIELS: Other comments? Geri?

DR. DAWSON: I just wanted to respond to Cathy's bringing up the point about what the IACC does, how does that fit into the whole issue of healthcare reform and positioning the autism field in a way that will take advantage of healthcare reform?

I think two issues seem to be really fundamental to the healthcare reform movement: one is comparative effectiveness research, and the idea that if one is going to be paying for or reimbursing hospitals or clinics for what they are doing, that there needs to be an evidence base that what we are paying for is

the most effective. So to kind of have that in the back of one's mind I think is very important.

Then the second thing is performance outcome measures. So clinics and hospitals, if the current healthcare reform movement goes in the direction that it appears to, then they are going to be accountable for showing that what they are doing actually is effective.

When you think about that, how would you measure effectiveness? What are the performance outcomes? With diseases like heart disease, it is easier to say whether it is cholesterol or deaths or something. What would be appropriate performance outcome measures for the autism field?

That is something, when I talk to people in the healthcare reform movement in D.C., this is something that they had stressed a lot. So just I think we might want to keep that in mind in thinking about these objectives as well.

MS. BLACKWELL: Geri, I just want to mention that, although, obviously, health reform legislation isn't finalized or passed yet, the Children's Health Insurance Program Reauthorization Act, the CHIPRA bill that the President already signed, does have some very strong measures consistent with the principles that you mentioned embedded in it.

So you might want to focus on that because we are really excited about those at CMS. Those are specific both to children enrolled in CHIP and Medicaid kids and other populations as well.

DR. DANIELS: Paula, did you raise your hand?

MS. DURBIN-WESTBY: No.

DR. DANIELS: Oh, sorry.

Anyone else at the table or in the audience with a question or a comment?

(No response.)

All right. Well, we are 15 minutes early, which means that you can take an extra

long lunch break. Hopefully, everyone will be happy about that.

There's a wonderful little restaurant right here in the hotel, and there are several different restaurants within walking distance. There was information up at the front desk, and I believe everyone at the table has a restaurant list as well. With the extra time, you can really take your pick of where you would like to go for lunch.

We will be reconvening at one o'clock.

(Whereupon, the foregoing matter went off the record for lunch at 11:18 a.m. and resumed at 1:07 p.m.)

A-F-T-E-R-N-O-O-N S-E-S-S-I-O-N

1:07 p.m.

DR. HANN: We would like to begin the afternoon session.

Okay, if I could ask for the presenters for Panel 2?

I feel like I'm at an auction.

Okay, it is my understanding that the morning went very well. There was lots of good discussion and a great way to get launched. So thank you very much, Panel 1.

We are moving now to Panel 2 to begin our afternoon.

Hang on one second.

And it looks like Alison is all queued up.

Alison, if you and your panel members would introduce yourselves, that would be

wonderful.

MS. SINGER: Okay. Welcome back from lunch, everyone.

I am Alison Singer, co-founder and President of the Autism Science Foundation, and I am a public member of the IACC. I served as an liaison for Panel 2.

The other members of Panel 2 were Dr. Pauline Filipek, professor of pediatrics at the University of Texas; Dr. Sarah Spence, pediatric neurologist from the National Institute of Mental Health; Dr. David Amaral, professor of psychiatry and behavioral sciences at the M.I.N.D. Institute; Dr. Emanual DiCicco-Bloom, professor of neuroscience and cell biology and pediatrics at Robert Wood Johnson Medical School; Dr. Ashura Buckley, research clinical fellow at the NIMH and sister of a brother with autism, and also Denise Resnick, who is the co-founder of SARRC, who is the parent of a son with autism and who, unfortunately, due to a family

situation, was unable to be here today, but who participated in all of our panel discussions.

Before we get started, I just wanted to thank all of the staff from the Office of Autism Research Coordination for all of the amazing energy and effort that they put into this. I know it was a tremendous amount of work. We really appreciate it.

I also want to thank all of the panelists from Panel 2 and all of the other panels, again, because this process really showed a lot of great expertise and energy, and all of the public members I know are very grateful for your input.

So, with that, I'm going to -- oh, sorry, I forgot the Co-Chair of our Panel, I apologize, Dr. Ed Trevathan from the Centers for Disease Control, who is the co-liaison for this panel, and also Dr. Cathy Rice from the Centers for Disease Control, who was the Co-Chair of this panel as well.

So, with that, I am going to hand it off to Dr. Filipek to begin our presentation.

DR. FILIPEK: Good afternoon.

Panel 2 started by first outlining, and we wanted to review for you, the research opportunities in the current IACC strategic plan.

Basically, this plan addressed multi-disciplinary longitudinal biobehavioral studies of children, youth, and adults, beginning during infancy, to characterize the neurodevelopmental and medical developmental trajectories across the multiple axes of the ASD phenotype, predominantly to identify ASD risk factors, subgroups, co-occurring symptoms, and potential biologic targets for intervention.

Such studies could include high-risk siblings of children, youth, and adults with ASD; children without a family history of ASD, as well as studies of typically-developing children, and to include multi-disciplinary

assessments of brain imaging, metabolic and immune markers, microbiomics, and electrophysiology, as well as behavior.

Research on females with ASD, to better characterize clinical, biological, and protective features; human and animal studies to examine immune, infectious, and environmental factors in the occurrence of ASD, and international public/private collaboration to expand postmortem brain and other tissue resources, for example, skin fibroblasts, to increase the acquisition, the quality, the type and availability of biomaterials relevant to the pathology of ASD, and research on unique strengths and abilities of people with ASD.

The noted research gaps in the current IACC strategic plan, as outlined by Panel 2, include the lack of studies focused on the underlying biology of co-occurring conditions. For example, but not limited only to seizures, sleep disorders, familial autoimmune

disorders, GI issues, as well as studies focused on underlying biology of co-occurring syndromes. For example, Rett, Fragile X, tuberous sclerosis complex, isodicentric chromosome 15, looking at similar or divergent pathways, both behaviorally and biologically.

The third gap was a clarification that the recommended study of females should also include studies focused on sex differences, encompassing clinical and basic research, in an attempt to explain the four-to-one male-to-female ratio.

The panel also noted a gap that the subgroup studies should highlight non-verbal or minimally-verbal autism, impaired sensory motor function; should highlight racial minorities and regressive autism.

That studies should address the collection of a variety of biomaterials to study the biologic signatures in patients with ASD, and the lack of studies focused on mitochondrial studies, mitochondrial markers,

and metabolic disorders using biologic samples.

I am going to turn it over to Dr. DiCicco-Bloom for the remainder.

DR. DICICCO-BLOOM: Thank you, Pauline.

So the new opportunities that we identified -- and we are keeping this, by design, relatively short, so we can have more time in discussion -- obviously, with the new discoveries, we would like to be able to collect and perform in vitro studies using new technologies to induce pleuripotential stem cells for neuronal differentiation from skin fibroblasts.

As you are probably aware, one can now use both human as well as mammalian model system fibroblasts, introduce no more than four transcription factors, and turn this fibroblast into a multipotential cell which can then be differentiated even into neurons. This would allow us to have opportunities, in fact, as a biologist might say, to have an

autistic neuron in the dish to actually examine, both for mechanism as well as to look at potential therapies.

The next opportunity -- and this really builds on the emerging evidence in genetics in animal models -- is now a goal to study an association between specific genotypes, whether these are common variants such as contactin-2 associated protein, for example, or serotonin reuptake genetic polymorphisms, or even specific rare copy variants, such as the neuroligin families, and associate them with functional and structural phenotypes.

So, for example, there have been some nice published studies on the serotonin transporter alleles and whether it is associated with macrocephaly, for example. Or another example is looking at oxytocin receptor alleles and doing functional imaging, and demonstrating that the amygdala has differential activation, and that there's differential association of that activation

with performance on cognitive testing.

So these opportunities were not specifically highlighted. I think they are emerging, but we should make them explicit.

The next opportunity also perhaps might be thought of as an unmet need, is to expand biobanking. We already heard this this morning from Panel 1, that we have, obviously, ongoing, large -- and this is really the same thing -- we have large, well-characterized populations, whether it is the National Children's Study, High-Risk Baby Sibs, the CDC CADDRE Study, the ATN Network, and other emerging ones, that we should be encouraging the collection of DNA.

One of the actual comments that came in was to include on perhaps even the consenting for families to have a stem cell biologist involved, so that we could actually consent at the time of having families join for the possibility of obtaining fibroblast biopsies for those who would be agreeing.

So, right upfront, we would like to try to encourage this, whether it is through supplements or whatever the mechanism. We are not here to talk about how to implement, but certainly we should encourage this, since this is a great opportunity.

So our suggestions for short- and long-term come on two slides. I haven't numbered them. It is really just to say a little bit more.

Skin fibroblasts should be obtained, and this will require, of course, the biobanks to store them. This technology is already emerging at multiple centers around the country.

A second priority is to understand the biology of non-verbal autism. As someone who doesn't see lots of children, this is not my area of expertise, but certainly we have already heard discussed this morning -- and I am sure we will hear a lot more -- being non-verbal does or does not associate with

differences in cognitive ability.

Those of you who are doing clinical assessment, we need tools that will adequately allow us to measure cognitive function in the non-verbal or minimally-verbal.

As a neurobiologist, if it is all domains, cognition and language and sociability, one thinks of a universal deficit, such as a synaptic molecule like neuroligin and neurexins, for example.

On the other hand, if it is a select language pathway, this might be a motor abnormality in a FIXP2 gene in the language circuit with no effect on other cognitive functions.

So it is important at the biological level to understand how these different regions work within mammals and then how we can start to assess them specifically in humans.

These studies to associate specific genotypes with functional and structural

phenotypes, I've already given some examples of that. This is really a natural emergence of the progress we have made to date, even based on only the data we have on 2008 funded grants. So I am hoping the ARRA grants will show us even more progress in that area.

We would suggest that research be specifically encouraged in co-occurring syndromes. We have seen that there is some research in this area. This really holds the promise by identifying pathways involved in each of these conditions, which we can study in detail, as is being done, for example, with Fragile X mice or tuberous sclerosis mice. By identifying pathways, we have actually been in the position to institute treatments in mice and reverse their symptoms.

In fact, as many of you are aware, there are actually ongoing studies with Fragile X children, based on work that Mark Bear has done in the mouse, looking at glutamate antagonist, because hyperglutamate

transmission is an underlying mouse defect which directly translated, because we knew the biology, into a human therapy trial.

In similar fashion to individuals with tuberous sclerosis, which manifests in autism in up to 40 percent of cases, have abnormalities of the mTOR pathway, and rapamycin, a drug which works on mTOR, actually, is undergoing clinical trial. In mice, it actually resolved tubers and improves their function. We are waiting for the human studies.

Also, we need to encourage research on the co-occurring conditions, including familial autoimmune disorders. I think there has been now replicated evidence, particularly in the advances over the last year, showing that familial incidence of diabetes mellitus or the maternal occurrence of celiac disease or rheumatoid arthritis may be predisposing factors for autism.

This, then, represents a subgroup and a

mechanism that might be relevant both in the families with these disorders, but also, as a biologist, it might identify pathways that we can focus on, even when the disorder itself is not manifest in the person.

So, in addition, as Pauline indicated, or as we know, seizures occur in up to 30 percent of individuals. These may come on later in life. We don't know if they are a symptom of a dysfunctional nervous system or, in fact, part of the etiology of some of the dysfunction. But this needs to be understood, both at the basic level, and I know there are some beginning efforts in having communications between scientists and clinicians studying epilepsy, but there's far less than we should see.

The American Epilepsy Foundation, some investigators are collaborating with autism experts to try to look at co-occurring symptoms and underlying mechanisms. This should be encouraged.

In similar fashion, the work that has been occurring now fundamentally in sleep disorders should be communicating with the well-known sleep disorders that are occurring in children. I think many of you, of course, were two years ago in London when Thomas Bourgeron talked about the clock genes and melatonin and sleep, and a real wonderful opportunity here to start to measure the biological markers he has discovered in mice and in human genes with individuals.

I know some of these slides at some level seem redundant. That is kind of the model that we have had, is to talk about gaps in opportunities and then to make specific statements of them as new objectives.

So, to expand subgroup studies and to highlight sensory motor dysfunction, racial minorities as well as regressive autism. These terms actually are in the plan, but after review of the funding for 2008 as well as the comments, the public comments, it was

clear that, at least based on the data we had, that there has not been much attention on these. So we would like to highlight them.

In the area of sensory motor dysfunction, at least as a neurologist, it is going to be a lot easier. I think the tools for measuring motor dysfunction are perhaps a little bit more advanced. Sensory dysfunction, although we know a great deal about it, as a complaint, I think we have a great deal of difficulty measuring it since it requires report by the individual. But enhancing analysis of motor dysfunction and whether it is imitation or abnormal postures would be important.

The racial minorities, I know that we are going to hear a lot more about this in other panels. Of course, this is a major need.

The very clear, it seems to me, evidence of regressive autism being associated with specific genotypes, here already there is data

on this. This warrants specific attention.

Because by understanding different subgroups clinically, and then looking for specific underlying biological etiologies, we are then in a position to begin to create selective interventions and treatments that are relevant for those subgroups.

To reiterate, the collecting of a variety of biomaterials, this we heard this morning, and I think we have talked about it. I would like to clarify something, a discussion we had on our panel, which was we had used the term "biomarker" and then we have replaced it with "biological signature". I think we can spend some time on this later.

But one interpretation of a biomarker is a measure that a clinician can use to detect a disorder and, therefore, treat it, or detect the susceptibility for a disorder and change lifestyle or environment.

That is a rather different meaning than the one we were thinking about here. Although

we are measuring biological markers, whether they are in blood, urine, or genes, we are at this point, at least for this question, No. 2, are using these as signatures of pathways, markers that this pathway may be different.

We don't know if they are good or bad. That needs study. But we are not encouraging per se that, if we find an elevation of a particular protein, that then the clinician will use that in the next 100 patients and make decisions.

This is an area, biomarkers for disorders are few and far between in general clinical practice. But, basically, we need to take advantage of collecting samples and having the kind of phenotypic analysis that is ongoing in a number of centers.

The final objective is to study females, to include more clinical and basic research that defines sex differences that contribute to the four-to-one ratio.

I want to take a step back from this. I

was not part of the original strategic plan. It is quite clear that very few studies are being done on women and girls with autism, and that this is an unmet need, which is where this came from.

From the biological standpoint, though, neurologists see many more mental disorders in males than females. We are aware that males have more mental retardation, more Tourette's Syndrome. So the male brain in general seems to be more sensitive to manifesting things we call disorders.

So there's an underlying biological difference. So we thought it would be useful to encourage analysis of sex differences in mental disease manifestation, and obviously, with a specific focus on autism.

So, for summary and discussion, one of the things that we were particularly concerned about is that the plan had, based on 2008 information, there was either little or no funding for brain and other tissue biobanks.

There were no studies on females.

I hope this may be changing, but I wanted to say something about biobanks and brain tissue, in particular. Actually, three of the six aims of Question 2 are related to tissue: 2.1, 2.4, and 2.6.

2.1 and 2.6, one is to establish an international network of biobanks, and in the long-term, 2.6 is to maintain it. Then 2.4 is to identify ways to increase awareness that donating tissues and brains are important.

I think we have a serious need to actually find ways of implementing these objectives, which are there since the beginning. I am hoping perhaps there is some evidence now, but it is going to be important that, when we implement requests for support of biobanks, that the biobanks are more than simply a freezer or a jar to maintain a brain specimen.

In fact, autism is going to require a significant investment in more than just

tissue. As we already know, the autism tissue program, which has been in existence since 1998, does deep phenotyping, including visits to the home and doing a whole ADI, for example, and collecting this data and making it available to investigators.

In addition, there are studies by MRI of the postmortem brains. There needs to be deep neuropathological analysis, and there needs to be a way that all this data can be shared among the investigators, including even having periodic meetings.

This kind of approach, actually, again, has been existent with some partial funding along the way both from NAAR and CAN originally and Autism Speaks now, and the autism tissue program.

This is a higher level of investment in tissue than is common in other common mental disorders like Parkinson's and Alzheimer's, where a level of phenotypic analysis and relationships with families is much less.

The other concern is that -- and I think I have tried to highlight this -- is that the studies that we are working on in the biological realm should be providing information about regions and pathways that will then inform us about selective treatments and appropriate services.

So, if we know that there are distinctions between language dysfunction and cognitive dysfunction, we need to be able to have tools to identify that in individuals. We need to have biological assessments that try to relate that to structure of function in an individual person, and then tailor our treatments accordingly.

So we need to be translational, something which certainly most of investigators, we all sit in our comfortable little niche, and crossing disciplines, as was pointed out this morning, interdisciplinary and multi-disciplinary is really the watchword for autism research. Of course, we know that

the INSAR and the IMFAR meetings are doing a lot to maintaining this communication.

And finally, we all feel a lack of ability at times to communicate the progress we think we are making. The studies we have designed to examine biological risk or genetic risk or environmental risk and effectively communicate that to the autism community. Advocacy groups do it. The NIH does it. This panel is another format.

But I wonder whether we need, we may need to think of some creative ways to more effectively explain really the progress we have made, but, also, how difficult it is to put 2,000 people in a dataset and analyze that and learn something over five to ten years, when, of course, many families would like to have results tomorrow. So we need to think about that as well.

I guess that's that. Thank you.

DR. TREVATHAN: We are going to open it up now for questions or discussion.

Maybe we should all move down.

DR. HANN: Let's just wait for them to take a seat, okay? Great. Thanks.

Okay, go ahead.

MS. McKEE: I just wanted to say that I agree with the high prioritization given to the biology underlying the non-verbal autism.

I know we are all aware that we received a large number of responses to the RFI on this issue. There are very few studies. Just from a community perspective, non-verbal children have very few placement options in the educational system. I think that anything we do to help increase our understanding, to provide them with better targeted services, including those related to augmentative communication, would be a huge benefit to the community.

DR. MADDOX: I don't know if I should get recognized, but I'm going to introduce myself. Is it okay?

DR. HANN: Yes.

DR. MADDOX: I'm Dr. Yvonne Maddox, and I'm Deputy Director of the Eunice Kennedy Shriver National Institute of Child Health and Human Development. I am sitting in for our Director today.

I wanted to make a couple of points related to the brain and tissue bank issue. I am very pleased to be actively involved in all of our Institute's activities, but certainly to be involved in autism research and the support of autism research.

I was telling Dr. Dawson earlier today that, when I first came to NICHD almost 14 years ago now, I was very actively involved in autism research outside of some of the other special projects I had. Now I find myself back at the Interagency Autism Coordinating Committee. So I am very pleased with that.

The NICHD just recompeted its brain and tissue bank for intellectual developmental disabilities to the University of Maryland. I think most of you probably know this already.

But I wanted to say that we are very pleased that we were able to recompete it and that we were able to support it for five years at a tune of about $7.5 million.

But one of the things that was very interesting to me, as I began to talk with staff as we thought about the whole idea of recompeting the tissue bank, and also how useful the bank might be, was the idea that we really do need to do more to work with the community, and not only the scientific community, but the advocacy groups, et cetera, et cetera, to let people know that this tissue bank not only has been recompeted, but we think that we have improved it quite significantly in working with the PI on the contract.

One of the things we have talked about doing is not only to enhance our own website to allow people to recognize that the tissue bank, indeed, is alive and well, but really to be able to speak to what the bank has been

able to do in the past. Because I think, when you put in place any type of sampling mechanism, folks always want to question issues associated with the acquisition of the sample as well as the distribution of the sample.

We have been very much concerned that many investigators who conduct autism research may not have had access or may not even know about the brain and tissue bank. So we are going to put forth a full court press, as they say, to make this bank much more visible. We would be very, very pleased to answer any specific questions you might have about the bank in terms of how it has been used to date.

As I said, or maybe I didn't say, but the bank has been in place for some 18 years. As you work in the biomedical arena, you know how important it is to improve all of the aspects associated with maintenance of a resource such as this.

So we are very pleased about this. We

hope that this bank will be used perhaps more aggressively than it has been used in the past.

A couple of the comments that were made earlier in this panel, I think we could address because we do realize that it is so important to be able to have the genotypes and the phenotype sort of confirmed.

One of the things that we have done has been to insist that, as we work with our investigators, that the medical examiners are actively involved in the process.

So, if you have any specific questions, I have staff from the NICHD here, and certainly the Project Officer of the brain and tissue bank, we would be happy to answer any of your questions.

DR. AMARAL: I would like to make a couple of comments also about the brain and tissue and biobanking in general.

First of all, I want to congratulate you for reinvesting in the NICHD brain bank in

Maryland because it is actually a wonderful resource. I think, of the many brain banks, it has actually been very facilitatory. So I am glad to see that it is moving on.

And I would like to say to the public members of this panel that this is actually a difficult topic, obviously, not only to acquire brains, which is obviously the most difficult, but to acquire biomaterials in general. I think what we need to do is we need to be able to communicate to families that science now has incredibly powerful tools, looking at DNA and specific cells, reprogramming fibroblasts back to neurons. I mean these are incredibly powerful techniques that we can use, but we can't use them if we don't have the raw material, the tissues from subjects who have autism as well as typically-developing subjects that we can compare.

So I think we are at a point in time in autism research where we need to engage families fully; the idea that it is not just

an advantage to be able to contribute tissue, it is mandatory. I mean we have to make it almost an obligation, if we want autism research to go forward, to come up with a method that makes it comfortable for families to provide these kinds of samples. You know, a skin biopsy is not a trivial thing, but it is not a devastating thing as well.

So what I would like to say is that I hope, as part of what goes forward with the IACC planning, that some attention could be made to communicating to families that they are a partner in modern research in autism, and they will partner by helping us through not only providing their time and effort in a variety of studies, but also providing some tissue, and that we need to be able to provide family support to make it easy and as uncumbersome as possible for the families to contribute.

It really is, I see, a collaboration between the community and science. If we are

going to make some progress here, we have to have this collaboration go forward in a more avid way.

So thanks.

MS. REDWOOD: I just wanted to follow up on that. There are several autism organizations that have formed a collaboration, and we actively support the Maryland Brain and Tissue Bank. We have developed a wonderful brochure that we give out at all of our conferences to thousands of parents, Autism Society of America, the National Autism Association, Talk About Curing Autism. All support the brain and tissue bank.

We were instrumental in developing a brochure for medical examiners and a poster. Actually, I have one up in my room I will bring down to share with everyone.

Personally, I went and met with our State Medical Examiner and asked him if he would please help us in this need to be able

to obtain more tissue and also control tissue. He was very responsive. We were able to purchase a freezer for storage of tissue.

I think signing up the state medical examiners and letting the parents know that this is available is something that we should really try to pursue.

I just want to put in a real plug for Dr. Zielke. He has been wonderful to work with.

So thank you for, again, supporting that bank.

DR. SPENCE: Thanks, Lyn. That actually is really very, very important.

I think the other thing that our panel spent a lot of time talking about is, following on Panel 1, the idea of value-added; that given that there are these collections, that one other thing to think about is other biological materials.

So, within the plan right now, there really is that huge focus on tissue, but I

think one of the other things that I wanted to make sure doesn't get lost in the discussion is other biological materials as well.

Because, as we all know, the phenotyping is sometimes the most expensive piece. If that is getting done, then having some other biological materials, and while we may not have the ability to have a biomarker yet, it might be a year away. It might be two years away. It might be two months away. If we have some plasma, serum, urine, I mean very easy things to collect at the same time that you would be collecting other tissue, I know that in genetics you can, in fact, get fibroblasts to grow postmortem. So the idea of getting postmortem tissue, the IPS cell lines, would be another thing that people could consider.

So I think we want to think more broadly about biobanking in general and maybe adding other biological materials on within even the postmortem tissue.

DR. SAMSTAD: Can I ask a quick question? In an adult outpatient clinic, would there be opportunities for folks to donate to these banks? If so, is there advertising material that would be available that we can provide?

DR. DICICCO-BLOOM: So not in autism, but in other mental disorders, I have seen brochures. I know we have one related to autism. But, usually, as you may be aware, this ends up being an individual PI at a specific institution in their own clinic, who then goes to the local community and gives out brochures, which are paid for by their grant.

So what we are, obviously, faced with, local individual motivated PI, based on their career and research, versus a national goal. So I think I am going to toss this to the Questions 4 and 5 panel. I mean, what is the appropriate way to approach the community, at what level, to institute requests in doctors' offices or studies?

I think the easiest place to build this in, as I think Sarah alluded to already, is using the National Children's Study, which is still emerging, or the High-Risk Baby Sibs. If they will, let's say, and we are not talking about implementation, but if there were ways of supplementing funds to Baby Sibs investigators with the goal of providing information and pamphlets with the investigators in those clinics, knowing that they should be encouraging this, or at least broaching the discussion, so that over time that these families are seen three, four, or five times, they will understand what the point is.

I mean the first thing is sticker shock. You want to punch a needle into my child's skin. Why?

But, you know, six months later, maybe there will be a better understanding of subgroup identification in children with or without GI or immune abnormalities. We may be

learning things.

So it needs to be a collaboration between the community and the investigators, but there kind of needs to be some kind of a national agenda of trying to institute it. I think these large cohort studies would be our best bang for the buck because they already have these established relationships. Adding the next layer to collect biological materials, fibroblasts, and prepare for that, would be great.

DR. TREVATHAN: While we are on the topic of biobanking, just to point out one of the things that came up in the discussions, it is listed on the slide, in terms of building upon some other large-scale studies in which there are well-defined children, and in some cases perhaps adults, with autism. The idea being there is a platform that already exists for identifying these children. Perhaps that would be one place to go to try to relatively quickly and efficiently collect biospecimens,

biological data from people that are already participating.

I think one of the things that is at least perhaps one, if not the largest complicating factors here, that I would hope as we move forward we can, at the IACC level and I hope all of our partners can think about, is that the coordination of all of these different platforms together, bringing together samples, and then perhaps even more complex, the long-term storage and maintenance of a facility to store, maintain, and protect these valuable samples for, realistically, a very long time, and making those samples available to qualified investigators, is really a major undertaking and a very long-term commitment, when done well.

So I think thinking about how that is coordinated and how we can really define a long-term commitment, and how the specimens will be used, can be very helpful. I think that coordination can also be connected with

some of these educational opportunities that get out to the community.

I wanted to just ask another question, not to move away from the biospecimens because it is, obviously, very important. But one of the comments that Manny made and was a topic of conversation during at least one of the calls was the whole concept of biological signatures and those studies. Some of us may not be as familiar with that terminology and what all that entails.

So I don't know if there needs to be some discussion about that or we may want to give some examples of perhaps biological signatures, both for good, both for bad, what you all are thinking, more specifically, that could be subsumed under that umbrella.

DR. DICICCO-BLOOM: Ed, I would love to, but I would actually, because I think this is a deep conversation, I think a number of us will have comments, but I am afraid we are about to move off biobank. So I, actually,

wanted to take this opportunity to touch base with Dr. Maddox about the CHD bank that has been recompeted, and I will get back to the biomarker, if that is okay with you.

So one of the things about the Maryland bank, which has been a wonderful participant in the autism tissue program, is that currently it has many, many responsibilities for multiple disorders, 60,000 samples of tissues from thousands of individuals, most of which do not have autism. Thus, its goal and direction necessarily has to be to continue to handle all these samples which are available for the asking by any investigator.

On the other hand, autism brains there and into the future are few and far between and need levels of analysis that are not in the RFA for the bank, and our current understanding is that the enhanced assessment of ADI, of the deceased, expanded neuropathology, analysis of clinical records, recording and correlation of MRIs and genetics

and data-sharing among individuals, all of this would actually require additional funding. My understanding from the ATP is that will cost $3,000 per investigator to get additional work done.

So, certainly, the Maryland bank is a platform, but, as a national effort, we are going to need additional resources or mechanisms to enhance -- and I am glad that we are all going in the same direction, but we are going to need some credible processes that don't exist right now. Some of those processes have existed in the autism tissue program, for lack of any other program, but we need to nationalize that. I am looking forward to working in the future on that and wonder if you have anything more to add.

DR. MADDOX: Certainly, understand that to do some of the enhancements that are necessary that it will take additional funding. Working with the community as well as with the other Institutes at the NIH, we

are hopeful that some of the other options that you have described will come forth with additional funding associated with them.

We have said specifically that we would like to work with other partners outside of the federal government. I think that is going to be a critical role for us to play, too, and it is opening up the tissue bank, the Brain and Tissue Bank.

I am glad that you mentioned that the tissue bank does collect tissues outside of the brain. Of course, we do have the capability to collect fibroblasts with the bank the way it is currently structured.

So we are very much aware that to do some of the things that I have heard discussed today, that we are going to need additional funding. I think it is going to be up to us to try to develop the right partnerships.

DR. DAWSON: So I just wanted to expand on this issue about biobanking and make two points.

One is I think, particularly with the recompeting of the NICHD Brain Bank and also with this identified as a very high priority in the IACC strategic plan, I do feel that it is time for us to develop a national strategy for biobanking in autism that brings together academia and the advocacy organizations and the government, where we can look at ways that we can partner across these three organizations to make sure that we develop a state-of-the-art brain bank.

This really isn't something, I think, that one of these groups can do alone because we each have different pieces of it that we can provide. I do think that it is time to step back and to develop that kind of a national strategy, and then, with that strategic plan, to think about funding and creative partnership.

The second thing is that, since we are at such an early point in the development of a biobank for induced pleuripotent stem cells, I

also think that this is a time for us to form a national committee or perhaps international committee to develop standards for how this particular brain bank would be designed.

I think there needs to be standards in terms of preparation, storage, in terms of even methods of inducing these. Because my initial survey into this is that there is a lot of controversy in the field about how one goes about and does this. So I see that we are going to end up having just a lot of variability in the data itself.

Similarly, some protocols that are standardization for phenotyping would be helpful at this point, so that we can start this new era in a way that is coordinated and standardized.

DR. HANN: David?

DR. AMARAL: So I just want to follow up on what Geri said, which I agree completely, and I just want to make the point that we heard a lot of comments during the original

task forces that developed the strategic plan that you have to think a lot about, for example, if you want to look for environmental toxins in blood samples from individuals with autism, you are going to have to acquire the blood perhaps differently or at least process it differently than if you are looking for something else.

There needs to be a lot of thought, I think, put into exactly how to optimize tissue acquisition. But, then, again, as Eric said before, I think there has to be a communication of those protocols down into the trenches. So, if there are going to be volunteers in clinicians' offices, there has to be some information passed on on how to collect samples and how to make the system work properly.

So I agree with you. Absolutely, we have gone beyond sort of a mom-and-pop kind of operation, and we have to do this at the national level. I think there's going to be a

fair amount of communication and thought and compromise in a sense.

I think what we heard is that it is going to be difficult to do everything everybody wants to do with available tissue. There's going to have to be a prioritization, but then thought given to, when a sample is collected, it is going to be able to be used optimally; it is not going to be wasted.

DR. DICICCO-BLOOM: Ed, I want to get back to you about biomarkers. Dave's comment seems to be the perfect platform.

So I want to re-emphasize what Dave said. He is right on target. I mean you collect a tube of blood. You get the plasma off of the serum or the cells. Each one of those gives you an opportunity, and also, you lose another opportunity. So it is going to be very important that a centralized committee make decisions about these samples obtained from the multiple populations that we are taking advantage of, the large clinical

studies.

The natural consequence of that is to detect differences in biological molecules, whether they are oxidation products potentially reflecting abnormal oxidative processes or organic or amino acids, changes in peptides, levels of immune molecules.

We had a pretty healthy conversation about a biomarker with the idea that if I see elevated IgG to "X" molecule, that means it is a causative molecule or, if you have that, then you have this kind of autism.

That, of course, is a very simplistic way of saying it, but there's not much evidence over the years of my training as a neurologist that we have a biomarker for any mental disorder. When I was in my training, nerve growth factor in the blood was going to be a marker for one cognitive disorder or another. Catecholamines, which are adrenaline, was going to be another.

We actually have very few blood tests

that have reflective molecules that tell us there's something wrong in the system and the brain. We've got anemia, not enough red blood cells. We have glucose and insulin which are in the blood for the systems that are in the blood, but the CNS is somewhat separate.

On the other hand, some of the genes we do well know, for example, the serotonin-related genes are regulating serotonin in platelets as well as brain. So there can be information there.

But I have actually asked a number of folks in this room whether you draw serotonin levels on the kids, does it help you get subgroups in your clinical populations, and most people look at me and shake their head or laugh. I don't see enough kids to draw these things. I wouldn't know how to interpret them.

So we actually have a biomarker that has been established for autism for 30 years, I think, and we don't know what to do with it.

So I am just slightly skeptical that we should think of biomarkers as a key to making the diagnosis of a child or instituting specific treatment. We don't want to have false hopes.

On the other hand, the changes in serotonin certainly foretold all the information we have been learning about serotonin reuptake and all the serotonin-related genes that now are genetically-established to be associated with autism susceptibility.

So it tells us about pathways and relevant information. So that is how we think of it as a biological signature of things that might be broken. We shouldn't have the misconception like alpha-fetoprotein for a pregnant woman, that that means a neurotube defect. That correlation is extremely high. It is one of the few biomarkers a clinician uses. There are very few others, but, more deeply, they can talk about pathway

differences that might be clues.

DR. HANN: Lyn and then the person down there. I can't see your name tag.

MS. REDWOOD: I just wanted to follow up a little bit on the expansion of subgroups and the addition of regressive autism. I am so glad to see that that is acknowledged.

I think there's a lot to be learned from an intensive investigation of children or infants during that process of regression. I think that is a big opportunity and something that we could leverage some of the existing studies, maybe the early study, going forward.

When it looks as though a child is starting to lose developmental landmarks and regress, that we capture them then and we do blood studies. We do scans, everything we can. We collect tissue and try to understand the mechanisms that are involved in this regression.

I also have parents contact me saying, "I have cord blood. I want somebody to look

at the cord blood and to compare what was going on at birth to what's going on during that time of regression, and to see what has changed over time."

I think that is another area where we could really make a lot of progress. It would help us, too, if we were able to look at several different parameters in terms of what may have changed in the epigenetics of the child, to help identify what environmental factors might be involved in this process of regression.

So I would really love it if we could flesh out that one particular recommendation a little bit more.

DR. HANSEN: I just wanted to pick up on the issue around translation, which I really appreciated in your group, and just bring up the back side of that, not just translating our science to the community, but sort of translating it both ways and sort of learning from our clinical experience to the science,

to the biological science.

So having a sense of looking at -- this comes back to having really good clinical phenotyping that is consistent over studies, so that then you can look either at biological signatures over time and longitudinal studies and see how they change over time, and they help inform you about potential pathways at different developmental stages, but also at different manifestations clinically of the core symptoms of autism, but also some of the co-occurring medical issues that are going on. So it might be the onset of seizures. So what changes over time when we have kids with autism who then develop seizures or who develop chronic GI symptoms?

So, again, linking that in a translational way, so that one informs the other, and we are not just left with some kids and adults have high levels of serotonin, but we don't really know what that means in terms of the clinical manifestations. So making

sure that we are informing each other both ways.

DR. SPENCE: I think, Robin, that that was one of the reasons that we put it as a separate opportunity, that studying the comorbid medical conditions specifically.

One of the things, when we were first talking identifying gaps, in our section the Question 2 was really very well-worded very broadly-worded. I think that, playing grantsmanship, you could pull something into all of our research opportunities.

But I think one of the things that we felt, especially the idea of doing a very large, longitudinal study in order to look for subgroups, that's one way to do it. You take all comers, and then you start to look. But that is going to be very, very big and very, very expensive.

Another way to do it is actually to go after the subgroups, and maybe in a case-controlled way, and say, what about the kids

with epilepsy; how are they different than the kids without epilepsy? What about the kids with metabolic abnormalities; how are they different from the kids without?

So that was one of the reasons that we highlighted it, even though it is kind of in there before, highlighted it as a separate issue.

DR. SWEDO: I just wanted to have a little clarification on your suggestions for prioritizing short- and long-term research objectives.

The fourth and fifth bullets there are research and underlying biology of co-occurring syndromes and research on co-occurring conditions, particularly familial autoimmune disorders.

When this slide was presented, some examples were provided, but I guess, specifically, I was curious why Rett was included in there, when such a small portion of the clinical phenotype of Rett disorder

overlaps with the autism spectrum.

And under the familial autoimmune disorders, I think the evidence there could use replication, if not expansion.

So I was wondering if, instead of pointing out those specific and possibly not highest-priority examples, it could be maybe more generic.

DR. SPENCE: I think Rett was included along with some of the other disorders where the pathway is very well-understood. I would agree with you that, in terms of timing, the phenotypic piece of Rett Syndrome as clinically-defined, there is not that long that those children would meet diagnostic criteria or those individuals would meet diagnostic criteria for autism. But I think we also know that there are individuals with autism who have MECP2 mutations, whether they are high numbers or not --

DR. SWEDO: And that would be a more direct prioritization. We think prioritizing

autism money for Rett Syndrome might be problematic in some ways.

DR. SPENCE: Okay. So clarification that we are thinking about the genetic disorders for the MECP2 mutation, the TSC mutations, the P10 mutations.

The idea that the pathways, those people who are working on those disorders now have a lot more knowledge about the aberrations in the signaling pathways and Fragile X as well, and Timothy Syndrome, to the point where they actually can go in and intervene in animal models, and now even in clinical trials.

So the point was, and maybe we need to be more careful with the choice of suggestions, but the point was to use those aberrant pathways with the idea that there's lots of other ways to cause a problem in that same pathway. It doesn't only have to be with the TSC gene. It can be with a different genetic problem.

So the question would be, looking to see

whether understanding those pathways and the aberrations in those pathways could help us with understanding autism, even if we didn't know that there was a single gene disorder involved.

DR. NEWSCHAFFER: I'm going to bounce back to a couple of issues related to the collection of biologic samples and building of repositories, moving away from biomarkers. Sorry for the back-and-forth.

But I just want to underscore the points made by Geri and then that David followed up. I think that the standards for developing these repositories are key. It has been a recommendation that has been in the plan over in the causes section.

I think that the brain banks and the stem cells, the standards around those repositories are very important. But David's point about serum banking, urine banking, critical. I worry that is going to keep getting overlooked.

It is extremely challenging. The issue of studying environmental exposures in biosamples, oftentimes it is not the way the samples are collected, but it is the pre-screening of the collection vessels that you use. This can be expensive and time-consuming and a limited number of labs that can do this.

So not all studies are going to be able to engage in that. Should they? Do we have some studies that build more robust repositories? A very, very tricky set of issues and really needs to be paid attention to. I am engaged in this kind of work, and I am worried about it.

The other thing I want to say, which also jumps on one of David's points, is about forming the partnership with families around building repositories. I think that there is a little bit of a gorilla on the table or elephant in the room, which also connects back to communications issues, which I am really heartened that keep coming up in a number of

the presentations.

You know, we have talked a little bit in this presentation about communicating our science, our findings out. Robin raised a point about communication between clinicians and researchers.

When we talk about building biorepositories and biosampling, we can't avoid the difficult, classic communication issue about results reporting back to subjects. You know, this is another difficult one.

There are two extreme positions that are report only things that are known clinically-significant, done in CLIA-approved labs. Then there's report everything. It's our samples; we have a right to know everything. Those are the extreme positions, and there are defensible arguments around both of those.

But I have a feeling that, you know, to move this forward, we need to take a hard look at those and we need to probably think about

intermediate positions. It is very difficult work, and I think that it should be highlighted as part of this nexus of communication issues.

Because, right now, studies are dealing with that, but they are doing it individually with their community advisory boards, and maybe coming up with different strategies and solutions, and just knowing what different studies are coming up around this and pooling that information would just be a good starting point, low resource, and potentially helpful.

MS. DURBIN-WESTBY: This is Paula. Can you hear me? I am not near enough to my microphone.

We have people, parents and people on the autism spectrum, that sometimes talk about being interested in contributing to this, but one concern we have of children, parents giving consent for skin samples taken from their children, is that the child does not have any say and, in some cases, is not able

to have a say. We would not want to see the situation where, if the child could decide, they wouldn't want to contribute a sample for something that would end up developing a prenatal test to select people like them out of the gene pool.

And people have a lot of questions about what will the research be used for. Maybe that sort of piggybacks off of what Craig said, but that is a concern.

And there are some people who say, "I would like to contribute to this research, but I would really like to know what it is going to be used for."

MS. SINGER: Can I respond?

Well, I think what you are describing is exactly why our panel talked about including non-verbal and minimally-verbal autism as a new subgroup.

I think that, oftentimes, studies are populated by individuals with autism who are able to, by definition, participate in studies

and who have to perform certain tasks, who have to meet certain levels of test ability. That reduces from the sample populations the kids who may be the most cognitively-challenged or have the most challenging behaviors.

So I think one of the reasons that we wanted to include this is we really have to have a better understanding, not just of looking at non-verbal autism with our eye toward communication, but really, also, with a focus on cognitive disabilities. So individuals who may be non-verbal or minimally-verbal with cognitive disability and without cognitive disability, and what is the underlying biology there? Because we want to make sure that that population is not excluded from studies.

As Ann was saying before, they are not able to sit around this table and advocate on their behalf. So, oftentimes, it is their parent or their sister or their brother who

has to come and speak for them. So that is, to your point, exactly why we wanted to include this.

MS. DURBIN-WESTBY: Yes, and also, we are speaking for them, too, and having the concern about some of the uses of the research.

DR. COOK: I'm sorry, I am not sure I can say this positively enough, but it does bring up the fact that we are not doing a good enough job disseminating the results of our research. So that, with the exception of the rare situations that are not very highly-predictive -- or there are some that are relatively highly-predictive, such as Fragile X full mutation, but I think we have not done a good enough job of getting out the point that the genetics of autism that we know, that we have learned quite well -- we knew this 10 years ago, but from the molecular side, we can confirm this further. There is no way the study of the genetics of autism is going to

eradicate autism.

It is simply too complex. It is likely that we all in this room, whether we define ourselves as having ASD or not at all on the spectrum, have at least one autism spectrum disorder variant. We are not doing a good enough job disseminating that.

This is an important issue. Just as was discussed before about dissemination, we are not doing a good enough job disseminating that reality.

Because I hear the concern, but we are not doing a good job, having studied it, to say, look, that's not what it is about; it's about understanding mechanism to provide treatment options for those who wish to take part in it.

Now I know there are going to be exceptions, and that is a much larger discussion. But, by and large, if somebody does not have one of the rare single-gene disorders, many of the big hits are de novo.

They are not even inherited. They are not going to occur again.

So I can't emphasize enough -- Sarah and I and others who are on the DSM V Committee to talk about whether there would be disorders caused by, such as autism caused by even Fragile X Syndrome. You can't even say that.

So, if you know somebody has Fragile X Syndrome, let's say, prenatally, you don't know they are going to have autism. And I doubt that this is going to change very much in the future. I mean you could get some argument about it. But we haven't done a good enough job getting that point across. What are the limits of our knowledge and prediction?

And I don't want mistakes being made because people think we do. So, in the planning for DSM V, we are being very careful to think about educating people: autism is not caused by X, Y, and Z. Even though Fragile X greatly increases the risk for

autism, it doesn't predict that autism will occur.

MS. DURBIN-WESTBY: I think some of the concern people have is media reports, and I don't know how accurately the media always transcribes what researchers really mean to say, but the comment being made: there will be a prenatal test in whatever, however many years from now it is supposed to be. So a lot of people took that and looked at it and said, well, yes, it is going to be a prenatal test like there is for Down's Syndrome, and you know the statistics on that.

So the concern comes out of that. If you are doing dissemination, you might take that into consideration.

DR. COOK: We might want to have a whole topic on how to make sure that what we want to convey to the media is properly summarized in whatever sound bites they choose.

(Laughter.)

DR. HANN: Sue?

DR. SWEDO: Not weighing-in on either side, but I actually share Paula's concerns about how this is being portrayed, and particularly, since now there are commercial entities that are offering autism screening panels to pregnant women, and women are making decisions.

So I think that this kind of concern is one -- I don't see it being a high priority for this particular strategic plan, but the whole issue of ethical handling of data and communication of results is one that absolutely has to stay a priority.

DR. HANN: Geri?

DR. DAWSON: Going back to Panel 1, if you recall, there was that one objective to address the wide range of ethical issues that come as we discover autism risk genes. This is exactly what we are talking about, is just to really sort through this, not only communicating to parents, but communicating to clinicians and the public at large about the

meaning and the use of this information.

I do think that the time is now to do that, that we want to be proactive. In fact, we are probably already a little behind to be forming that, and I know some activities are going on around this. Craig is going to be sponsoring a conference next week that many of us are participating in that has to do with this issue of the ethics of risk communication. We will be sponsoring a second one on genetics.

But I think that there are going to need to be guidelines and things that the community provider can turn to to really understand and interpret this kind of information.

DR. SHORE: I think this speaks to the importance of having a set of standards that we can all agree to and trust, that everybody is going to use. So communication is key, and that is part of dissemination.

DR. MANDELL: The discussion of the relationship between researchers and the

people they are researching made me wonder if Panel 2 had discussed adding a longitudinal component to any of their work at all, for two reasons.

One is many of these processes that are described, especially the co-occurring conditions are not static, and how they unfold may have important implications for how they are linked to biomarkers.

The second is it also gives the opportunity, as the baby sib studies are starting to think about, of linking these kinds of studies to providing treatment and support.

So a huge issue is recruitment, and you have a lot of difficulty recruiting for complicated and potentially painful procedures. We have no difficulty recruiting for treatment studies.

So, if there is the potential to link those, so that families feel cared for, there is a sense that they are not just getting

money for participating, but their child is getting something for participating, that increases recruitment. It also allows the potential to look at the unfolding of autism, thinking about these processes rather than autism in the cross-section.

I would be curious for your thoughts.

DR. SPENCE: We actually did talk about longitudinal. It is in there. We didn't necessarily go back through. I think somebody mentioned it this morning. It was Matt who said we didn't mean to say, if we didn't put it up there, that the plan, as it exists now, that we thought that that should be de-emphasized.

So the first long-term objective for Question 2 is complete a large-scale, multi-disciplinary collaborative project that longitudinally and comprehensively follows kids through. So that absolutely was something that was important to do.

Then our point of discussion was,

however we are understanding what is happening here, all of the biological piece to this should be done with the idea that we are informing treatment and we are informing services.

DR. MANDELL: Right. So I wasn't just thinking about informing treatment, but that autism might unfold differently in different environments. So, unless the environment is standardized in some way, it is not clear whether you are seeing, quote, "the natural progression of autism" or something that is in response to changes in the environment.

So, by standardizing that, you both encourage family participation, make them feel that they and their children are cared for, and also sort of take that usually unmeasured variability out of the equation.

DR. TREVATHAN: This has been a great discussion. I hate to even come close to interrupting it, but I know we are running a little bit behind time. I want to make sure

we have plenty of time for public questions, discussions, and comments.

DR. HANN: We have the microphones for members of the public available.

DR. TREVATHAN: Right. Perhaps if we still have extra time after that, we could come back to this conversation.

But we have the two microphones. I think, as before, if you can come to the microphone and limit your question or comment to a maximum of two minutes, we will make sure everybody has time. Thanks.

You can introduce yourself, please.

DR. RING: My name is Rob Ring, and I head New Disorders Research at Wyeth Pharmaceuticals, soon to join Pfizer in the coming weeks.

I was struck by a couple of things and I have one comment. I am struck by really the absence of voices from industry in the conversation. I certainly appreciate the historical context that might account for that

absence. Really, there hasn't been much genuine drug discovery being done in this area since time began really.

But this is changing, and I think many of you already know that Pfizer has started the first really research unit of its kind, an autism research unit, early this year.

I think I can communicate it is likely that you are going to see an increase in the clinical development of agents in this area that are not just repositioning of old mechanisms, but novel agents.

I bring that up because I think there may be an opportunity that I would challenge the community to take on. I was struck by the biosamples discussion. Particularly what struck me is, as these clinical trials initiate, there is going to be very rich datasets generated, not just in terms of safety and tolerability, but efficacy and the evaluation of instruments that evaluate efficacy, things that are going to shape how

these agents could be used in the future.

But if we think ahead prospectively, there is a real genuine opportunity to partner together to try to collect samples and work together to make sense of these trials as we go forward.

I just want to make sure we don't lose sight of that opportunity and we look for ways to create communication between this additional partner and the problem, because I think we really are a shareholder in the problem as we move forward.

Thanks.

DR. TREVATHAN: Thank you.

Anyone else? Yes, Peter.

MR. BELL: Peter Bell with Autism Speaks.

I think it is great that this group identified how we all can be better communicators, communicators between the science and the consumers and communicating between the scientists and the clinicians, and

so forth. Those are all very important.

So, with that in mind, and because so many great ideas came together in this panel, I wanted to just give you my own personal kind of layman's version of what I heard. Hopefully, it will be helpful.

What I heard here is that one of the most important things is resource development. We need to have the resources to study, and that, obviously, can come through brain banks or biomaterial collection. I think Geri's suggestion about having a national strategy on that is tremendously important.

Once we have those samples, we need to research them. Our goal is really to understand the underlying biology of autism. Unfortunately, right now, at best, we can look at someone and say, based on their behaviors, this person has autism, but we can't look at it at a molecular and cellular level. That is really what is impeding our ability to make tremendous strides in our understanding of

autism.

I think that is also what is going to spearhead a lot of the development that will happen both from a pharmacological standpoint as well as a behavioral standpoint in terms of research and intervention.

The other thing is that phenotyping and subgroups is tremendously important. We heard a couple of subgroups that were identified today. The non-verbal or minimally-verbal patients, girls, is important.

Lyn also reiterated the importance of looking at regression. I would add another one, in that we also need to look at those patients that make significant progress.

I would add another one, in that we also need to look at those patients that make significant progress, some of which make actual recovery, thanks to some of the wonderful work that Professor Fein has been recently publishing and talking about.

I think we need to understand why that

takes place and what biologically is happening in those individuals that do make that kind of progress.

The last thing I would like to mention is that I think it is also important to recognize that autism is not just a brain-based disorder, that it affects all systems. Whether it is a cause and effect, we don't really know. But we really need to look at the fact that autism, obviously, is very pervasive, that there are a lot of situations that happen or complications that happen, comorbid medical disorders that happen, in addition to what happens just in the brain. I think that is important for this group to recognize.

So I just took a stab at trying to summarize what I heard from this panel. Hopefully, that is helpful.

DR. TREVATHAN: Thank you.

Yes, can you step up to a microphone perhaps over here? I know we have two.

MS. DAR: Marian Dar, and I have an autistic son.

I wanted to suggest that it is already recognized that GI is an important issue; that GI be part of not only research, but part of routine medical checks with autistic people, children.

Perhaps specimens, the biopsies that are done, if further investigation is warranted, be one of the biological areas that are studied, along with blood and urine.

I am lucky in a bizarre way that my children were born and spent their early childhood in China. We lived in a culture that was logical, literal, and very disciplined. Most importantly, it was gluten-free. So they had a rice-based diet and congee.

It was only when I was in my late forties that I realized that I was a celiac. A month ago, a consortium of a number of medical centers came out with some research

linking gluten-intolerance with schizophrenia. The research suggested that perhaps there is a relationship between gluten and other neurobiological disorders.

So, if we look at this whole area of study routinely and through research, we may gain important insight into a number of neurobiological diseases.

Thank you.

DR. TREVATHAN: Thank you.

Jim?

MR. MOODY: Thank you, and thank you for the interesting discussion so far.

I would want to address one of the short-term objectives. It is on page 12 of the existing plan, the one that begins with four studies.

I think the research has advanced to the point where at least one of those can be made more crisp and specific. There was some discussion about this at last year's science meeting, but it didn't really get to the point

of a specific research project.

But the idea would be to, either here at NIH in the intramural program or as a multi-center program, develop a protocol of specific clinical investigations, of specific studies that could be developed under contract or developed here at NIH, but run around the country to look at children during the actual process of regression.

Rather than looking at them years later or looking at biological samples years later, try to study in real-time, probably in a hospital setting for at least a few days or a few repeat visits to gather MRIs, sleep studies, GI biopsies, CSF, if necessary, things like that, but a specific program of real-time clinical investigations during the early process of regression.

I guess we are a lot better able now to identify children at the very earliest opportunity, sort of catch them right while an interesting biological process is going on:

the loss of language, the loss of skills, the development of some of these comorbid conditions. I think a lot can be learned from a specific real-time program of investigations, and that could be one of the four sort of general projects listed on page 12.

Thank you.

DR. TREVATHAN: Thank you, Jim.

I might just add, while we are waiting for someone to come to the microphone, because I know Lyn mentioned a similar issue, although not definitely under the category of autism research, so it may have missed the attention of a lot of us.

But, three or four years ago, there was an article published by the group from Einstein looking for acquired epileptic aphasia among a group of children who experienced language regression, both with autistic features and without.

One of the things that was within the

report that got a lot of attention in the child neurology community was that the time between the onset of regression and the time children were referred for evaluation for relatively-sophisticated neurological evaluation, including EAG, ranged from many months to a few years even.

So there is a major challenge in doing the studies that you all are suggesting in terms of our delivery system and getting children who experience regression to appropriate diagnostic evaluations quickly.

So that sort of bridges into some of the service issues that I think will be addressed later, but I would at least suggest that maybe we make sure we address that in multiple areas, as is appropriate.

Are there any other questions from the group? Yes?

MS. BLACKWELL: Ed, I just have a point of clarification. It is a little bit outside the discussion about regression, but when I

was listening to your panel talk, several times you mentioned children. I just didn't get that out of this chapter. I wanted to make sure that the discussion does, in fact, apply to everyone with ASD.

DR. TREVATHAN: Yes, it does.

Any more questions or comments from the audience, the public?

(No response.)

Christine?

MS. McKEE: I have a question, whether there is enthusiasm on the panel to study females? Out of our last work groups, we had the females studies in, and we had it in as a short-term; I think it was a short-term objective. When it came around to IACC voting, no one really knew what to do with it, and I think it got two votes, both from moms of little girls with autism.

So I want to hear from the panel, since we have the experts here, is there something unique, is there something exciting about

studying females? And give us that language, so that it doesn't get in and get bumped again.

DR. COOK: There are many reasons, but one that I want to focus on that I heard today, which I think is extremely important, and I think very important relative to the infant sibs project, is that I won't be surprised if the Infant Sibs Study finds more females that are identified as high-risk based on their early behavior, and that their progression looks better in a longitudinal sense.

The reason I think this is so important is that what we may learn from those females is what is very protective or, in a sense, innately therapeutic, that may be applied to everyone.

Now you could say, well, the females that don't have a positive course, how will that help? In a sense, they are left where the males are.

That dovetails with studying more carefully, male or female, those that have had very positive outcomes. That is just one thing I can think of, but I do think it should be at least balanced somewhat, but I think that what we will learn will apply to everyone with autism.

DR. LORD: I think the other thing about females is just that they are people, too, and they have a huge range of spectrum of autism. So part of the problem so far has been that there are fewer females with ASD than there are males, and there's a huge range.

So, when you are trying to look at gender differences or sex differences, they get washed out because you have a smaller number. So the trick is not just to study females, but to have large enough samples that you can look at them with the same range and control from that to some degree, if you are looking for subtypes or looking for specific findings, rather than trying to do the same

thing we do with the males with smaller numbers.

Whatever is going on, that is not going to be enough, to just take the small number of girls. So it's got to be a big study and probably across sites.

DR. SPENCE: I think that actually came up on our calls as well, that kind of feeling of, do we only want to study girls? Because that is the way it is written in Question 2, is launch four studies in females.

We kind of wanted, and one of our opportunities or priorities was this clarification that part of the reason of studying girls, other than to just study girls because they are people with autism or females because they are people with autism, but was the idea of this: the four-to-one male-to-female ratio is something we have known about for a long time and really has to give us a biological clue that we haven't figured out yet.

So we wanted to make sure that it was clear that it wasn't just studying girls, but also studying female versus male and what it is that might be protective of a female or detrimental in the male brain.

DR. DICICCO-BLOOM: And I just wanted to expand on that. We also included, expanded a little bit to include, some of the basic biology because there's no question that the underlying genetics is going to interact with the underlying gender decision.

I mean there's one striking study, which has now been replicated, that one gene that has been associated in some cases with neuron migration called reelin, if you look at a mouse model of this where one of the two genes is missing, the males, as they develop, they lose purkinje neurons, but the females don't.

So it is a terribly exciting model, just for understanding the difference between genes that regulate the brain formation, how they interact with sex even before sex hormones are

there.

So we need to understand that. And maybe Ed can speak about the incidence of male versus female mental retardation. I don't know if it is that skewed, but this is an underlying biological difference. So understanding that will help us identify fundamental mechanisms, but also maybe protective factors that could be used.

DR. TREVATHAN: Well, in brief, there is a gender difference. It is about two-to-one overall in intellectual disabilities, but it is not just limited to autism mental disabilities. I mean there are a lot of these neurodevelopmental disorders and neurogenetic disorders more common in boys. I mean, if you look at Tourette's Syndrome, for example. So there is, obviously, a lot that we don't understand with gender differences.

DR. SOLOMON: I think there are really two types of issues are. One are the kind of clues that you can get from the different

incidence of the disorders by gender. But, also, I think the point that Cathy made is extremely important, and that we do need to make sure that we have large enough samples of girls, because not only are there protective factors, some early work in our lab, funded by the Birch Program of the NIH, is showing that there may also be some specific risks associated with gender. So I think it is very important that we have studies of girls.

DR. AMARAL: So I want to agree with Marjorie that we do need large enough populations. I think, when we initially discussed this in the task forces, it was that studying an adequate number of females might actually give us some insight into obligatory trajectories, if there is such a thing, in autism.

So the male brain and the female brain develops differently. There are some issues that are important, that we think might be important in autism. For example, abnormal

development of the amygdala. Well, that is sexually-dimorphic. So the male brain amygdala develops completely differently than the female brain amygdala in terms of time course.

We know nothing, or virtually nothing, about the development of the brain in females with autism compared to males. So we are making assumptions about females with autism based on this male population. We just haven't studied them.

So I think, for a whole variety of reasons, and I don't want to reiterate what people have said because I agree with all of those, but I think to understand the basic biology of this disorder, to determine what is the trajectory, what are various potential trajectories, are they different in males and females, or do they have a final common pathway, we don't know any of that because we haven't studied females adequately at this point.

DR. LORD: Not to just beat this into a pulp, but I think one of the odd things I have seen, just in this field over the last few years, is we are seeing fewer and fewer girls in research samples. So our latest research samples, I mean looking at CPA and MSAC and all sorts of studies, the ratio is more like seven-to-one, sometimes ten-to-one across different sites.

I mean the girls are there, but they are not getting into the research studies. So that does suggest that having a study that is started with girls at least would be a worthwhile thing. Because if you start with boys, somehow the girls just don't make it in there.

DR. AMARAL: Or, Cathy, just have added incentive to include the girls in the studies because, oftentimes, the incentive is to get a homogeneous group in your study, and you are going to spend your money on getting the best, largest group that is homogeneous. But if you

could actually incentivize people to include an adequate number of females, and doing it across sites, then I think the number is going to go up, and it is important.

MS. WISEMAN: I would also question the ratio. This past year, I would say, I am hearing from more and more families who have girls, much more so this past year -- I don't know if anything has changed -- than I have ever heard in years past, but I know they are out there.

DR. SAMSTAD: Not to change the subject, but I am wondering if I can follow up on Ellen's point.

How does the panel see the role of adult patients in elucidating mechanisms for autism? Is there a role there? Or is it too late by that point? Any thoughts on that?

DR. AMARAL: So this is a really difficult issue. I guess I don't know if many would agree with this, but from a neurobiological point of view, the brain is an

adapting organ. I guess one of the reasons that people have migrated toward looking at the earliest stages, in terms of looking at the etiology and the biological problems, is that, No. 1, you are in a period of dramatic change in the period from birth to about five years of age. Then, if a disorder is manifest, then, from that point on, you are looking at an organ that is adapting to the fact that it has a disorder and trying to do the best it can with the environment that it is situated in.

So, the longer you go in many senses, the more you are looking not at the disorder, but the disorder that has gone through a process of adaptation by life.

So, I think, in a simpleminded way, it is easier to look at the biology of a neonate or a toddler with a disorder and then to follow that progression. It is not to say that it isn't important to look at that progression, and even try to optimize it, to

try to see how you can maximally adapt to your environment, and there needs to be more research, and we talked about that in the panel sessions.

But, in terms of looking for etiological facets, I think people have focused on the neonate because it is a simpler system.

DR. DICICCO-BLOOM: Well, I guess you set me up. But I basically agree. However, another aspect of the neurobiology is that certainly so much of the clinical development and even the neuropathology indicate abnormalities of the original brain formation before birth.

But I think one of the exciting observations, particularly with some of these specific animal models, the genetic models, whether it is tuberous sclerosis, Retts, and Fragile X, where animals have been studied, what is a surprise to many of us is that, although we know the development goes awry and you can sometimes measure differences in

numbers of cells, locations, the way they branch, what is really amazing is that you can take the postnatal animal and adult mouse, a two-month-old mouse, repair the gene abnormality, and, voila, many of the symptoms of the disorder, whether it is measuring neurophysiology, electrical impulses, or watching the behavior, can be reversed.

I certainly, as a child neurologist, never thought that a developmental gene disorder could ever be repaired because you just didn't build it right.

So what we know is that the genes that we have identified regulating the production of neuron survival, migration, connections, they also have a separate role probably in ongoing information transferred at the synapse.

So, even with, let's say, a deficiently-built brain, if you can correct the functionality of the synapses there, you will enhance function. So there is a tremendous

amount of plasticity. The fact that you could reverse Rett Syndrome in an adult mouse is just very difficult to swallow. It is not the way we prepared.

So it is also a wonderful opportunity, right, so that now we can actually talk about, okay, you may be different, but we understand the pathway. Let's try to treat that pathway now, based on what we know about what is wrong with it.

Hence, for example, in the Fragile X, the use of glutamate drugs in individuals, and including older people, to see if it improves function. So you won't repair the way it was built, but you may repair its function now. So we need to think that way.

DR. PERNER: From my personal experience, I have presented some EEG research, and being on the autism spectrum and being relatively verbal, and also coming from a research background myself, I think one of the roles perhaps for adult involvement is

that many of us may be able to comment to researchers about some of the things going on.

For example, at one time, there was a recognition test. So the measure was, to respond, one would push a button. But I noticed several times that I nearly pushed a button and didn't completely do that. So, in a sense, to understand some of the errors that went on, if you assume that starting to push a button and not completing that reflects an instance of -- like the error, which I was actually able to give comments back several times on that.

So one of the possibilities might be that, even if you run studies in children for heterogeneity, if you can run those through verbal adults, and see how they respond and what kind of feedback they can give on what they experienced, that may help and purify, to perfect the mechanisms to better make sure what we are really looking at and recognizing that many times the dependent measures, as a

matter of pragmatics, turn out to be surrogate measures of what is really going on. So that might help reduce the gap somewhat.

DR. DAWSON: I just wanted to follow up on Manny's point about the importance of studying adult models; but, more importantly, the idea of studying development longitudinally in autism through adulthood.

I think we have to be careful about applying our models around neuroplasticity that applies to typical development to the development of a brain in the case where there is autism or any other kind of developmental disorder. We may find some real surprises, not only the surprises that we are finding in the animal model studies where adult animals can lose their symptoms when certain kinds of biochemical manipulations are made, but also in terms of our clinical lore.

So, for example, we thought for many years that, if a child had not developed language by age five, that they would likely

not develop language. But now what we are finding, by following people longitudinally, is that a significant proportion of individuals develop language in elementary school or early adolescence.

So, again, our models about neuroplasticity and developmental windows and sensitive periods may be very different in a brain that is developing differently. So I think this longitudinal and also being careful about being very open-minded about development in autism is really important.

DR. INSEL: I just had one comment that is off-topic. So let's see if there's anybody who has an additional comment about development in adulthood.

(No response.)

Okay. One of the things that Ed and Alison will have to do is to take this to the IACC and kind of convey the complexity of this discussion.

In looking at the slides, I was trying

to match up research opportunities with recommendations, and trying to figure out whether, when you take it back to the Committee, they will look at this and say, well, you said this was an opportunity, but where's the recommendation?

And there was one place that it does show up. There's an opportunity around microbiomics, which you had listed as one of your bullets. It really wasn't very much on the agenda a year ago because this is a field that is exploding in the last six to nine months.

Is there something there that you would like, that the panel wants the IACC to consider as a way to implement that? Or what did the group have in mind when you thought about that as an opportunity?

DR. SPENCE: I think that, actually, was on the first slide. That's the existing plan.

DR. INSEL: Right.

DR. SPENCE: So we didn't talk a lot

specifically about the microbiome. We talked a lot about collection of materials that could be used later with different technologies. So microbiomics, proteomics, other technologies of looking at samples.

And what has come out in this discussion, and I just wanted, before we end, to kind of ask Craig where he said collection of samples is hard, and you have to make sure that you collect them in the right way.

I guess the question is, if we bring back to the Committee that maybe there needs to be expert consensus on what to collect and how to collect, and maybe we won't be right every time, but at least we will get started, is it so hard that it is not worth doing?

I mean I remember in our original strategic plan meeting Alison made just a beautiful comment that I will never forget. She said having it be hard doesn't make it worth not doing.

So I think that that is one of those

things. The idea was, given the new technology, we need samples collected in order to perform those technologies on those samples.

So maybe the next thing to do is to have a big biomaterials meeting or initiative or something.

DR. DICICCO-BLOOM: Tom, let me point out that the slides, the handout has actually not been updated. We changed the slides and added more information on our short- and long-term objectives.

DR. INSEL: So I guess I was thinking this is an interesting new area, and it is something that we didn't talk about much in the original plan.

The presentation refers to other disorders, celiac disease, diabetes, and others in which microbiomics are really very hot as an area of investigation. I don't think we have ever received an application to do this for autism, but I am wondering, so

this didn't come up in any of the panel discussions about a particular way to do this? Okay.

MS. REDWOOD: I just had a quick comment with regard to one of the recommendations to associate specific genotypes with functional or structural phenotypes.

I was just going to also add that I think it might be important to also look at behavioral phenotypes and try to also sort of link those to medical phenotypes as well. Whether or not we see certain behaviors in children, whether it is head-banging or self-abusive behaviors, with certain medical comorbidities, and I don't know that we are really doing that right now.

So I would really love to see all these different phenotypes linked in some way in a broad database.

DR. DICICCO-BLOOM: Just as note, I don't think we were separating out behavior from function. So it was a broad application,

but certainly adding those extra terms would clarify.

So genotypes with function includes a functioning individual in their environment. So just trying to make it a bullet, but you are correct.

DR. TREVATHAN: We are almost out of time, and the group it uncharacteristically quiet. We have actually been using the public discussion time when there were no further people at the microphones. I just want to give people another opportunity in the audience if they would like to make a comment or ask a question.

(No response.)

Any further comments from the panel?

(No response.)

It is good to see Story.

DR. LANDIS: It has been a busy day at NIH.

(Laughter.)

As I am sure you heard, the President

and the Secretary came to visit the campus, which was extraordinary, and complimented the NIH on getting $5 billion in stimulus money out the door, and a big chunk of that, as I am sure Tom probably told you this morning, $92 million of that were new initiatives in autism.

So I am sorry that I am just getting here.

DR. TREVATHAN: Well, I was really impressed that, when you and Tom left the meeting, you got $5 billion.

(Laughter.)

So I now have to leave to go do a CDC meeting. I'm hoping I can do almost as well.

(Laughter.)

I doubt it.

DR. INSEL: So maybe it is worth pointing out, since you have been in the meeting all day, that at the President's announcement this morning, he talked only about three disorders. He talked about

cancer, heart disease, and autism.

He spoke specifically about his commitment and concerns about the numbers that he is seeing and the need to do more. So I think that is the first time we have heard this from the White House in such a public way.

And the Secretary as well, who we did a briefing for her this afternoon about autism, very engaged, very interested.

So a lot of interest in what we are doing coming from both HHS and from the White House.

DR. HANN: Okay. On that very positive note, why don't we go ahead and break? We are scheduled for the next session to begin at 3:30. We may be able to bump that up a bit and be able to begin more around 3:20.

(Whereupon, the foregoing matter went off the record at 2:57 p.m. and resumed at 3:32 p.m.)

DR. LANDIS: If people could take their seats, that would be wonderful. And if the panel three members could come and sit up here for the presentation, so everybody knows who is on Panel 3, and then once the presentations are done -- no? You want to sit down there? You get to come back after the presentation, right, but you have to come up here now. Come on, Robin.

So I'm Story Landis, Director of NINDS. I am -- Lee Grossman. Say who you are.

MR. GROSSMAN: I'm Lee Grossman. Hello, everyone. Hi, Della.

I'm a public member of the IACC. I am the President and CEO of the Autism Society, and I have a 22-year-old son with autism.

DR. LANDIS: And this panel was: what caused this to happen, and can this be prevented?

And maybe the rest of the panel members could introduce themselves, and then Sue Swedo is going to make the majority of the

presentations.

DR. STATE: Hi. I'm Matt State. I'm a child psychiatrist and geneticist at Yale University.

MR. SELL: Hi. I'm Jeff Sell. I'm the father of twin boys that are 15 with autism and also two little girls as well, a 16-year-old and a 12-year-old, going on 25.

(Laughter.)

I'm the Vice President of Advocacy and Public Policy for the Autism Society of America.

DR. HANSEN: I'm Robin Hansen. I'm a developmental behavioral pediatrician at the UC Davis M.I.N.D. Institute and an autism researcher.

DR. PERNER: I'm Lars Perner. I'm an associate professor of clinical marketing at the University of Southern California, and I'm fortunate to have a job, a dream job, getting to talk about my special interest in great detail, and actually get paid a little bit.

(Laughter.)

DR. NEWSCHAFFER: I'm Craig Newschaffer. I'm an epidemiologist at Drexel University in Philadelphia.

DR. SWEDO: I'm Sue Swedo. I'm a pediatrician, and I work in an intramural program of the NIMH.

What caused this to happen and can it be prevented? We have a large number of gaps, recommendations, and opportunities. So I am just going to read pretty much literally off of our slides.

If it gets too tedious, you can just raise your hands and you can read it silently. No, I'm just kidding.

Gap one, we tried to organize them by those that could have a similar approach. So gap one was need to further take into account heterogeneity across autism spectrum disorders to identify risk factors.

The thinking here being that different subtypes might have different etiologies, and

that, in addition to paying attention to the behavioral similarities, we might want to pay attention to phenotypic differences in individuals with ASD.

Gap two is need to identify factors that influence heterogeneity across autism spectrum disorders and the possible bases for the identification of autism subtypes.

Again, here our lesson is that the same genetic lesion is often known to produce very different clinical manifestations, different phenotypes; the same thing might be happening in the autism spectrum disorders.

And another factor of interest to us was the impact of protective factors or resilience on a less severe manifestation.

Next slide.

The opportunities here would be to study the phenotypic variation across ASD cases with known shared genetic and/or, if established, epigenetic variations; to support the ability of ongoing studies of genetic and/or

environmental risk factors; to conduct analyses stratifying subjects according to behavioral or cognitive characteristics and clinical features.

And as implied in that opportunity, that would require very large sample sets and very large collaborative efforts in order to have enough individuals that might form a subgroup.

Next slide.

An additional opportunity for gaps one and two is to support studies designed to identify clinically-meaningful subgroups based on trajectory, intervention response, et cetera, as these may also represent etiologically-distinct subgroups.

Then, finally, large-scale studies that aim to address gene/environment interaction as well as the role of epigenetics in ASD.

Again, all these things are thought to contribute to the heterogeneity and that, by studying those, we might be able to find the window into the larger spectrum.

Gap three was to enhance information-sharing and coordination across etiologic research studies. As you heard earlier today, the national database for autism research is making some progress toward this, as is the Autism Treatment Network, sponsored by Autism Speaks, which is collecting 100 cases per site at 15 different sites across the country, and doing very extensive common measures and information-sharing.

However, not enough consideration has been given nationally to the best array of common data elements, collection forms, and measures for etiologic research. There are no current mechanisms to track potential risk factors and ASD features being measured and analyzed in ongoing studies, so that we have some islands among a larger sea.

To ensure that, when possible, etiologic information be gleaned from intervention studies, so that we take advantage of every research subject who has volunteered to

participate.

And finally, a gap that the delays in data submission and accessibility impair timely meta-analysis. Here the opportunities are to monitor the portfolio of ongoing studies to identify gaps in the potential risk factors and ASD subtypes or the features that are being assessed, and to promote information exchange among investigators conducting etiologic studies.

It might be something as simple as conference calls, a little more involved with planned and organized meetings, since the collaboration enforced from above might not work, but definitely those encouraged from below might.

Next slide. Yes, this one.

Examine the existing array of common data elements, collection forms, and measures and consider expansions and adaptations.

Facilitate data-sharing and rapid access to shared data for research use through

resources such as NDAR and the Autism Clinical Trials Network and the Autism Treatment Network.

Gap No. 4, appropriate assessment of vaccination as a risk factor. There is a need to focus on strategies to identify potentially-susceptible groups, a need to better characterize responses, including immunological, behavioral, symptomatic, and developmental, to both vaccination and to naturally-acquired illnesses that challenge the immune system.

Next slide.

Measure post-vaccine responses in children already diagnosed with an autism spectrum disorder and to incorporate measures of post-vaccine responses and factors that may be predictive of adverse responses into the existing baby sibs studies.

Another opportunity would be to examine data as they become available from ongoing longitudinal studies, such as the CHARGE or

SEED studies, that are collecting information on immunization histories. Provide additional support or supplementation, if required.

And to continue to coordinate with the National Vaccine Advisory Committee and support efforts in public health surveillance of vaccine safety to develop the best strategy for including developmental end-points.

Our final gap, gap five, was incentives and mechanisms for rapid and responsible translation of findings from etiologic research to prevention and intervention strategies designed to limit disabilities due to ASDs.

That was a very carefully-worded gap with the emphasis there on limiting disabilities from the autism spectrum disorders, and that was done intentionally, with recognition of the fact that that is our true target.

We would like to develop mechanisms to enable rapid initiation of replication

etiologic studies, to develop effective and responsible means of applying validated findings on genetic and environmental ASD risk factors to prospective developmental diagnostic and treatment studies.

Jeff, do you want me to keep going or are you going to come up? Okay, I will just finish them up then.

Areas of continued need related to existing objectives and opportunities: studies to identify and prioritize among potential environmental risk factors to consider in ASD research. Efforts to promote expansion of genome-wide association studies, to identify gene/environment interactions and epigenetic processes. And as we have heard several times today already, biobanks and standardized procedures for collecting and analyzing tissue.

Rapid and reliable diagnostic tools for use in large etiologic, both genetic and epidemiologic studies. Assays for assessing

environmental exposures and procedures to measure longitudinal postnatal body burden accumulation in relation to immune and physiological status, to identify vulnerabilities that may develop over time from an ongoing exposure.

In summary, we believe that ongoing research is making progress toward identifying genetic and environmental risk factors, but could be enhanced by improvements in: one, understanding of heterogeneity across autism spectrum disorders; two, coordination and communication across studies; three, diagnostic tools, measures of exposures, and their physiological and immune impact, and biobanking capabilities and standards, and, four, methods for investigating gene/environment interactions.

The second summary point: opportunities exist to better understand whether vaccines are a risk factor in some subgroups of autism spectrum disorders. To promote translation

into preventive strategies, research results related to ASD risk factors should be consistently replicated and then responsibly communicated.

We had some additional summary points. Yes, there, discussion points. I knew that was what was next.

So the questions that we were still struggling with at the time that we finished our last phone call: how can we balance the need for deep phenotyping with the need for large samples in epidemiologic research? How should we identify new potential risk factors and set priorities for which ones to study?

And finally, all panel members recognized and endorsed the opportunities to address gaps in our understanding of whether vaccination presents a risk factor for autism spectrum disorder in specific subsets of children.

Alternative strategies were proposed, including a study of vaccinated versus

unvaccinated children. The panel discussed the concerns that ethical and selection biases might limit the utility of such a study.

We still have 18 minutes and 59 seconds, if the panel wants to say anything.

(Laughter.)

DR. LANDIS: So are there points that the panel would like to make in addition to the consensus that you see, mostly consensus that you see on the slides, before we open it up to the whole workshop?

MR. SELL: I just wanted to thank my fellow panel members. I mean, obviously, it is late in the afternoon, and sometimes to liven up the discussion, I just like throwing the "vaccine" word out there, especially in the confines of an IACC Committee meeting.

But it was given some serious consideration, as is reflected in the summary that Sue just gave, and it is one of those issues, from a community perspective, I think it is very wise, when we were understanding

our task, what we were charged to do, identifying the gaps and recognizing potential research opportunities, that that be brought up and be given serious consideration.

We had a nice, robust debate and discussion about it, trying to reach consensus. Sometimes you just cannot reach consensus, but the upside of that is we certainly did not stick our heads in the sand and just ignore the issue. We talked about it and then recognized areas where we need to do better and where there are existing gaps and, as a Committee, decided that this would be something that would warrant discussion amongst the group here today.

So I am sure a lot of you are probably tired. It has been a long afternoon. Hopefully, we will have some rather healthy, robust discussion on some of the areas that our task was charged to look at, what causes this, and one of the areas which is very important and was worded, the consideration

was taken very seriously: how can we prevent this from happening? Or better said probably, how can we prevent some of the symptomatology that affects individuals with autism?

I have a head-banging, non-verbal son who regressed into autism. So some of the discussion already today has been very meaningful to me because I think there are certain subsets of the population that we have just not looked into in a manner that is robustly, I guess -- I hate to use that word twice in the same ramble -- but as robustly as much of the community would like to see.

So I am hopeful that the direction that IACC is going, based upon the recommendations of this scientific workshop, will be received better by the autism community and we will be able to communicate better and actually figure out a way to get our arms around this huge problem that our nation is facing.

DR. LANDIS: Maybe we could ask the rest of the panelists if they would like to add

anything. Craig, Lars, Robin, and then Matt? Or, Lars, if you would like to start?

But I think the discussions were extremely lively. We took more than the full two hours each call and lots of emails. I think people who are on the panel probably have additional comments they would like to make.

So, Lars?

DR. PERNER: Yes, I would like to emphasize the idea of the need for subtype research, recognizing that a lot of disparate groups of individuals who are classified within the autism spectrum, that some, in fact, may need the polar opposite treatments of some of the others.

It is interesting that, actually, there's some similarities in this area to my field of marketing. We went through, about 20 years ago, an issue of aggregation bias, which is used a great deal in economics. I understand it is not used as much in the

biomedical disciplines.

But, basically, what that shows is that you may, if you look at two subgroups individually, you may see an effect. Then you add the results together, and the effect disappears. It could also happen in reverse. So that, say, a treatment would be ineffective when viewed in each group, and then you put them together, and you get a misleading result that they are, in fact, effective. This often comes about when the dependent variables are a non-linear function.

So it is important that we identify these subtypes. Now that raises a question of: what are subtypes? We today used both the term "subgroup" and "subtype". I would like to make a distinction that a subgroup could be defined, for example, as females or, for lack of a better term, high- or low-functioning individuals.

With respect to the subtypes, it is not as obvious what these might be. Obviously,

they are likely to be defined to a large extent by readily-observable characteristics, such as, for example, gluten-intolerance. But to take all the variables that influence the autism spectrum and look at combinations, we would likely get too many subtypes.

We need to find a group of subtypes that have within each a certain measure of similarity and the tendency to respond similarly across a number of different areas of research.

Now this is an area where there has apparently been made some progress in the area of depression. I would like to address one practical issue here.

There's been a lot of discussion about the practical versus the theoretical value of research. A lot of people have been concerned about some of the research and, for example, the origins of autism perhaps being less practically relevant.

I want to emphasize here that subtype

research, there's probably nothing more practical because it will, ultimately, if we are successful, allow us to more quickly identify the needed treatment for each individual. So, again, it is one of the more important areas.

Also, when we assess, for purposes of running an efficient study, the idea of within-group homogeneity, again, we want to be careful we don't select that on a dependent measure pre-treatment without regard to other forms of heterogeneity that may exist within the population of interest.

DR. LANDIS: Craig or Sue?

DR. SWEDO: I just had two comments. One, I wanted to just echo the importance of the heterogeneity. As we struggle to better define similarities in the behavioral expressions of autism spectrum disorders, it is important to pay attention to the vast variety of affected individuals and move away a little bit from the "if you've seen one

child with autism, you've seen one child with autism." There's probably at least another child with autism that has similar characteristics, and that might help us understand who they are.

The second thing, since Story offered the opportunity, is just to express the fact that I was a dissenting vote on the vaccine gap. I feel that I would like to see vaccines not set apart as a separate environmental risk factor, but considered within the framework of other environmental toxins, other environmental factors that are impacting on the children from, actually, long before the mom becomes pregnant and the father conceives, through the pregnancy, delivery, and postnatal period as well as these crucial developmental periods.

So, for me, pulling vaccines out and giving it special attention made me concerned that it might follow with funding or prioritization that would maybe decrease our

ability to study other environmental factors.

DR. LANDIS: Craig?

DR. NEWSCHAFFER: Well, following that, I basically am happy to let the consensus slides more or less speak for themselves.

I think that, if you look for recurring themes, things that resonate across the other presentations we have had, clearly, we have heterogeneity; clearly, we have biosampling, and then we have this newer issue of communication which has shown up in several presentations.

I guess, just on heterogeneity and connecting it to the vaccine issue, I think, even in an area where there are divergent views such as the vaccine area, I think -- I may be tested on this -- but I think that the one area where I think there is consensus is the importance of heterogeneity in looking at this particular environmental exposure, and probably the importance of heterogeneity in looking at any environmental exposure.

So the priority listed on the slide, to focus first on understanding mechanisms of possible susceptibility to immune challenge, be it vaccine or be it environmental chemical, seems to be a clear area upon which everybody can maybe agree.

So that's all.

DR. HANSEN: Well, I guess the point that I would make, as someone who is involved in a large study looking at gene/environment interactions, as a clinician, one of the things that we have struggled with is, how do you really do deep phenotyping in a way that isn't just completely shotgunning and really trying to be consistent across how are we collecting historical data; how are we collecting and reviewing medical records; how are we being consistent in terms of our clinical exams and our medical histories, and all of those issues that I think we struggle with?

Yet, we really need to try, I think, to

come to some common understanding of how are we collecting data, just like we talked about previously around banking samples. We have to be very careful about data collection and storage.

The same thing goes true for the clinical data. I think it would be nice to have some common forms or collection instruments that we are using across multiple studies, so that we get the biggest impact for the number of subjects that we study. Since it takes so much time and effort on the families' point of view, it would be nice to be able to have some common datasets that we are all collecting in terms of deep phenotyping.

DR. STATE: Yes, very lively, it was a lively discussion.

(Laughter.)

So just I guess I would stress a couple of quick points.

One, I think everyone has talked about

the importance of biobanking. I think that the devil is really in the details. If I had one thing that I could really stress, it is that now is the time as studies are getting going to really tackle this issue. It is going to be tremendously important to understand anything that we want to understand about heterogeneity going forward.

The second thing, just on a positive note, is that, as a geneticist, I think that we may not be there today, but I think very soon we really are in a position to stratify people based on an identifiable genetic risk, not a genetic cause, as Dr. Cook pointed out, but a genetic risk.

Those kinds of studies are going to require a lot of effort and coordination, but are a tremendous new opportunity that we didn't have two years ago, probably didn't have a year ago. I think they are quite important.

Then, you know, the elephant in the

room, I have to say something about the vaccine issue. I was more on the Dr. Swedo side of the debate. I think that the issue of gene/environment interaction is tremendously important. I think new twin data is going to come out showing that it is tremendously important that we understand environmental risks.

But it is a very fine line. On the one hand, we didn't want to skirt the issue because it would feel like we left it undone. And on the other hand, I think that we don't know a lot about other environmental risk factors that may be far, far more important, based on what we do know already, I think in large groups of samples about the risks of vaccines.

So I was hesitant about separating it out for the same reasons, but felt like it was important that we not leave it unsaid.

MR. GROSSMAN: Yes, I wanted to point out to the workshop participants, because it

is not adequately demonstrated in the slides that are presented here, that we did have a very thorough discussion on the prevention topic. That is what we were tasked with, and it was one that was a challenge for us.

We did have unanimous agreement, I believe, on the fact that what we meant by prevention was looking at a way to diminish or remove the more negative aspects that are associated with autism. I like the term that we came up with, "limiting disability".

And I would imagine that, as we go through the discussion with the rest of you today, that this will be something that you will probably want to ask much more about.

There were some ideas that were presented that we discussed, and it appeared as though these issues around prevention fell into what Panel 4 is looking at and went beyond what we were tasked to do.

So that is part of the reason why we perhaps didn't tackle this to the vigor that

should have been attached. But, if Panel 4 has not dealt with this issue, then it is probably something that is a greater gap than what we had dealt with, and it should be something that would be under further deliberation with the entire IACC.

DR. LANDIS: Any more comments from the panel?

(No response.)

So I guess we now get to sit down and open up the whole discussion.

DR. HANN: Thank you, Panel 3.

We will give them a minute to sort of get readjusted at the table, and then we will open it up for discussion amongst the participants here at the workshop, to be followed, then, by the public comment period and question period, the same format.

Okay, Ellen?

MS. BLACKWELL: Thank you so much for your very honest and straightforward discussion.

I know that you said several times you are really attached to this language in gap five about limiting disability, but I just wondered if I could sort of reframe it for you in a different way that would be consistent with our discussions in Panel 5, which are that you might consider prevention and intervention strategies designed to maximize quality of life and health outcomes associated with ASD.

I think that might be -- I don't want to speak for you all -- but I think that might be what you were trying to get at, but perhaps said in a more positive way.

DR. LANDIS: Responses from our panel?

DR. SWEDO: Sue Swedo.

Ultimately, I would agree. I think that disability was actually already moving away from sort of the possibilities of identifying risk factors and then preventing the onset of symptoms. So I think that either would be acceptable.

I think that our choice of disability really did speak to the issue of trying to prevent only those aspects of autism spectrum disorders that are actually disorders or disabilities, and those that are on the continuum with much of the rest of the population would not be targets for attention.

MS. DURBIN-WESTBY: Hi. I like Ellen's language, maximizing the quality of life, but I understand you have a different focus with limiting disability.

Once again, I'm going to say that I think it is important that people on the autism spectrum have a voice in talking about what constitutes disability. I have had parents who have instituted a strict regime to keep their child from flapping their hands, and the child flaps his hands because he is really happy.

And I said to the mother, "What do you do when you're happy? Do you laugh? Do you smile?" And she said yes.

She set herself up. I said, "Don't do it. Next time you're happy, don't smile; don't laugh. I can't follow you around. So hire somebody for 20 hours a week to make sure you don't do it."

(Laughter.)

And she kind of got my point, but she said she didn't want people to tease him. So there's that whole piece in there about educating and acceptance and awareness that needs to come with that.

So, when you talk about limiting disability, and there are disabilities that are significant for some people, then just remember to do some consultation or have us involved in the research.

DR. FEIN: I had a question about the vaccine issue. So, just to clarify whether I am getting what the panel is saying, I take it that the disagreement was whether vaccines should be pulled out of the whole environmental panoply of possible risk factors

versus left in the panoply of possible risk factors.

But was there unanimity that we need more research on environmental risk factors, including vaccines, that that question is still an open question? Was that unanimous for you? I'm just curious.

MR. SELL: Yes, in terms of environmental exposures, I think, clearly, the panel, there was consensus that there are just a whole host of environmental insults that are affecting the prevalence numbers that we are seeing. I think you just have to look at it from that angle.

We agreed that the environmental exposures that our population is facing is a huge area that warrants further consideration and much more research and much more spending on research.

I think the angst was more related to the vac studies, putting that back into the strategic plan and making recommendations such

as that.

DR. LANDIS: This is Story.

One of the more interesting discussions that we didn't have time to really pursue in any depth was there seems to be a list of commonly-studied environmental risk factors, and that by looking at the usual suspects again and again, we may be looking under the lamppost, where we think the light is, and missing things away from the lamppost which could be much more important.

There was some discussion about a more open, broad-based survey of what could be risk factors. I think some of those might well come out of the longitudinal epidemiological studies that are underway, including a study that NINDS is funding in Norway. But we need to be very broad-minded and not just focus on a small subset of potential risk factors.

DR. FEIN: Well, let me begin by saying I think that it is important to study a wide range of environmental risk factors. I

applaud the group for underscoring that.

It also seems important to study the potential role of vaccines in the context of other environmental risk factors. So, with that in mind, I wonder whether there was discussion as a research opportunity, again, about the National Children's Study, the advantage being, first of all, it is population-based, which is, I think, really important because what we find in the high-risk populations may or may not generalize to other populations.

But it also speaks to this issue of looking under the lamppost because there's a wide range of environmental factors that are being examined. And it also speaks to this issue of how risk factors that may play a role in autism may also play a role in other kinds of health outcomes, and how autism overlaps with other health outcomes, whether it is autoimmune diseases or others, in ways that can help us better understand underlying

mechanism.

DR. SWEDO: We actually did talk a bit about the National Children's Longitudinal Study. As I mentioned this morning, one of the frustrations there was the length of time that it might take to get these important answers.

So, in addition to looking at ways that the NCLS could be utilized, we discussed the ongoing epidemiologic population-based studies in Denmark and in Norway, where those children now are actually past the age at risk. So we would have a good ability to determine whether or not they had the outcome of interest, but we also have biologic specimens and very careful environmental exposures from the prenatal period.

DR. INSEL: So this is sort of building on Geri's comment. I understand the reservation about pulling out vaccines as one particular environmental factor, just the way I didn't hear you pull out any particular

genes as worth pursuing specifically.

But it also strikes me, as you describe it, that even when you talk about the environmental factors, there seems to be that there's only a single outcome that you are wrapped around, which is absence or presence of autism.

So I wonder whether the way this might be reformulated is to think about the dilemma that parents face, particularly with a younger child if you have an older child with autism, in the decision about all sorts of things because it is always a risk/benefit.

I don't know of any parent that says that they don't want to vaccinate their children at all. They are worried about safety. So what they want to know is, what are the consequences of doing it? What are the consequences of not doing it?

So what I am suggesting is, would it be better to sort of reframe this as looking at health outcomes generally, which

presence/absence of autism could be one such health outcome, but there could be a hundred others, including meningitis and many other things that people could be concerned about, and providing information, actionable information, that helps people make decisions about risks and benefits of a whole range of things that they would be facing with younger siblings?

DR. HANSEN: Just speaking maybe not for the group, but I don't think that we were thinking necessarily about limiting outcomes to just a spectrum diagnosis, but really looking at a variety of developmental outcomes, including autism spectrum, and also a variety of environmental factors that may or may not be associated with vaccine status.

So we were thinking about looking broadly and just having that be one factor that needed to be looked at.

DR. INSEL: So maybe I guess this is where we need some help from the panel

because, at least in listening to this, and I don't know if other people have the same confusion, it is not exactly clear what message you are sending to us.

Is the concern about the grain size of recommendations? That is, as Sue mentioned, that you want to talk about environmental factors broadly and you don't want to drill down to any specific ones? Or is there something specific about vaccines that you want to convey to the IACC?

Because I'm not real clear what the message is, if this is going to be conveyed forward, how to do that.

Story?

DR. LANDIS: There was one, I think, specific recommendation which was that we should continue to work with NVAC as they do population-based safety studies for vaccination to make sure that there is an assessment of developmental delay, behavioral disorders, autism. I think that there was

consensus on that, that there will be broad-based population studies conducted and that we could contribute to a measure of that safety.

The second piece was, I think, and I don't remember if it was Matt or Craig who was most vehement about this, that there have been lots of epidemiological studies which have not given compelling evidence for a role of vaccines. That suggests that replicating those kinds of studies again would not be a good investment of money, but if there were mechanisms by which we could -- so that means you are looking not at all the hay sticks in a haystack, but you're looking for a couple of hay sticks. If we had some idea of what would define the hay sticks we should be looking for, then we could design a study that would actually make sense.

Was it Craig? You know, on the telephone, it was real hard, once the fur began to fly, to figure out who was most articulate.

DR. NEWSCHAFFER: When it is particularly controversial, I tend to disguise my voice.

(Laughter.)

So, if I could just step back for a moment, and I don't want this to sound like a copout, getting at the heart of your question, the point about whether or not the vaccine is highlighted as a title in a slide, personally, I was not involved in that discussion. This is just me personally. I joined late on the first conference call. So I came in once that was labeled up top. I'm happy to weigh-in on that issue, but I do want to highlight what was said about the vaccine issue, the three recommendations, and just try to drill down on those a little bit.

The first focused on -- and again, as I said when I sitting up here, I think that there was close to consensus among this group on this point: that given all we know about the possibility of vaccine being linked to

autism spectrum disorders, if there is a link, the link -- and it is a big "if" -- if there is a link, the link is going to be in a susceptible, vulnerable subgroup, which gets us right back to heterogeneity, the overarching theme.

We recognize that, if we are staying under the heading of vaccines, we are talking about susceptibility probably related to immune response susceptibilities, and we recognize that there's other research pointing to potential importance of immune-mediated mechanisms in autism spectrum disorder. It is by no means fully accepted, but it is an area in which there is good research going on that really doesn't have anything to do with vaccines.

So our first recommendation was to focus on the importance of studying susceptibility for immune response as one form of potentially-important heterogeneity. We took pain to add in other immune response-evoking

exposures, like infection and certain environmental chemicals. All that would fit under that first recommendation, but that would also go to the issue of vaccines, if you were going there.

The second thing -- I think it is the last one we listed -- was this point about NVAC. From a public health perspective, and I am a public health professional, the issue of vaccines and autism from a public health perspective and vaccines and autism from a research perspective are very different.

The public health system has different priorities and needs. They need to respond to public concerns. When it comes to vaccine safety, they have an ongoing duty to monitor the safety of vaccines, regardless of whether autism is on the map or not.

So we looked to the NVAC Vaccine Safety Work Group Report and felt that where they were heading, which was more consideration of how they can build better monitoring of

neurodevelopmental end-points, and potentially autism, in ongoing vaccine safety surveillance efforts, it was important that the research community support them because there are real challenges to doing that, right, in ascertaining end-points in a valid and reliable way, and that what we do should cross over and support that effort. So that was the other recommendation.

And the third recommendation that we put, which is, in my mind, the one that I would put as the lowest priority, is there are a number of existing epidemiologic studies that will have data on vaccination.

I come from a school where I feel like, if you have the data, you are going to look at it, and you should look at it. There are real limitations to what we can do in terms of contrast with respect to vaccine exposure in these existing epidemiologic studies, but I think it is silly to say we're not going to do it.

What we need to do, when we do it -- and I think it will be done -- it gets around to the communication issue; we need to be very careful that we can communicate what the limitations are of these analyses and where we think there might be potential for these to be early-stage signs, discovery science types of signals, if, in fact, we see something.

I don't think, I know we are not going to see a clear signal of, vaccinated versus unvaccinated, a difference in autism risk. I mean the deck is stacked against us in terms of sample size and other things in these existing studies.

But to say we are not going to look at them seemed a little bit just silly. So I think we will, and I think what we need to do is just be careful about how and be prepared to communicate the findings that emerge from those looks in the ongoing studies.

I will say one more thing, and then I will be quiet. Geri, when you raised NCS, you

weren't talking specifically about vaccine? You were talking about NCS in general?

DR. DAWSON: Well, I was talking about the NCS as one mechanism where potentially we could look at vaccine and also a variety of other environmental risk factors that may play a role and interact with vaccine exposure susceptibility, but it would also, this sample would also have the genetic data. So it would allow one to potentially pull out vulnerable subgroups.

So it just has the advantage of a lot of different components of the different hypotheses that you have been discussing.

DR. NEWSCHAFFER: Right. So, I mean, I think we did talk about NCS in general. I think that may have been on the portion that I was not involved in, but I don't think, when we were formulating the recommendations around vaccination, we certainly didn't talk about adding resources to hone in on vaccination and NCS.

I think that is something that, if you look at the three recommendations that are up there, that was something that we felt is not a direction that we wanted to go, devotion of new resources around specific vax/unvax contrasts. We focused, again, on susceptibility, existing studies where it is going to be done anyhow, and then the connection between research and public health surveillance around vaccine safety.

DR. DAWSON: I just wanted to make one clarification about the National Children's Study, which is that I think the supplementary funding would have mostly to do with collection of medical records. The advantage of that is it would allow one to look at many things that may be potentially important.

You would have better records about maternal infection during pregnancy. You would have better records about the prenatal and perinatal status, and so forth and so on.

So the medical records I think is the

broader issue. Within that, vaccines is one component.

DR. NEWSCHAFFER: We are having maybe a little sidebar here, but absolutely. I mean I personally am a strong supporter of adding that information to the National Children's Study, but that bus is not driven by vaccines.

DR. LANDIS: And I would say that there's some discussion right now about what an affordable price tag for that study is. Given what that price tag is, what's the best way to invest those dollars?

So I don't think -- I don't know if Yvonne is still here -- I don't think there's a final decision that has been made on what that is going to exactly look like. I mean I think it will be funded. There's a lot of money that has already gone into it. But what the "it" is is not clear.

So I think we didn't feel comfortable handing off to the National Children's Study when its exact shape is not defined.

I think Matt had a comment.

DR. STATE: Actually, it is slightly orthogonal to the vaccine question you asked, Tom. Also, I just wanted to clarify that I think in our discussion, when we were thinking about gene/environment interactions broadly, including vaccines, that the issue really was not categorical diagnosis.

In fact, I think one of the things that we were really interested in -- at least I was; I don't speak for the rest of the group -- is the fact that at least the emerging data suggests that the same genetic lesion can lead to a very broad variety of neurodevelopmental outcomes.

How that happens is a tremendously interesting question. So it really blows apart the kind of idea that the only end-point is categorical diagnosis of autism.

So I think exactly how we get there, I think, is a bit unclear, but I think we are starting to see that there are possibilities

to take a look at a genetically-defined group and to look at a very broad range of outcomes, and then to try to start addressing the question about the role of gene/environment interactions in those longitudinal studies, and get away from the thing that you were concerned about.

MR. GROSSMAN: This is Lee.

To address this point, I would like to express to the rest of my workshop participants, you should feel very grateful that you weren't tasked with this issue of vaccines.

(Laughter.)

And I say that because it is a very difficult question. It is fraught with controversy, as we all know.

But the way that we approached this, and I think that it was actually a fairly easy step, is that when this gap was presented to us, appropriate assessment of vaccination as a risk factor, maybe if I could speak for

everybody, but it was an immediate unanimous response that, yes, this is a gap and we should treat it as so. It should be something for further consideration for the IACC.

Whether we like it or not, and many may not like it, there is a concern, and expressed rather vocally by many people in the autism community, that this is an issue that needs to be addressed and dealt with, and that their children have been vaccine-injured, and it has not been dealt with.

I think that, as far as I am concerned as a public member of the IACC, that it is an issue that we need to look at further. I personally know of families whose child was seemingly normal in the morning, had a vaccination at noon, and developed autistic symptoms in the afternoon. To sweep that under the rug I think would be doing our community and the community at large a disservice.

So what you are hearing from us is, how

do we approach that? We are struggling with it. There is no consensus among this panel to do that.

But I would strongly recommend to the IACC that we don't push this under the rug and that we deal with it head-on, and come up with some suggestions on how to move forward.

DR. HANN: David has been waiting for a while.

David?

DR. MANDELL: I want to congratulate Panel 3 on dealing with, clearly, having a spirited discussion and managing to include both honesty and civility, which is often rare -- (Laughter) -- probably for all of the groups.

So I was wondering whether in your mind, and this gets to Tom's question, whether this report replaces what was in the strategic plan prior or augments it? Because one of the things that may have been intentional or unintentional in the way that this report is

structured, in dealing with the issue of vaccines, just by virtue of the amount of space it takes up, it becomes the priority.

And there were other things that are hinted at and came out really nicely in the discussion following about, for example, quantitative rather than qualitative measures that are really needed for us to understand etiology, or looking at interactions, stratifying by genetic risk to look at the environmental causes of autism, or even mentioning other environmental causes where the data would suggest more promise for an association with autism than the studies to date, similar studies of vaccine, have.

While all of those are hinted at in a lot of the bullets, none of it is specifically laid out the way the study of vaccine is laid out. So I am curious if that was intentional, and I guess whether or not it was intentional, I would certainly advocate for being as specific about the other issues that you would

want studied as you were about vaccines.

DR. HANN: Panel 3, comment?

DR. LANDIS: So I would just say that vaccine as a specific issue was deferred to a discussion with the NVAC and additional information. We, I think, as a panel, took the need to actually discuss this, and it was clear that it is obviously not the only environmental factor, that there needs to be attention, but to try to come up with one or two concrete things that would make research sense, where there would be questions that could be asked and questions that could be answered. Measuring immune responses seemed like a question you could ask and answer, rather than an open-ended, unlimited discussion of this issue.

But I resonate with your concern that in this report it receives what could look to be an undue amount of attention.

Sue?

DR. SWEDO: I would just second that and

say that that is actually why I presented myself as the dissenting vote. I felt it was important enough that, unlike I think it was Panel 1 that had a whole bunch of recommendations and they didn't group them, we did group ours. So we have five gaps and three sets of recommendations in response to those, and one of those huge categories is vaccines. To my mind, that gave too much attention to it and might convey to the IACC that we thought it deserved that kind of prioritization in terms of research funding.

But I like the way that Craig summed it up and said that there isn't anything in our recommendations that suggests new funding for this. It is very much directed toward making sure that we don't close our eyes, plug our ears, or have any impression that we are not willing to look at this.

As somebody who identifies odd environmental triggers for mental illnesses --

DR. LANDIS: Maybe you can explain that,

Sue.

DR. SWEDO: Okay. Yes, you're right.

(Laughter.)

It could be many things, couldn't it?

When I started my research on OCD, the only environmental triggers that were considered to be worthy of attention were psychosocial risk factors, such as punitive toilet training or a harsh parenting style on the part of the mothers. Yes, I am old. Sorry.

(Laughter.)

But it has only been 15 years since we started those studies. The thing that really took off was the fact that we broadened our mind to the point where we were looking at all kinds of things and all kinds of patterns.

Panel 2 talked about biological signatures. I think I got that right. I would say these were phenotypic signatures, that there is a particular pattern of clinical presentation as well as history, and that is

what we are hunting for. If it turns out that it is a single vaccine, it will be like finding a single gene; we will be able to fix it quickly. It is much more likely that it is going to be a combination of things. I just don't want the attention on vaccinated/unvaccinated children to sort of get in the way of a larger frame of view.

DR. HANN: Okay, I am going to do this a little differently. Other people on Panel 3 that want to express? Okay, Craig?

DR. NEWSCHAFFER: Yes, just following on what David said, David, if you had been listening this morning -- so much for the civility there, David -- (laughter) -- I can't see him down there.

You know, this is very much a concern of mine. I was at least going under the operating assumption, and I think this is what most of the group was, that we were focusing on gaps and, in fact, does not in any way supplant the existing report.

I think, in reviewing the existing recommendations, there were none that we moved to strike. There were some that we highlighted as perhaps not seeing as much action as we would have liked to, including the standards around biosampling.

But this is not, I can't say it strongly enough, meant to replace the existing recommendations. I think, as Story suggested, vaccine was there, and we came up with what we thought could be the best recommendations, and Sue just highlighted, to focus on vaccine. But it does not mean that it supplants other things that are in the existing strategic plan in any way.

DR. STATE: Can I just quickly second or third that? I mean we talked all morning about the fact that, if we didn't highlight it, it wasn't because it wasn't important. Because it is already in the plan, and this was something that we felt that we needed to address.

I also want to make sure -- I worry that, the longer we talk about this, the more that we are going to challenge this. You know, it is all going to splinter and the civility is going to --

(Laughter.)

But I just want to I think make clear that I think the consensus, at least in my view, was what Craig enumerated, which is very, I think, specific and delimited, and that any broader conclusions about reading of the broad epidemiological data or anything else, it was not intended by the group as a whole, maybe by some members of the group. I think that is important.

DR. HANN: Stephen?

DR. SHORE: This perseveration on vaccinations would do any of us on the autism spectrum proud.

(Laughter.)

But, getting back to what Lee was talking about, I am glad to hear that we agree

that it is something that needs to be looked at, but we are still unsure as to exactly how that is to be done.

I bring this up because one of our panel members from Panel 4 is not here because she took a flu vaccine, a thimerosal-free flu vaccine, and it blew her system out. That is why she is not here. Sharisa, yes, Sharisa Joy.

So it is something we need to look at. I don't think anybody, I hope nobody is recommending wholesale non-vaccination. That is dangerous. So, you know, we still need to look at it to some extent.

But what I wanted to get at was I am really impressed with the work that you are doing on subtyping. It is really, really important.

My focus is on, roughly, behavioral developmental educational approaches. I do know some developers of some of these approaches who are subtyping behaviorally.

They've gotten to a point where they can say A, B, C, or D, and given these types of behaviors, we are going to recommend this package of interventions. And it seems to work.

So, the more we can get into that and the more that we can port that over into biomarkers and other areas of concerns of autism, I think the better off we will be, matching diagnosis to treatment.

DR. HANN: Lyn?

MS. REDWOOD: Thank you, Story.

I just wanted to go back to this vaccine issue again. If you read through all of the RFAs in this huge notebook, almost every other page is look at vaccines, look at vaccines. So I really want to thank the Committee for taking time to look at that.

And I agree with what Craig was saying about these large population-based studies. If you actually read some of the reports, they actually acknowledge that they wouldn't be

able to pick up susceptible subgroups that might be more vulnerable to vaccines, what Stephen just mentioned about one of his friends.

So two questions I wanted to ask that particular panel. One is that we have something like 1,322 children who have been compensated through the Vaccine Injury Compensation Program for vaccine injury. Many of those also are diagnosed with autism. Whether or not they had some type of underlying vulnerability, mitochondria, there were several that had acute disseminated abnormalities in their brain and inflammation, ADEM, that went on to develop autism.

Why can't we look at those children who we know, for one reason or another, were more vulnerable to vaccines, and figure out what those factors are? So then we can screen children to be able to identify the ones that are not going to respond well to vaccines.

I mean that seems like it takes out the

fishing expedition for, is there a problem or not a problem? We know there is a problem. We know that children have been vaccinated, similar to what Lee was saying, and that they have developed autism, either within days or weeks afterwards. I think we really owe it to those families to look at this.

So I think if we look at the children who have been vaccine-injured, it is going to offer us a huge opportunity to be able to determine what mechanisms might have caused those injuries.

The other thing that I think we have overlooked is the utility of using animal models to look at vaccines. I know there was a study that just came out today, published in Neurotoxicology, which just looked at the administration of one hepatitis B vaccine in infant primates. They found several of their critical mechanisms, like rooting and suck, were abnormal. So I think we can utilize animal models, expose them to vaccines, and

look at them as they develop and be able to test some of these hypotheses.

So I would really like to see an emphasis on animal models and also looking at the children that we know have been injured. Yes, that does get away from some of these other issues. I think it is a way to sort of solve the problem.

I would like the Committee's feedback, the panel's feedback.

DR. LANDIS: Yes, so I would be pleased to address the second question. We did not consider studies in animal models during any of our phone conversations.

I think one example that has been interesting to me is that there was an initial report from Pasko Rakic in mice that ultrasound caused abnormalities in neuro-migration and could represent a potential risk factor for autism. He has now replicated those studies, has done similar studies in primates, and hasn't published the results,

although the preliminary data and the grant make it clear that those abnormalities are not evident in the primates that he has been studying.

So I worry about the generalizability of animal studies. We thought it was better to focus on a subset, a simple set of questions that could be rigorously posed and answered in the context of the studies that we described.

I would say that one of the points that Sue Swedo made several times is the issue of selection bias. She did it in the context of vaccinated/unvaccinated studies, that it is almost impossible to get away from the issue of selection bias. Not knowing enough about the decisions on vaccine injury, I would have some concerns, without having adequate knowledge, that there might be bias in the selection of that subset as well.

But I am just the liaison. So I shouldn't have said any of that. I will pass it down to my panel.

DR. NEWSCHAFFER: That is fine because I was going to address the first part. So I think, Lyn, you are right, that if you focus on the existing autism epidemiology studies, your SEED, your CHARGE, your EARLIs, and if you have a specific focus on susceptibility in vaccine, there are going to be limitations to those, true.

However, there's potential in those studies to look at susceptibility to immune challenge. Once you broaden it and include things like infection and other immune-challenging exposures, your numbers go up.

And if -- and it is a big "if" -- there is something to be learned there, it may be generalizable to vaccines, just as it may be generalizable to prenatal infection. So there is that hope.

Then, in the high-risk sibling studies, where you have, albeit it through a very crude proxy, the fact that there's an existing sibling, you have a genetically-enriched

susceptible population, and you have a commitment to look at, as Tom and Matt emphasized, not just autism/no autism, but you have the benefit of being able to look at continuous end-points, which give you some advantages both conceptually and also from the perspective of statistical power.

You may in those studies be able to focus on vaccination, maybe the best rationale being because vaccination in those perspective studies is a measurable, quantifiable immune challenge and becomes a good exposure to look at if you are interested more broadly in immune susceptibility.

And you may, because you are dealing in this population where there is enriched susceptibility, it may set up a circumstance where you might be able to learn something about that.

So I do think that there is some potential for science to be advanced around the general issue of susceptibility mechanisms

to immune response in these existing studies in those ways.

DR. HANN: Sue, did you have a comment as well?

DR. SWEDO: I was just going to clarify a bit about the known and unknown risk factors. That had been my objection to the very specific suggestions that kept coming up in the RFI of a vax/unvax study, is that that was going to demonstrate something for us that the previous studies had not.

In addition to the concerns about the unknown differences between those two groups in exposures, in prenatal history, et cetera, I think the bigger question is how you would ever find a group of unvaccinated individuals large enough to make sure that you actually were having an appropriate assessment of frequency.

We haven't seen it in any of the huge epidemiologic studies that have been done. So I object to it on many different levels, but

do not, as you know, Lyn, I do not object to the idea of making 100 percent certain that vaccines aren't contributing to autism.

I worry sometimes that, even if we got as close as scientifically we can, since scientists never say never except just then -- (laughter) -- nothing is 100 percent and nothing is zero percent because of those chances, and that equivocation continues to impact on public health questions.

So, the longer this remains on the table, the worse it is going to be for America's children. If there is anything the IACC can do to make that definitive answer come more quickly, I do not dissent against that.

MS. REDWOOD: I guess my question was whether or not we could use children who have obvious vaccine injuries and investigate those. That was my question.

Also, about using animal models, I don't think there's any perfect model, but I think

it is a good place to start.

DR. SWEDO: Right. So that is actually why we had stepped back from that and said that we would like to know the susceptible factors, and we would like to know the immune mechanisms by which this might be happening and actually look at those same questions, not just in vaccine-injured children, but in the larger population of children who have, as Tom asked earlier, a continuum of responses, a continuum of variability, and then focus in on those as perhaps the signature that will allow us to go out and get additional kids.

The problem becomes how to get those vaccine-injured children into studies. We can talk more about whether or not that might be something, a targeted investigation that could be done in collaboration with immunologies.

DR. DICICCO-BLOOM: I wanted to address a slightly different issue, one of the areas of continued need, and particularly related to some earlier comments by Ed Cook and the

issues of genetics.

One of the needs is rapid and reliable diagnostic tools for use in large etiologic, both genetic and epidemiological studies. I just wanted to understand, what are we thinking for rapid and reliable genetic diagnostic tools? What's the rush to rapidly know my genome if we, in fact, think that these are susceptibilities which aren't going to change decisions we will make?

We certainly can now identify five genes for Alzheimer's disease. I don't know how many people are changing their lives on that basis.

So I just wanted to know how to translate that into actual goals.

DR. STATE: Yes, I think you misunderstood the point. What we were talking about was rapid, and maybe not even categorical, but a rapid assessment tool that would serve large-scale genetic studies. So it does not have to do with genetic testing.

DR. DICICCO-BLOOM: Sorry.

DR. HANN: Okay, Bob was next, and then Geri, and then Alison, but we are running out of time for this part of the discussion. So, when the little light goes red, we are going to open it up for public.

DR. HENDREN: Thanks.

When I first heard the presentation, I had two questions. One of them had to do with a kind of overlap between Panel 2 and Panel 3. Yet, I realize now that, with vaccines being assigned to your panel, you've got more than enough to deal with.

(Laughter.)

So just vaccines could be Panel 3, and I guess there could be plenty to discuss. So I am going to move on to my second question or comment.

You had talked about trying to facilitate data-sharing with resources like NDAR and ATN or the Autism Clinical Trials Network. Then think about all the times that

we have tried to do over the years some kind of facilitation like ISAAC and all the other things. Did you just decide to give up on that? I mean it has just been too much energy and effort put in to try to say, could we have one database that we could all share data with? Or you didn't make that recommendation?

DR. SWEDO: I'll just jump right in and just say that ISAAC actually has been folded beautifully into NDAR. Folks are entering -- sorry, ISAAC was the Cure Autism Now-sponsored database for clinical research on autism, as opposed to NDAR, which not only has the clinical data, but genetic, neuro-imaging, and biologic data all on the same platform.

So ISAAC has morphed into NDAR in some ways. Our group actually uses three systems right now, but they are all compatible, so that we can end up putting the data into NDAR.

DR. HENDREN: And is NDAR widely available? Does everybody use NDAR? Or is it only in NIH studies?

DR. SWEDO: Do you want to --

DR. INSEL: We're hoping everyone everywhere will use NDAR. It is available for everyone. The question is, who is willing to share and when?

DR. LANDIS: There was some discussion at an NDAR meeting about offering small awards. You would apply and you would get a grant that would enable your deposition of data in NDAR.

One of the nicest things about NDAR is it has these GUIDs. I don't understand what they are, but it means that there's one file for each patient. So you don't end up with one patient appearing as 20 different cases and skewing the interpretation of the data.

DR. HANN: Okay, I'm going to need to stop this part of the conversation. I know it is very rich. We will turn it over for public comment. Then, if we have time, as we did for other panels, if the public comment doesn't go the full length, we will come back to the

panelists.

So if I could ask if anyone from the public would like to come up to the microphones?

DR. HARRY: Jean Harry from NIEHS.

I think I am going to go back to an earlier part of the presentation for this last group and just applaud the group for making the statement of trying to broaden your scope of what you are looking for, rather than looking under the lamppost.

A lot of discussion was made on the vaccines. But when I was thinking about the chemical exposures or environmental exposures, most of those, realize, as they are designed, are also somewhat looking under the lamppost because it is either what we can measure, what we can have a biomonitor for, or might be able to pick up in the blood tissue or urine.

There are a number of things which need to be considered in the fact of a single acute hit at a critical time of development. Many

of those things, you are never going to find later on in any sort of biological sample that you find. There are a number of compounds that are actually going to get into the system, do their damage, and be out within just a few hours.

So, if you would keep that in mind also when you are thinking about environmental factors, that it is not just long-term, persistent, chronic exposure, but you can also have those acute exposures, a lot of your metals, your organo-10s, your mercuries, things like that, which we now know are very, very toxic and can happen at a very acute exposure.

So I just wanted to bring that out for consideration as you are going for the environmental factors as far as the chemical exposure.

DR. HANN: Additional public comment? Questions?

MR. MOODY: Thank you. And thank you,

Della.

I would like to make a plea to bring the tools of science to bear on finding a rigorous answer to the vaccination question as it relates to autism. The issue should be depoliticized as much as possible. Every time it comes up, it is like we are all of a sudden walking on eggshells or it is something to make fun of or laugh at; it is such a controversial issue.

I would suggest that, until the tools of science are brought to bear to answer the question of causation in a rigorous way, the controversy will only grow, and the harm to public policy, both in autism and in the general case of the vaccine program, will only grow.

So IACC has an opportunity here to take a leadership role and not kick the can back and forth between a variety of people. IACC has the strategic plan. It has the funding mechanism. It certainly has the interest in

the community to get this done.

The question was referred over to NVAC at last January's meeting. It was answered in a pretty rigorous way. In June, the Committee voted unanimously, but the lack of baseline data on unvaccinated children was an important scientific gap.

NVAC has no money. NVAC has no strategic plan. NVAC has no say-so over what NIH does.

IACC has the tools and has the plan to get this study done. So I perceive from what the panel members have said, albeit on tippy toes, that this is an important issue of public policy, that understanding baseline data on vaccinated children is crucial to public policy. The question is really more the mechanics of who will do it and how it will be done.

Now I would suggest, in response to I think it was point two on the slide, that the existing studies, EARLI, CHARGE, and NCS,

given as examples, the first two are not designed as far as their protocols and will likely not have the statistical power to answer this question.

The third study, NCS, as Sue points out, it will take a long time. It potentially will have the statistical power to answer the question. But, as far as I know, in 2002, there was identified for NCS a vaccine autism core hypothesis, as well as a vaccine timing core hypothesis. Somewhere along the line, that was deleted from the NCS. It is not part of the core hypothesis right now.

Unless there's a specific protocol put in place that will ensure recruitment of a sufficient number of unvaccinated children, NCS won't have the statistical power to provide these answers, even if you guys are successful in convincing them to spend the $20 million to collect the medical records.

So it is protocol problem. So NCS may be useless.

But, other than that, there's an opportunity to do a retrospective study, say of 10-year-olds, even fairly randomized, if you use a large HMO or something, that would avoid some of the selection bias issues and look retrospectively at their health outcomes and use the waiver cards as a way of selecting unvaccinated children.

There are selection bias issues in almost any study design for epi. As someone said on IACC, I think, this is NIH; this is the leading research institution in the world. These issues can be dealt with. The differences in unvaccinated kids are not unknowable. They can be known. They can be discerned and teased out.

The one thing we do know, we know from vaccine court that vaccines do cause autism. The question is, how many kids are affected?

We know that ADEM is a risk factor. We know that mitochondrial disease is a risk factor. These are all things that can be

looked at in a rigorous disease study of vaccinated versus unvaccinated children.

So I would challenge the Committee to sort of do the hard thing and step up to the plate and respond to the community concerns and the agreed-upon scientific concerns, and set up a panel of experts, an independent panel of experts, that can bring the tools of science to bear to get these answers.

Thank you.

DR. HANN: Additional public comment?

(No response.)

Okay, I will take the absence of that, then, to take the prerogative to go back to the panelists.

I believe, Geri, you were next in the queue.

DR. DAWSON: Well, I, too, wanted to applaud this group for handling this controversial and challenging question I think quite well in many respects.

I wanted to follow up on one of the

points that you made, the idea of making recommendations to NVAC about the potential of understanding vaccine injury or children who have been vaccine-injured and entered into the database that is kept, like the Vaccine Safety Datalink database.

One of the possibilities would be for this group or IACC to actually write a recommendation to NVAC which advises the CDC around vaccine safety monitoring, about how they could augment the current system in order to begin to prospectively collect data on children who are reported to have had an adverse response to vaccine where it has resulted in a diagnosis of autism.

I think about a year ago the CDC started its own kind of genome project where individuals who are having an adverse response to vaccine, the goal is to genotype those individuals, so that you can begin to collect data over time about potential genetic susceptibility groups.

It might be helpful for the IACC to recommend to the NVAC that they recommend to the CDC, because they are the ones that are commenting on their strategic plan right now, that there would be ways of enhancing the monitoring system as well as making sure that the genotyping is done on those kids, where they are entered into that database of individuals who have reported that they have had a response to vaccines which resulted in autism.

That would also include, I think, recommendations, hopefully, that have to do with the phenotyping that would be done around a child whose parent reported that they had an adverse response. So one might want to, for example, go out and actually do a diagnostic evaluation or maybe even a medical workup of this child.

But, if we could start collecting these cases prospectively, and do a better job of this kind of safety monitoring, this might be

another way of leveraging an existing system in such a way to understand better whether there are vulnerable subgroups.

DR. HANN: Alison? She was next in the queue.

MS. SINGER: In addition to looking at research gaps, one of the charges to all of the panels was to look for new research opportunities. One of the ways that we did that on our panel was to really look at the 2008 Summary of Advances.

In the Summary of Advances, you will notice that the greatest number of advances came under Question 3. So I was wondering if the panel had -- I know you had a lot of time spent on other issues, but did you take any time to look at some of the new advances that were highlighted in the Summary of Advances and see if they led to any new ideas for new things to add to the plan?

DR. HANSEN: Well, yes, we did. But I think we really saw our task as really looking

at the advances and then identifying areas where we needed to really focus for new opportunities to advance in those areas.

So I think we struggled with the same thing I think all the panels did. By not mentioning it, we weren't saying that it wasn't a priority. So, if we are trying to identify gaps, not going back and reiterating what has already been done and how we have moved forward, but how can we keep moving forward by just highlighting on the agenda where we want to really identify additional opportunities.

I mean I think we did, as a group, look at how far we have gone, not just since the strategic plan was put together, but just pooled our knowledge in terms of subsequent to the strategic plan. What do we all know that has been out there in the literature that is addressing these issues?

DR. STATE: So one of the points we were trying to make in terms of opportunities that

I think is new and emerging does come from this recent set of genetic findings.

So this thought that there is an opportunity to turn things on its head, to identify kids who have a recurrent structural abnormality or have potentially a common variant, now that we think that we may have had one that will be present in a significant number of individuals, that that does present, we think, a new opportunity.

One of the things we didn't know is whether or not that has already been sort of dealt with in ARRA. Because, I mean, this is something that has happened over a short period of time, but I think long enough that there may already be studies ongoing there. But we saw that as a way to leverage some things that were not present at the time that this was written or were just coming to the fore.

I guess the other thing that didn't come out so much, but Bob was making the point

about the intersection between our group and Panel 2, I think we had a lot of things to deal with, but I think there were several discussions about the fact that one of the things that we are finding out, I think, about the underlying genetic architecture of autism is that there are a lot of different individual things or genetic variations that are affecting a small group of people. The real leverage may be in identifying the common pathways as opposed to identifying common genetic variation.

So we do think that a big, emerging opportunity is the same -- I don't want to speak for the whole group, but I will say, in my mind, a big opportunity was already addressed by the kinds of things that you were talking about in terms of translating from a genetic finding to a neurobiological or biological understanding of pathway.

DR. HANN: Comments? Questions?

DR. INSEL: I would like to just follow

up on Alison's comment. Is there anything, as you look at not only the recent advances, which were actually 2008, I think, so over the last nine months -- this is, obviously, such an active field -- is there something that has happened more recently that we ought to know about and that you would want to work into an initiative for the IACC to consider for its update?

DR. STATE: I mean there are probably a variety of brand-new findings, I think the first solid evidence for a common variant, but we already I think talked, highlighted in our slides the necessity for replication as a first step.

But that certainly has come up since 2008 and could turn out to be a very important finding, particularly because it would allow you to power studies, given that the allele frequency is reasonably high. So I think that is one thing. I don't know what other people --

MR. SELL: I would just echo something that Lyn had brought up earlier. I find it fascinating that today the monkey study came out, out of the University of Pittsburgh. I hate, at this point in time in the afternoon, to bring up the "V" word again, but just reading through it -- it was handed to me earlier today -- I think there's some fascinating findings that are contained in it. I think it leads to some promising thoughts with respect to utilization of primate studies, animal studies.

DR. LANDIS: If I could go back to the question that you asked, Tom, one of the highest priorities for this group, although we didn't list priorities, was to come up with ways to get replication done as expeditiously as possible, recognizing that time is children's health and that a genetic finding in one population, if others who had genetic groups that they were studying could, on a pre-publication basis, then look in their

populations to see if the finding was replicated, could save a year or two years. The same is true for environmental risk factors.

I know it is really difficult to share with your competitors pre-publication data, but if there could be safe harbors for doing that, I think it would just be really important and would instill into those kinds of studies the urgency that I know we are supposed to be thinking about so seriously on this Committee.

DR. INSEL: So, if I can respond, I mean I know that people think vaccines are contentious, but, actually, data-sharing is a far bigger problem, amongst scientists anyway.

(Laughter.)

It is conspicuously absent from the conversation that was in your report. So, if we have the time, I thought it would be useful to hear -- you mentioned it as an important gap in something that you think is an

opportunity, but it would be useful for us to hear about the details of that. Because everybody likes the idea of data-sharing until you start to say when and how and who.

We have seen this with NDAR, that, yes, we have 12,000 GUIDs, 12,000 subjects entered in, but we are being told that there won't really be any data to go with them for two to three years because everybody wants to hold onto their data until it is published and the replication is published. Then maybe they can share it.

So was there some conversation about this?

DR. COOK: Tom, I have to weigh-in here because it is my expectation that the data that I deposited last December would be available to everyone now. So, to hear that it is not available because of resistance to sharing, I am just concerned about that message.

DR. INSEL: It is available, some of it

is, but there are many people who have sent GUIDs with the idea that they will not be sending data for some period of time.

So I bring this up because this is a chance that, if the panel felt that we really needed a policy like we have for genomics, where we do have a very clear policy about data-sharing, we don't have it for clinical trial data, and whether the panel felt that we needed to actually move in that direction?

DR. LANDIS: So, if I could just -- this is Story -- point out that the first bullet under opportunity for gap five is to develop mechanisms to enable rapid initiation of replication of etiological studies.

That could be supplements to grants. I just think there needs to be rewards, and we may do better with rewards than sticks. But wouldn't it be nice to know that in June you publish your data and, by August, because people knew about it ahead of time, there had been an opportunity to replicate, or not, a

particular set of genetic or environmental risk factors?

I just think that that would be really, really important to do. NIH is like the land of mechanisms -- (laughter) -- but we should think about how to do that because it doesn't help the field if it takes two years for someone to go through and find out that what Matt may have found doesn't replicate in a different set of autism spectrum patients, but that could be because of the heterogeneity issue that we have talked about.

So I mean we did do more than pay lip service to that issue of sharing. We had a bullet.

DR. HANN: Sue? I think, Sue, didn't you have something? Yes?

DR. SWEDO: I was going to respond directly to the question and just say that, as someone who deeply believes in NDAR and the need to share data, and has some of those GUIDs that don't have data behind them, our

rationale, I believe, is quite solid. That is that those GUIDs represent patients that we were asked to put into the NDAR who are participating in our subtyping study. So, if I put their clinical data into NDAR, I would expect that the scientists in Bangladesh would go ahead and start analyzing it when the sample is not complete.

We have not yet reached our milestones for collection of the first 100 children with autism, 50 controls, and the matching developmentally-delayed individuals. As soon as we do that and we analyze the data, then they can be put in.

Our panel talked quite a bit about enhancements and rewards or non-sticks to help people gather additional phenotypic data at baseline for other kinds of studies. So I know that the ACE centers have many different goals and aims, but are being encouraged to share common measures of the behavioral assessments as well as some clinical data,

enriching the common measures to include other factors of interest, such as environmental exposures, when that can be done in a way and a means that is both reliable and doesn't require a tremendous investment on the part of the respondent. Then that should very quickly move into the common measures.

So I think asking investigators to share common measures as quickly as they are collected is absolutely appropriate, as Ed said, putting genetic data in, once you know what it is, but we do have a very real constraint here. If the whole purpose of your study is to phenotype a group of patients, it doesn't work to put those data into NDAR until the primary analysis has been done.

DR. NEWSCHAFFER: Yes, I want to talk a little bit about environmental exposure data in relation to this issue. It gets back a little bit to -- Manny first raised the point about homogenating and standard measures.

So, for environmental exposures, that is

tricky. We realize, of course, too, that the science of investigating environmental exposures in this field is a little bit behind that of genetics, but we do have large studies that are now out in the field.

If we look at research in other disease states, there is a history of efforts of trying, for example, to come up with a common lifestyle, exposures questionnaire for breast cancer. That was a mixed success. There were some advances. There was an instrument developed. It was not widely used.

I think, though, that we should pursue it. I mean some of the stories of mechanism -- I do think that the folks investigating environmental exposures in autism should be encouraged to discuss a baseline set of potential common exposure measures and see where that goes.

In the meantime, I still think the issue of replicating environmental findings moving forward is going to be very important. People

are going to start looking at things, and preliminary results are going to come out.

On the genetic side, they are doing pretty well with replication. Some standards have been proposed, and there's the ability to replicate because data-sharing exists, and it is relatively easier to do data-sharing because I know there's difference in platforms, but, essentially, we are dealing with more homogeneous measures.

So we've got a while to get there on the exposure side. I think we should look at that path. But, in the meantime, the kinds of things that came up in our conversations were just ways of having the investigators -- and there aren't hundreds of them -- who are looking at environmental exposures be in communication about preliminary findings, and seeing if there is some way that we can promote quicker response in other studies that are out there, instead of having to wait until a paper in NFAR to see that there is an

interesting parathyroid finding in CHARGE, so we are going to focus on that in another study.

If there was some way to get ahead of that a little bit, it may help the issue of replication on the environmental exposure side. I'm not sure what that mechanism would be, but I think that that is worthy of exploration. At the same time, I think we do need to start looking at common measures and see where that might take us.

DR. STATE: So I guess I am going to give kind of the glass-half-full interpretation, at least for genetics and genomics right now. I mean I think that we have made that distinction already, but I think it is important to talk about the different challenges for different datasets.

I think it is interesting, though, to reflect, when you think about how we might move ahead with broader data-sharing across phenotyping and environmental exposures, kind

of what's gone on with the genomics field.

I think there has been a combination of a kind of mandate from the NIH to move much more quickly along with just a general expectation in the field. Then the outline, the Ft. Lauderdale agreement on genomics is now serving as sort of a basis for people within autism to feel like, on the genetic side, or the genomic side, to feel like they can share large datasets, that they are not going to be scooped by the next guy over.

So there is some very large-scale meta-analysis going on right now, where a lot of groups are giving preliminary data, unpublished data, you know, from AGP, Simons, and a variety of other structures.

So I think it is an important issue, but it is also important to see or maybe to try to trace how it has gotten better over the last four or five years in genetics and in genomics.

DR. DAWSON: I just wanted to mention,

in terms of this issue of data-sharing, we had a meeting recently of the folks at NDAR and the folks at the Simons Foundation, and then the bioinformatics group at Autism Speaks, to really talk about broadly what are some of the challenges in data-sharing not only within the NIH, but thinking about the field as a whole.

I think some of the challenges are coming up with a standard for the field about a common phenotype battery. I don't mean down to the specific detail. We made great strides, for example, when we had an ADOS and an ADI. There was a sense that we need to take that now a step further and to say, if you are involved in an autism study, these are the expectations in terms of how you might want to go about phenotyping that will allow you, then, to share and merge your data with others.

Then, in addition, it is kind of how that data is entered into a database actually makes a lot of difference, because the

difficulty is often at the level of trying to combine these data and whether they were coded in certain kinds of formats.

Then you get down to the next level of how you put in place the information technology infrastructure into the database itself that either facilitates or doesn't facilitate information- and data-sharing.

So we thought about the idea of the group of all of us who are interested in data-sharing to come up with some standards at the level of phenotyping, but also at the level of, if you are doing an ADI, let's agree that every item should be entered, and it should be entered this way. If we can do that, then, five years down the road, when we want to combine these datasets, we are not going to spend two years trying to map your dataset onto my dataset.

But it gets even more, I think, complex at the IT level. But, certainly, for people in the area of IT, they have standards like

this in other areas that allow very easy data-sharing.

So I just think that the autism field in general could benefit from this, again, stepping back and coming up with a coordinated strategy on this.

MR. SELL: I just would like to highlight that. I kind of felt Dr. Cook's pain as well with respect to the data and the frustrations, at least from the community's perspective. There is, I think, a clear need for a strategy around clarity and speed with respect to getting data in and data out.

I come from Texas. So I always have all these goofy little sayings. I have always had issues with data in/data out. That is kind of the expectation that I think the standard needs to be based on: the data goes in; the data comes out. It is made available as widely as possible. It is clear. There are clear expectations going in what that data is and what it is going to be used for, and some

timeline associated with it, when we can start seeing results.

I think President Obama coming up to NIH and talking about autism today really highlights the need with respect to IACC taking charge and really trying to press this data issue and speed it up just a little bit.

I think the community's concern is data in and data gone. We want to start seeing results. We don't want to see the data just going in someplace and then hear folks come and tell us, you know, about the problems or the issues.

I mean IT has made some very substantial advances, obviously, as I think Geri highlighted. There are ways of doing it, and I have seen IT guys get all excited because they can explain it -- I'm not understanding it -- but they are explaining they can do it, and they can do it in rapid speed if they just had a little bit of funding to do it, and they had clarity with respect to what goes in.

It is just we want to see data and results actually coming out. I hope I kind of encapsulated a little of this from when Dr. Cook first mentioned it is very frustrating to put the data in and then finding out it is not being shared. I felt that. That kind of hurt.

MR. GROSSMAN: I don't know if it is because it is late in the day or what, but I am finding this conversation extremely frustrating. I think what the IACC is considering right now in terms of looking at a strategic plan, that if there is ever an argument for an increase in devoting more attention to services, this fact that the science community is at odds and is arguing about data-sharing, when we have such an urgent crisis in front of us, it is unconscionable.

So I would prefer that the resources, not that they should be diminished on the science front, but much more attention be

given to the service side, so that we could move forward on doing what needs to be done for people today and address that, and not have to deal with these issues of who is going to see what data at what point.

I just find it, as a parent and an advocate, I just find that this type of discussion is just not appropriate, considering the issues that we are dealing with.

DR. INSEL: Yes, so I'm not sure this is an either/or choice, Lee, but I think everyone realizes that there are great needs on both sides.

Let me just clarify. I didn't want to give the wrong impression about NDAR and data-sharing.

The fact that there are not the data that we would like to have in NDAR, when we have so many individual subjects already entered, is largely because the studies haven't been done. So the data haven't been

collected.

That is because it takes three to four years to do much of what is intended for the people that have been entered. So much of the ACE data and other studies that are underway now have a framework where all this will get loaded up, but it takes time to get the studies done and to get the data in there.

The gist of my question to the panel was simply that I don't think we have come up with perhaps the most modern or contemporary guidelines about what to expect in terms of data-sharing. We do have guidelines that we have provided to the field, but this is a moving target. Genomics has really pushed the edge of what we expect. It may be worth recommending to the IACC that we revisit this.

I think a lot of people feel, as Sue Swedo mentioned, the concern about being scooped. The community, of course, is hoping that everyone gets scooped. I mean they are hoping that someone in Bangladesh or Bombay or

someplace will see in the pattern of data that are there the very thing that everybody here is asking for, which is a way to slice this very heterogeneous pie so that you understand the subgroups.

That is going to take a lot of people looking at the same data in different ways. We have already seen this in other illnesses, where often the big discovery about how to break apart an illness comes from somebody who didn't collect the original dataset. It sometimes occurs in a place where there's the most data to work with.

So creating that playground for smart people from all over the world to begin to enter in here and tease this apart is something that the IACC could begin to promote as a vision for how this would be done. But it would require, I think, providing somewhat different guidelines about what the expectations are.

And, Story, I agree, I think we can

provide rewards as well for being able to play in this playground and to be able to enter data in as quickly as possible.

DR. LANDIS: And if I could come back to the issue of sharing risk factor data and epidemiological data about factors that might increase incidence or not, maybe some sort of a consortium with money attached for all the people who are doing those kinds of studies to meet once or twice a year with their fellows and share where the state-of-the-art is. If there were detectable money in it, they probably would be enthusiastic about doing that.

The other thing is, didn't you change the guidelines for data deposition for ARRA, the ARRA grants?

DR. INSEL: Right. So exactly. ARRA, everything is required; all clinical data needs to go into NDAR. I can't remember exactly what the timeframe is, but it is pretty tight there. So that would be one way

of populating the database.

But we have this beautiful framework that takes in imaging data, clinical trial data, 15,000 data elements. Back to Geri's point, there's a data dictionary that defines exactly what every one of those elements means. So, if you are measuring head circumference, exactly how that is to be done.

So that sits there. What we want to make sure is that it is fully populated, so that anyone anywhere who has a really interesting idea could go in and begin to mine the data for some new approach to understanding the subtypes.

DR. HUANG: I find this conversation really fascinating. We are not a research agency; we are a services agency.

So I am particularly interested in this gap five and looking at the prevention and intervention strategies that might come from this research.

I think the research, we are talking

about the genetic research, the pathways research. We are still a quantum leap from that into the researchers who are going to do the diagnostic strategies or the intervention or the treatment.

So what I am wondering is how all of that gets connected or if there is a recommendation that really links the translation of that research into intervention strategies.

I was really interested, also, in this prevention concept in terms of prevention, onset or prevention of certain kinds of symptomatology.

DR. HANN: Tom is sitting here going that sounds like Panel 4. So that is the panel that is meeting tomorrow.

I think, as we have walked through a number of these panels today, we have seen that issues that get brought up in one sort of get picked up in the next one in terms of then taking it off into whatever their direction

is, if it is diagnostics, if it is pathways, in this case, risk factors.

So I think that your question, actually, is a natural evolution. It is like, once you start to get a handle on some of those things, how does it then get into treatment strategies and interventions?

DR. INSEL: And prevention as well.

So Stephen is going to take us through that first thing in the morning.

DR. HUANG: I was just bringing it up because it was mentioned in this gap here under this particular panel.

DR. INSEL: Yes, actually, I thought that was one that they could have just handed over to Panel 4 because that is where we --

DR. LANDIS: But we wanted to make sure that what was discovered under Panel 4 didn't just sit in somebody's journal.

DR. INSEL: We got it. So you will hear tomorrow. That was actually a big part of the discussion, was making sure that we pulled out

pathways, targets, and moved them into new interventions and new approaches to prevention. So we will get to that in the morning.

DR. HANN: Any further comments or questions for Panel 3?

(No response.)

I can tell there's a fatigue factor that is setting in and a hunger factor I think for some folks.

Okay, then let's call it a day. We will see everyone bright and early tomorrow morning.

Thank you all very much.

(Whereupon, at 5:25 p.m., the proceedings in the above-entitled matter were adjourned for the day, to reconvene the following day, Thursday, October 1, 2009, at 9:00 a.m.)

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

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INTERAGENCY AUTISM COORDINATING COMMITTEE

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SCIENTIFIC WORKSHOP

+ + + + +

THURSDAY,

OCTOBER 1, 2009

+ + + + +

The workshop convened in Salon E of the Bethesda North Marriott Hotel & Conference Center, 5701 Marinelli Road, Bethesda, Maryland, at 9:00 a.m., Della Hann, IACC Executive Secretary, presiding.

PROCEEDINGS

(8:59 a.m.)

DR. HANN: Okay. Well, I hope everyone had a good evening. There was lots of excellent discussion yesterday and I am quite confident will continue today. We will pick up this morning with a presentation from Panel 4.

And I will turn it over now to Panel 4 and Stephen, I believe. Stephen, do you want to have each of your panel members sort of acknowledge who they are? And then we can roll into the presentation. DR. SHORE: By the time the sound gets here, you have no idea what you are staying.

So yes, we are Panel number 4. And Panel number 4 consists of the hard work by Robert Hendren, Eric Samstad, Edwin Cook, Bryan King, Joyce Chung and Sharisa Kochmeister and was coordinated by Dr. Thomas Insel and myself.

So just to get oriented, Panel 4

focuses on when should treatments or interventions be started? What are the medical issues I need to know about and how do I know that treatments are both safe and effective?

So before I begin, I want to read a statement by Sharisa Kochmeister, who as I mentioned yesterday, was unable to come. She is ill and this is her statement.

I am quite sorry that continuing health issues are preventing me from being here with you all. I want you all to know that I am honored, pleased, and proud that the NIH and NIMH appointed me to an advisory panel for the Interagency Autism Coordinating Committee for helping determine federal policy and research targets spending.

Apparently, they think I am an expert on autism. I am excited and humbled about this appointment, have enjoyed giving my input to this committee via phone meetings and email. I think the panel for listening and

incorporating my ideas about communication needs, adults with Autism Spectrum Disorders and ensuring quality of life is honored.

I sincerely wish I could be there with you right now and I intend to keep working diligently and unstintingly on behalf of all people on the spectrum, their families and caregivers through continuing to be an advocate for all people and invite people to contact me with their ideas and feedback. Signed, Sharisa Joy Kochmeister.

So, now let us begin. Through out conversations, we noted that there was no mention of emergence of new technologies as interventions in need of study. We also noted that there was a greater need to focus on data for decision makers regarding comparative effectiveness, how to sequence in interventions. That is something that is not really looked at. Is it reasonable to expect to use intervention B after intervention A? Is there any sort of sequence that we can put

together in order to make a treatment algorithm?

There is a startling absence of interventions for adults in nonverbal individuals. And we had quite a bit of conversation about how nonverbal does not equal low functioning. And we heard that quite a few times yesterday and I am sure we will hear it several times more today, the terms low functioning and high functioning don't adequately describe what we are trying to talk about, what we are trying to conceive of as we want to help people with autism lead fulfilling and productive lives. We might be better severed with the idea of a spectrum of functioning.

And this wide spectrum of functioning, we are at a point where we now consider autism as a spectrum but the spectrum has gotten too wide for its own good. So yesterday, there was a lot of talk about sub-typing and I think that is really good. So

the more that we can work towards matching diagnosis to treatment, the better off we will be.

We need to focus on potential novel treatments emerging from mechanistic studies. We spent a lot of time talking about sensory integration. And that is just one example of the many approaches that are out there, where don't have hard core evidence-based studies on them but there is a heck of a lot of clinical evidence that something is working and we need to take a look into those.

We need trials with predictors of outcomes and assessments of functional outcomes. And another way to word that is "quality of life."

Continuing on, we need new technologies. So let's take a look at them. Emerging tools and devices for communication, social skills and cognition. As technology improves, there are more and more opportunities for people in the autism

spectrum and, by extension, others who have difficulties communicating verbally to have other functional ways of communication.

Comparative effectiveness research agenda. So, by using administration data, by putting data into registries, let's take a look at how interventions are working for people on the spectrum across interventions. There is no research out there. And this is something that I focused my dissertation on. Comparative studies, comparing studies. And I took the educational, behavioral, developmental realm and as I was doing my dissertation, I did see calls for the need to compare interventions but nobody had ever done -- nobody has done comparative intervention research. Integrating predictors such as biosignatures, family history, clinical features and all of the trials. Molecular based novel therapies and, for example, fragile X, tuberous sclerosis and so on, and registries to integrate data across trials.

We need to integrate short-term objectives. Objective number one -- and these objectives can be found on 21.

Integrate short-term objectives, number one, the one about biosignatures with two through four, RCTs and add quality of life and function to outcome measures. Because that is what it is really all about, quality of life. How are people on the autism spectrum leading fulfilling and productive lives?

We talked a lot about adults yesterday and that emphasis continues. Adding adults, adding studies in adults to objective number four, the three randomized control trials of interventions for school-aged and/or adults by 2012.

So what do we need to emphasize? We have a need for new treatments and comparative effectiveness. In other words, what do we need? And there is an urgency of testing widely-used interventions. And this

urgency that speaks to, you know, often we have heard that autism is a national emergency. And I think the way to look at that national emergency is that we have an entire population of people on the autism spectrum who are not leading fulfilling and productive lives and contributing to society because we are not doing the necessary research to help people in the spectrum reach their maximum potential.

And now we get to the summary, the major points and we heard this yesterday quite a bit. The heterogeneity of the autism spectrum. The need for personalized interventions, life-span studies. You know, back to adults, we spend 70 to 80 percent of our lives as adults. Outcomes and how are we going to measure function.

How do we balance the portfolio between novel, targeted interventions and testing of currently modestly helpful interventions? How do we fulfill the need for

personalized information within these large scale randomized controlled trials?

And finally, we need a broad portfolio that provides actionable information about a range of interventions, including medical, behavioral, and technological policies.

Now, I have only taken about ten minutes because I feel we are going to have a good amount of discussion on this. So, let the discussion begin with the panel.

DR. INSEL: Stephen, if I can start off. That was a great summary. And I wanted to thank the panel that worked really hard on this set of questions.

It was a series of I think very useful and rich phone calls, some of which occurred at six o'clock in the morning Pacific Coast time. So we are really grateful to those people from Seattle and San Francisco who were able to join us at that difficult hour.

Also, it is a shame that Sharisa couldn't be here because I think you get a flavor for some of her recommendations in these bullets but the bullets don't full capture the quality of the discussion we had on the phone, where she was very, very helpful.

But as you said, maybe we can open it up and just go down the row to get specific points of emphasis from anyone in the panel who wants to say more about the bullets that we have already presented.

Brian, do you want to start?

DR. KING: Thank you and good morning everyone. I think one of the take home messages for me in thinking about the groups' discussion and looking at their recommendations is that they don't depart very significantly from what was there before. That what we have done is try to enrich and broaden the coverage, based on a lot of themes that have been coming up through the course of

the conference thus far, making sure that adults are represented, for example, making sure that nonverbal individuals affected by autism are also adequately represented and so on.

One of the feelings that I feel obligated to share though in looking at this list is that it is really daunting. We think about the needs that we need to address in terms of treatment and, arguably, everything that we do rolls up into this need to deliver treatment for folks in need.

But it is an extraordinarily long, long, list and it feels like it is going to be very difficult to prioritize within that list where we focus our efforts. We clearly have to do that.

One of the points that I made yesterday and will reiterate today is that a worry that I have when we start to include all of the things that need study is that we may not have a well-developed workforce yet that

can actually do some of these studies. So for example, the point that Stephen made earlier about sensory integration, Roseann Schaaf spoke to that as well, but we have a lot of occupational therapists out in the workforce that are delivering treatment every day but not necessarily ready to jump in and do controlled trials of those interventions. And we need to figure out how to be supportive and help that research take place, along with many other things on the list.

So, I will stop there.

DR. SAMSTAD: Yes, I think overall it looks very good, especially if the goal is a 1.1 rather than a completely right. I am very pleased to see that adults are represented and that is a major concern for me was their inclusion.

I did have one comment. I am imagining that item number six in the short-term objectives that that would also -- that is the one about widely used treatments. I am

imagining that implicitly that adults are included in that category but I don't know for sure. Maybe it would be nice to call that out explicitly.

My only other comment, and maybe this is getting too fussy, but there is in my mind some blurring between the items that discussed randomized controlled trials and item number six which talks about definitive studies and widely used treatments. I am not exactly what the distinction is between those two categories but perhaps that is harmless.

Overall, I think it is a very positive step forward and I am quite pleased. Those are my thoughts.

DR. CHUNG: Hi. So one of the things I wanted to maybe highlight is, having done clinical trials myself, I know that it is a very long tedious process to run a trial, get people enrolled and get the results. It is years and years in the making. So one of the things that is hard in doing treatment

research is that meeting a sense of urgency with a kind of need to carry out a well crafted, well designed study.

So the urgency issues, the timeline issues around trials is always problematic I think for people to get impatient. When is that five year trial going to be over? When are the results going to be completed?

So there is that. I think the issue of technology is something that I wanted to raise because I know that the technology field moves very, very quickly and develops very quickly. So I think we need to capture that somehow in ways that allow these maybe more rapid turnaround of those types of intervention type studies because those are going to move very quickly. And if you wait five years, you know, everything is going to change. So I think those are things that need to have maybe a slightly different approach to how those are funded or carried out.

And I guess with regard to the issue of comparative effectiveness research, I think that I wanted to make a clarifying point that some people think that this means that we do prospective trials using different types of modalities that are compared. The problem with that again is the time frame. It is not just doing prospective head-to-head trials. It is also using a lot of existing data on utilization, on what people are doing actually in real life situations to be able to capture these large data sets.

So that information could be a little quicker in coming around to helping inform what we do, rather than waiting five or ten more years for some head-to-head trial.

And I guess my last point I wanted to make was the issue of just diversity with regard to our subject population. That I feel like we need to do a much better job of expanding who we reach out to with regard to subject recruitment, the diversity of our

samples. You know, that part of heterogeneity is not captured all the time. We talk about clinical heterogeneity, I think socioeconomic, and ethnic heterogeneity is not really discussed in the same kind of way. And we really need to think about disadvantaged populations as being a really important group to include because the disparities of their care are found.

So that is the major point I wanted to make.

DR. COOK: Yes, I agree with everything that we have said. I wanted to focus a little bit on an area that has to do with emphasizing the translation of current already available and rapidly expanding knowledge about genetic variants associated with Autism Spectrum Disorders.

Yesterday I made the point that this is going to impact. Basically we should be less concerned about how much these should be thought of as causal variants but the

reality is a number of them provide us many clues to treatment development.

And as someone practicing in the field, I guess I came up, with others, with this concept of modestly effective treatments. Because the reality is that if we had such effective treatments, you know, we would be in a diabetes conference talking about what we do beyond giving insulin and we are not there yet. I don't know that we will, given the heterogeneity.

So one of my questions is how do we accelerate the translation from some of the basic knowledge. There are a lot of steps. I am reminded maybe 15 years ago coming to Washington for a similar conference and really feeling pressured to do things tomorrow or yesterday now. And Donald Cohen, who is quite wise and quite influential, said that here is so much we need to know about the development of the brain, this may take a very long time. Of course, whatever length of time that is,

we should try to accelerate it.

Some of this is dependent on knowledge and basic neuroscience and it is good that that is advancing rapidly as part of the underpinnings of what we are trying to do. But there are other impediments such as accelerating translation, even let's say looking at, for example, we mentioned fragile X, more specifically the metabotropic glutamate receptor 5 antagonists, which frankly much of the delays of getting those to trial I would consider administrative. It would be good to involve the FDA here.

Some of these things have to do with a manufacture of drug. And frankly, a lot of it has to do with the fact, and I am glad this is mentioned in a public comment, that the reality is autism has been almost completely ignored by pharmaceutical companies, in spite of the fact that we know from a recent study in England that confirms a lot of our impression that it has always been

an important problem. So one percent of adults in England with ASD. So the question is, how do we form those partnerships and get the interest.

Another issue is how do we get the message that I heard yesterday to Pharma that the goal of each treatment is not to cure autism but to reduce disability and distress. Now in addition to concerns that people with autism who are appropriately proud of their identity of having ASD should not be cured, the issue is that when you set up a trial for curing autism and you are only going to reduce something as important as extreme distress, you are setting up that trial for failure. You are not setting up the right outcome variables. So this is an important message in needing to partner.

And then another point, actually I am going to shift a little bit from that, could be called, you know, those of us involved in this could always be ridiculed for

reaching too far in this quest for something much more effective. But the other thing is this comment about existing treatments ranging from what would be considered relatively mainstream that still need to be studied more to some that some would call complementary and alternative, other people could consider mainstream. And that has to do with the support for -- and this gets back to Brian's point -- the support for people doing well constructed clinical trials. We really don't have that infrastructure. And it would be good to think of a mechanism to provide what basically amounts to mentorship in this area. The studies are hard. They are very hard. So, those like myself who would like to know much more, they are not simple but the principles are a lot simpler than what I see from the perspective of reviewing articles or IMFAR abstracts. Some of the basic principles it would be helpful to get across to people to save time and to make those studies more

meaningful.

Thank you.

DR. HENDREN: Thanks. Some of what I say is going to echo what Ed has just gone through. You covered such a broad area, it was hard to not repeat some of what you have already said. So, it was very good.

But there were two things in Panel 4 that really struck me. Two points. And under the gaps it talks about need to focus on novel treatments emerging from mechanistic studies, is kind of what Ed was saying in translational studies. But I think that is a new possibility that hasn't really been present until recently and it helps open up new ways for us to think.

And then under summary and discussion questions where it says how to balance the portfolio between novel targeted interventions and testing of current modestly helpful interventions, in the place where people put their responses on the website, you

know, people wrote in and wrote their comments, there was a thick group from the treatment section of the plan and there were hundreds of responses. But I would say well over half of those related to what Ed was mentioning in terms of what we sometimes call complementary alternative medicine or what sometimes we call DAN treatments or what we sometimes call as biomedical treatments. And I think those treatments are being used a great deal with very little evidence or ability to help people make good decisions. And yet I feel that people out there want that information. And I think they are not unrelated to these two points because I think many of those treatments are targeting things like inflammatory processes or immune function or oxidative stress. So there is ways to begin to think about these trials in a translational way that may find ways that they could be helpful and work.

And I think the mentoring that you

mentioned, Ed, the opportunity to work with people who have passionately been out caring for people but have never been trained to do good research, perhaps we could have a way that we could give family members, those out there trying, anything that might help their child, a better group of things to look at.

If there were things that obviously cured autism, we would have probably done some studies on them by now. But they seem to have enough of an effect on enough people that all those people wrote in and said we would like to have more information about this area. And I think to me that was an important thing to think about our public and who is interested in treatment.

DR. INSEL: Well, I think you have heard a pretty good summary of all of the points made on the phone calls. Let me just pull a few things together because some of these things are very consistent with what you heard yesterday, the need for registries, the

focus on heterogeneity. The comment that came up in each of our phone calls that we needed to move from symptom reduction to thinking about quality of life issue, improved functioning, how do we provide the right measures and interventions that ensure that that happens?

I think one thing that we didn't talk about yesterday that you did hear in this discussion and Joyce mentioned again, I will just emphasize that as an opportunity is this comparative effectiveness research agenda. This is an area of huge interest at CDC, at NIH. And it is a place where there certainly will be additional funds coming through, no only through ARRA but it is quite clear that in this time of talking about healthcare reform, people are looking for research that informs the decisions that policy makers have to make and comparative effectiveness research is, at the end of the day, precisely that. It is research that helps someone, a decision-

maker know whether that decision-maker is a clinician, a family member or a payer, whether intervention A is better than intervention B.

The only other thing I will add to this conversation which I think we didn't capture as we talked here but we did talk about it a bit on the phone was that we wanted to separate out treatments, which is most of what we have been discussing here from the broader term of interventions because interventions can also be preventive or preemptive. And we thought it was important to think about innovation, going way upstream. And as we get form annals two and three, better ways of detecting ASD at an earlier stage, thinking about ways that one might be able to provide a kind of preemptive intervention that would ensure if someone was at high risk, that they wouldn't actually develop some of the symptoms of the disorder.

So, that is certainly a gap. I don't think anyone at this point is focused on

this. But it could be part of a strategic plan, an effort that is part of a vision for where we would like to go in a way that just puts us in the same league as the rest of medicine. That is the way we are thinking about cancer, heart disease, and many other medical problems. And I think the group, as we talked about where we wanted to be with autism, clearly wants to bring the best thinking and the best tools from other areas of medicine to bear on this problem, which is a little more complicated but certainly no less important.

So let me see before we take our seats whether there is any other additional comments form the panel.

Eric?

DR. SAMSTAD: Now I feel heretical or something because I was going to agree with, follow up with what Joyce was saying. I think at least in the case of adult autism research, there are so few data out there that

I think before you can do comparative effectiveness studies, you really need to know what works and what doesn't.

As a clinician, if I have at least good studies of various treatments, I can offer these to a patient. I can say here are the risks and the benefits and we can make some decisions that are customized for that patient. But I guess the push is one for comparative studies so that makes it a little more complicated. But I am not sure it isn't premature in the case of adults but that is just in my thoughts.

DR. INSEL: Other comments? Stephen?

DR. SHORE: Yes, just some comments about comparative studies. I think the reason why we are so challenged with doing comparative studies is because of the nature of autism in human development. It is temporal. It is temporal in nature. You can't go back. You can't do ABA for six

months and then go back and then try something else to see how it worked. So I think that is one of things that challenges us with comparing studies in more traditional evidence-based sense that we are more used to.

And also, I think the goal is there is a number of approaches out there. And really what we are looking at is matching best practice to the individual needs of the person. So the question is not which is the best approach but which is the best approach for this person at this time because it is probably going to change over time. And that is something that also needs to be included in our work.

DR. INSEL: Any other points from the panel? If not, why don't we take our seats and then we will open this up for the rest of the participants.

DR. HANN: Okay, as the panelists take their seats, questions from the fellow -- yes. Right there.

DR. LANDA: Yes, I am Rebecca Landa and I just wanted to thank you for a lovely presentation. This is so exciting.

One of the things I wanted do is to echo whoever brought up the notion of infrastructure. It seems that as we are getting advances in the field in technology, we are also advancing in methodology. And if anybody submits a treatment grant, you can tell by the different reviewers' comments that there is still some disagreement in the field around basic things like design, exclusion criteria, establishing your outcome measures, what your fidelity measures should look like, how you are randomizing, you know, a whole technology around randomization and your analytic procedures. And I just would love to see somehow some work being done to come to some agreement around some of these things in the field.

And also I think it was maybe you, Ed, that was talking about how we really need

to bring along junior investigators. Because if the senior investigators are facing these kinds of challenges, I really am concerned about how the junior investigators are going to learn how to get onboard. Because as you have all said, I mean, doing this research is very time consuming. It is very expensive not just on our part, on the part of the taxpayers, but also on the part of the families as they wait with baited breath for the answers.

So I feel that this is a matter of some urgency. I would also like to see the possibility discussed of having like a data coordinator center or a multiple of these who could advise investigators early in the stage of their grant award. Perhaps one would wish that we would have all of that worked out before the review but sometimes through the review process there are new enlightenments that come out about things that could be altered. And it would be nice if we could go

before a real sophisticated DCC, present other viewers' comments, our intentions, and have one last go to make this thing as wonderful as it could be before we embark on this process.

That is my comment.

DR. HANN: Any comments back from the panel?

DR. COOK: It is interesting because in some ways, you were asking for -- I am going to interpret what you said and put it into some reviews not of my own grants but of others that I have seen and say that there probably is a need for some consensus building around clinical trial best practices.

I have seen comments from reviewers that make me think it would be impossible to do a trial correctly. Most of us who have ever, some of us submit, there are many situations where it is six of one and half a dozen of the other, this is certainly not restricted to clinical trials but could also, I mean, I could tell you similar stories

about genetic studies. But six of one and half a dozen of the other, one reviewer picks six and the other picks half a dozen, and between the two of them, you have no chance.

So development. I think there are some basic principles. Obviously others who are half a dozen instead of six disagree with what I think is obvious. And there probably is some need for consensus building. And in the same way that I don't think he would put in most grants without an ADI and an ADOS, there are certain basic principles of clinical trials that need to be set out as this needs to happen. And others say there is a range here. This is not as important as some reviewers think.

So anyway, I just want to echo what you said. You need to be able to come in with some sense that these basics have been taken care of. And you are speaking much more broadly of the peer review system than I think we can talk about.

But in this specific issue, I think there are things that we could list out as essential versus, you know, there is a difference of opinion and particularly people coming from different directions need to have some flexibility.

DR. CHUNG: I wanted to say something about maybe there could be a discussion about sample size considerations for studies, clinical trials.

I know that Dan Hall, who is manager of NDAR, the IMFAR data did a post for IMFAR looking at sort of the mean sample size of trials and it was quite small. So I don't know how that could be improved. And I wonder if there could be some discussion about recruitment and expanding our outreach and just maybe people who have done trials talk about how to do that better.

DR. HANN: Lee?

MR. GROSSMAN: Thank you. I have two questions. I will reserve the second one,

if you could put me back in the queue, whenever it opens up again.

The first one relates to this idea of new technologies. Our panel was tasked with this idea of prevention or limiting disability or improving quality of life. And again, there was this discussion that we had where it seemed like some of the information that we were talking about broached into what Panel 4 was going to cover. So, really didn't go into the depth that we could have, deferring to your panel.

So, I want to see, I want to get a little bit more into what your conversations were on new technologies and to see how specific you had gotten into that area because it is identified here as a gap and an opportunity.

And let me throw out, and not necessarily discussion specific but just to kind of throw out what I have in my idea for what specifics would look like. One of the

things that we had talked about was laboratory methodologies to be developed and implemented to adequately and appropriately and cost effectively measure body burden and types of load in large numbers of people. So that was one of the things that was thrown on the table for our panel.

Was there any consideration or any thought or specifics in terms of these emerging fields and the development of those?

DR. SHORE: Yes, Lee, what you bring up is very important and needs to be considered but we didn't really include that material in terms of intervention. But I do think it is something that is worth looking at in our discussion, that is.

DR. INSEL: There may be other people on the panel who want to speak more to this. I think what impressed me the most in the conversation we had in Panel 4 was how quickly the technologies for improving communication were evolving and people felt

some need to know more about those, have some comparisons. Is it worth spending the extra money to get X?

And there was the point that there really have not been many studies. Someone on the panel brought up robotics as a kind of example of where things could go. And they were saying the need to increasingly harness technology to help people in the spectrum be able to function and to participate in areas where they couldn't currently. Again, let me defer to others who were part of that discussion.

It's too bad that Sharisa isn't here because she was somebody who was able to give us some great examples of how that has worked for her.

But I must say, body burden, we didn't talk about that.

MR. GROSSMAN: I was just using that as an example for some sort of new or emergent technology that can be exploited to

our benefit.

DR. COOK: I guess my comment about that is it sounds more on the technology affecting what was being covered in 2 and 3, in terms of more cause of progression. So our emphasis was more on intervention, whether it is helping with technology to help with social skills development, communication development.

DR. HENDREN: So, I do think there was a lot of discussion in the group and in comments that were sent in about assisted technologies, trying to help with speech and language what could be done with computers, what could be done with interactive programs with iPhones, yes.

But there was a lot of discussion on the comments that were sent in and a little discussion in our group about some of the assessments that are being done and the ones that you are talking about with body burden or people that are sending to labs that aren't the largest labs but yet values back and what

do those mean. I don't know whether that would be a target for study but parents were certainly interested in that because many of them were spending large amounts of money to do these tests and it is not clear what the value is.

But I think other technologies that we at least mentioned and that Ed mentioned earlier, too, were things like genomic microarrays that could be used for a variety of purposes, including perhaps seeing who might respond or better personalizing medicine as being done in other areas, or perhaps imaging in ways, functional MRI and other kinds of MRI are now slowly being able to predict kind of responses and more effort in those areas of using the technologies and trying to support that as ways that might lead to more personalized medicine was, I think, a lot of the things that we were referring to. More the latter than specifically what you were saying. And yet the public really wants

some of those other tests validated.

DR. HANN: I believe Story was next.

DR. LANDIS: I was struck in some of the letters in the RFA RFI that we received and also in another mass emailing of the issue of diet and how changing diet can have for some children undefined what proportion or why a profound effect. And I am thinking this is -- if you could identify the children who would benefit from changing diet, it is certainly a low tech way to address better treatments and better lifestyle.

And I don't know what the etiology of that change, why a change in diet would necessarily make a difference but if you had screens that would identify those kids. And I know we have talked about this before, that there are reports, case reports, individual anecdotal reports of very important changes in outcome for children, based on relatively simple interventions. And I don't know how we

could pursue that but it could be potentially a lot less expensive and effective for some kids than thinking about some of the other high tech things that have been discussed, except for the assays, obviously.

DR. INSEL: We had talked. We didn't talk so much during the phone calls but in the IACC discussion for the strategic plan, we talked quite a bit about the “n of one” approach and being able to find a way to aggregate individual experiences like that so that it could become the foundation for an RCT. But actually it doesn't show up much in the plan. It is still in the plan but it doesn't have much of an emphasis and it is not something that we talked about in the panel discussions this time around, partly because it was already there.

DR. COOK: Well, I think it is an excellent -- it is really what I was trying to address when I talked about mentoring for trials because this is an area that has been

there for decades with parents being told that this definitely works with me having parents come in, having their life rearranged around all the food being in the trunk and the child being very distressed by this. Parents concerned that if the pleasures they would like to offer their child, being able to eat out at a regular pizza place that doesn't have gluten free dough would be nice. Parents, as Bob mentioned, don't feel permitted to not do this.

And with all of the promotion of this, there has been one study I know of by I think it is Dr. Elder, a nurse in Florida, which was negative and admittedly under powered. There is a second which I haven't seen. I don't know the results and that is just one dietary approach.

So again, there is a lot of effort and energy out there. There is a lot of use of treatment and how do we help support people in studying what they feel so strongly about?

DR. HANN: Ellen, were you going to follow up on the diet issue? Okay. Were you going to follow up on the diet issue, Lyn?

MS. REDWOOD: For those of you who don't know me, I am one of the public members of IACC.

And I just wanted to share with you a story about a little girl in Georgia who was 12 years old. She was being taken care of by her grandparents and they could no longer control her behaviors and she was admitted to a state psychiatric institute. And within a matter of months, she deteriorated. She became very ill. She writhed in her bed all night long. She vomited and by the morning she was dead.

When an autopsy was done, this little girl was obstructed and she had infarcted her bowel. And that was never treated and never acknowledged.

And I am sharing this story with you because I feel so strongly that these

children have many, many underlying medical problems that are being completely overlooked because the focus has been on the brain and not the body.

And I think it is an area where we can make so much difference. There is not any amount of behavioral therapy, or speech therapy, or assisted communication devices that is going to help with a child who is impacted and has infarcted their bowel. And we are missing so many opportunities to improve the health of these children.

Oftentimes when we these underlying medical conditions are addressed and treated, their behaviors get better. Some kids have even lost their diagnosis. So we know they have immune system abnormalities. We know they have ulcerative colitis. They have metabolic stress. They have low levels of glutathione. They are under-methylated. And there is so little focus on addressing those medical issues.

We have protocols in place now for treating inflammatory bowel disease. But it is not anything that is even considered. And I know Yvette mentioned yesterday the pediatricians are so stressed, they don't have time to really look at these children medically and it is an area where we could make a tremendous amount of improvement and it is not anything that requires a genetic test or an MRI or anything except a good physical exam and some laboratory work.

So I just want to put in a plug to please look at the children's bodies as well as their brains.

DR. JANVIER: This is Yvette. Since you mentioned my name, I can't resist.

As a developmental pediatrician, I have worked with children with developmental disabilities for 20 years. And you talk about comparisons, I have certainly dealt with children with many different brain disorders and many of them have GI issues, reflux,

constipation, et cetera, that I really take offense to this description of children with autism as being ill and sick. I mean I personally treat over a thousand children. They are the healthiest children I know. They are beautiful children. Immune disorders; I don't think I have a single child with a significant immune disorder.

So you know, maybe we are talking about subgroups, subtypes, I don't know. But it certainly isn't common. But I really don't think that GI issues, if you looked at the total population of children with developmental disabilities, that there is really any difference.

So you know, I mean I totally understand the desperation on many parents' parts to improve the functional life of many of their children but you know, I don't think that we have been able to understand what the cause is here, what the cure is, if there is a cure, a way to prevent this. But going off on

tangents where a rare child who should have had an examination and picked up a bowel obstruction is really not where we need to be going.

MS. WISEMAN: Nancy Wiseman. I have to respectfully disagree with that. I see so many families. I talk to families day in and day out. And I cannot emphasize what Lyn just said.

I have lived this with my own child, who is almost 14 now. She was diagnosed at the age of two. We got an early start. By the age of six, she was considered off the autism spectrum. Great story. What we didn't know, and she was being treated with one psychiatric med after another, was that she had an underlying autoimmune disorder called PANDAS. It was not diagnosed until she was seven. It was not treated properly until last year. This is a child who had violent, violent, rages, tics, OCD. Very, very bright child. Everybody just assumed it was part of

the autism. Nobody looked at it in terms of it being an overlapping disorder.

I see so many kids and talk to families every day who are hurting, who are medically unhealthy. Yes, there are some kids who are not dealing with some of these serious medical issues but I would say more of the kids that I deal with are.

So one of the things that I wanted to say to emphasize what Lyn said was that we have to have higher prioritization on getting at the underlying immune, metabolic, and gastrointestinal issues. It didn't look like my daughter had gastrointestinal issues when she was two but when I started peeling apart some of her foods, it turned out she was highly allergic to most foods.

Also, I think we need to have an understanding of which treatments helped kids who have comorbid disorders because so many of these comorbid disorders, whether it is immune or gastrointestinal can impede the progress

that these kids make and set them back.

I never imagined that my child would be set so far back so many years after overcoming her autism diagnosis. But for some reason so many of these kids seem to be susceptible.

Also, one last thing. I know you said that you are going to be doing comparative studies, one treatment versus another. And thank you, Stephen for addressing the importance of looking at individually tailored programs for the needs of the child.

My other question was, are you looking at integrating some of these treatments and how it helps these kids?

DR. HANN: Panelists?

DR. INSEL: Yes, if I can. I am not sure we really want to get stuck on the discussion about the medical issues here because we didn't talk about it in the panel. It is in the plan already and it was actually

in the second point that the IACC made. It says under short-term objectives to support at least three RCTs that address co-occurring medical conditions associated with AST. We didn't revisit that except to note it and to say that we weren't sure this was the highest priority but it was something that was in the plan that we didn't feel any need to change.

So unless you feel that needs to be changed, perhaps you want to tell the IACC to take it out or if you want to say leave it in, we actually didn't deal with it. And we are in the business of updating the plan. So we didn't think there was any new information that we could bring to bear to change that particular recommendation. But I will let Stephen respond to your specific question.

DR. SHORE: Yes, implied with matching best practice to the needs of children on the spectrum, I believe, does include mixing and matching methodologies as needed.

And an example of that is the SCERTS model developed by Barry Prizant, where essentially it is not so much a methodology but it is more of a philosophy. In brief, the idea is to give the child a really good assessment in the areas of socialization, communication, emotional regulation, and transactional support. So that is where the acronym SCERTS comes from. And then after that good assessment is done, take from existing interventions and give the child what they need.

So, that is a good point to bring up. Thanks.

MS. DURBIN-WESTBY: This is Paula. Is anybody on?

DR. HANN: Wait a minute Paula. Wait a minute.

MS. DURBIN-WESTBY: I am just going to jump in. They haven't invented the technology that lets me know when to jump in, in a panel with 30 people. So I am just going

to start. This might take it in a little bit different direction. Now, I wrote down language changes I would like to see. And I might as well bring it up here, after listening yesterday from disorder to disability or, in some cases, difference. We already talked about high functioning and low functioning.

Nonverbal, I prefer to think of it as people without a communication system that is understood or well understood. Because there, I don't think a divide between verbal and nonverbal always captures what needs to be researched.

We could get rid of mental illness. I know it is in the DSM but it could be developmental disability, which I think is more accurate.

And no autism patient. A lot of us aren't patients but if I keep having this throat, I am going to be a patient. But I am not going to be an autism patient. So,

sometimes people are patients and sometimes we are just autistic people.

And deficiently built brain. I don't really think of our brains as deficient. I don't consider myself to have a deficient brain or anybody else anywhere on this spectrum. There are people that have more significant challenges.

And I think the language is important because how we talk about disability is important because it can open up new ways of thinking about it that could lead to paradigm shifts and lead to real research breakthroughs.

So things I have read in studies like "locked in a world of their own" and the "costs of autism to society." Or one was "our findings lead us to the rather sad hypothesis that . . ." And a hypothesis to me isn't sad or happy, it is just a hypothesis. But if you put a value judgment on it, that can limit the way you look at it. So that is my language

thing.

And then one point I want to make is, as a representative of the Autistic Self-Advocacy Network, I am not here just representing people who can speak or people who can talk and communicate in a way that you can understand. And I think largely of people who are autistic who are not able to communicate and who are, perhaps, the most vulnerable to potentially inappropriate interventions and treatments. And I have talked to parents who have tried this, that, or the other, that is a widely touted intervention, or medication and it doesn't work for their child, or it backfires, or it has the opposite effect. So, I think we need to think about that.

And also once again, I say because my brain does function differently, I and other people on the autism spectrum can offer valuable insights when it comes to developing interventions and treatments. And ASAN does

not support normalization to make autistics indistinguishable from non-autistic people. I don't think that is really a reasonable goal. And it puts a lot of stress on people to try and imitate and figure out how to do that and if it is not really part of our neurology.

And at a time when there are so many exciting breakthroughs happening in autism research, it is absolutely urgent that we be involved in the research and perhaps no place more urgently than in the treatment and intervention research. And especially when young children are involved, I think it would be very urgent to talk with autistics, older people, adults who can communicate with you and kind of translate some of what we can see.

And it seems to me that only in the autism world do people say, well, you are not autistic enough so you can't really have any input. And if you looked at another disability like blindness or deafness, you probably wouldn't say if you were consulting

somebody who is blind but they can see a little bit of light or something, you would not say you are not blind enough to be able to help with our study. You can't really have any input because you are not deaf enough. So, I think it is something that people need to quit making a divide between who can talk for somebody else. And I think we have a really important state in the research that affects people everywhere on the spectrum.

And my comment on pharmaceuticals. I think this is my last comment. Pharmaceuticals need to be safe, designed for specifically autistic brain neurology, and not plans to prevent autism or not necessarily to stop behaviors that are just socially stigmatized. But if somebody can get some relief from some kind of sensory overload, that is beneficial.

I take a medication that is really an anxiety medication but I take it so that I can stand to feel my clothes touching my skin

all day. So I am not like opposed to pharmaceuticals but they need to be developed in a safe manner. And also, I think there needs to be a focus on developing, or looking at the significant number of people on the spectrum who have epilepsy. Because what I understand, they are usually excluded from drug trials, which makes a lot of sense. You don't want to put somebody in an unsafe position but there needs to be a way to research that.

And then in the consolidated analysis of strengths, weaknesses, opportunities, and gaps from last year, there was the sentence: "The majority of targeted children and adults in schools and communities are also going to be on psychopharmacological treatments." And that is a really sweeping statement.

If people need some kind of psychopharmacological treatment and that has been determined that that is the best route

for that person but it is not like you get handed your diagnosis and your medication. So, it is just something to think about when developing what you are trying to do with that development.

DR. HANN: Any comments with regards to the panel -- from the panel? Stephen.

DR. SHORE: Yes, something, just a few observations based on what Paula mentioned.

ASD is still a good way to refer to people on the spectrum. I, too, like to think of it as being an autism spectrum difference. Now that said, the reason why we are all here is that there is a number of things about autism that are horribly disordering. And one of them, as Paula mentioned, this business of a number of people on the spectrum who we have been referring to as nonverbal but I really like to think of it as we haven't figured out a reliable means of

communicating with them yet.

And I have heard how many stories where a person who doesn't have the ability to speak and just by chance they end up in close proximity to a keyboard of some sort. A generation or two ago, they just happened to be next to a typewriter. Now they just happened to be next to a computer and they are pushing buttons and suddenly they are typing out words that nobody suspected that they even know.

Getting to medication, I don't take any medications for autism. There is no medication for autism, specifically, but we know there is a lot out there for some of the effects such as anxiety and so on as Paula just mentioned. But it seems to me just based on anecdotal evidence that a lot of people on the spectrum seem to have atypical reactions to medication. And I think that is something that needs to be explored. And that is something that medical doctors would be much

better than I to sort out but it is something to be mentioned. Thanks, Paula.

DR. HANN: Anything else from the panel? Okay, Ellen Blackwell.

MS. BLACKWELL: Have a couple of questions. I wondered if, in your discussions regarding treatment you talked at all about integrating a cost-effectiveness component, especially in the comparative effectiveness research.

And second in your discussions regarding the new and novel treatments you discussed the importance of assuring the health and safety of the folks that you were going to be looking at.

DR. HENDREN: I think those are good points. I think that looking at the value of treatments or looking at the cost effectiveness is something that I don't think we emphasized but should be there. And what we are saying is any outcome needs to look at a clinical outcome compared to financial

outcome and then to safety. And safety, I think is always part of the trials. So it is something that we discussed but didn't emphasize as much as you are suggesting. So I think that is a good suggestion. Both of those.

DR. HANN: Anything else from the panel? Okay, Peter.

DR. COOK: No. Sue has had her hand up for a long time. I'm sorry.

DR. HANN: Sue.

DR. SWEDO: Thank you, Ed. I actually was just going to try and make a suggestion that would incorporate many of the remarks this morning and it goes actually with your summary and discussion questions.

How to fulfill the need for personalized information within large scale randomized clinical trials and also sort of what you were talking about in terms of individualized therapies.

I'm not sure it can be a function

of the IACC. Although, I guess between our services side and the research side, it would be lovely if there was a clinician's toolkit in terms of these individualized comorbid conditions but also just the mainstream approach that we heard from Yvette this morning. You know, if 950 kids are very healthy and have no physical illness as a part of their autism, then there should be a standard approachable therapy for that. AND within that, we need to be working within that population of people to improve outcomes and functions. So that that would be one group for a study.

But there may be kids who have additional needs. And one of the difficulties that Ed was speaking about was to design some of these very individualized treatment trials becomes, A) a design nightmare but also just a feasibility difficulty. And maybe that would be another place where some multi-site collaborations could be useful and also some

help in talking with review groups. Maybe there would have to be a contractor or different mechanism.

And then the second point I wanted to make was about the encouraging technology as aids to maximizing outcome in autism. It would seem like that would be something that maybe there could be a special outreach to the technology community, letting them know about the SBIR and some of the other awards that NIH has because I think a lot of folks kind of struggle in their basements or -- probably not basements, in their offices trying to get this done and may not know that there are grants available for that kind of thing.

DR. HANN: Any comments from the panel on those issues?

DR. INSEL: Maybe I can just respond quickly. Sue, I think this is an issue way beyond autism that we are struggling with. How do you develop the interventions approach in the era of personalized medicine

and how do you create a pathway that allows you to move quickly for subgroups that you might identify on the fly, so that you have designs that are more adaptive?

There are some pretty good templates. So, I-SPY 2, which is developed by NCI for breast cancer is probably the best example right now of adaptive design driven by these small -- in their case, using biomarkers to decide who should go into which arm and then quickly moving around to go into different arms.

You know, I think remembering the conversations we have had on this panel, the concern was that we are still very limited here. We don't have targets. We don't have novel therapies. We are still largely limited to behavioral interventions and tweaking them this way or that way.

And you know, where ended up over the course of our phone calls in the final phone call is the sense that we just really

need to back up here. Go back to Panel 3 and Panel 2 and ask for some help to come up with some target identification, some pathways, some novel entities that maybe could be done in collaboration with Pharma or other ways so that we will be able to push out these kinds of adaptive designs with an array of options for treatment that we don't currently have. That is, at least, how we ended up in the conversation.

DR. SWEDO: I actually agree completely and one of the things I had forgotten to say was that many of the families I talked to would find it most helpful to have some of the things that don't work known and made clear. Kind of what Ed was saying.

If you have had your child on a gluten-free, casein-free diet and you think maybe you saw a little improvement when the child first started, how do you know when you can stop? When is it going to be safe to stop?

And for families who don't want to take that chance that their child might regress and get worse again, that is a very heavy burden to bear.

So as we get the results from the dietary trials or other negative studies that have been well done and not definitively, but at least for the group that was tested, demonstrate that if you have these symptoms, this is not that helpful.

I think that would be huge because right now you only hear about sort of the anecdotal cases of this helped my child. And the moms are saying, I have to try it all because what if I don't try it and it might have worked. So to be able to give some validated information of what it isn't necessary to try, I think would be as helpful as when we can feel like the cancer institute and just, you have got this cell type, let's march you in this direction.

DR. HANN: Peter?

DR. GERHARDT: You know, it says need for greater focus on data for decision-makers, comparative effect in those sequence of interventions are prescription algorithm, etcetera, etcetera.

This was brought up yesterday, too. I really think that in that particular area, this need for not only interdisciplinary cooperation but also modes of effective translation into practice. We are already a very fragmented field. And each path should read speech path journals and be around all those journals.

You know, so if you are doing a dietary intervention and you have only people who think dietoric, then the other group isn't go to buy it. And if you have only people who don't think dietoric, then they are going to say it is a flawed study. And it is not going to change anything independent of -- I mean, I think that is part of our challenge with the vaccine question right now is that we continue

to find flaws with the studies based upon our philosophical orientation, as opposed to the actual basis for the studies.

The other part with the translation. In terms of intervention, I don't know who the decision-makers are and how they are accessing information. The principles aren't reading journals. Classroom teachers may read Exceptional Child. The other analysts read JAMA. How do we get that information into that information into the hands of people who can most benefit by using it, who can actually do this?

You know, the concern, and you know, it used to be said there was a 12 year gap between research and practice. And it has decreased. I sometimes think in autism we have like a 20 year gap between what we know in the research and what is done in classrooms.

So I think that really should be part of this. And I also think it would be

interesting to look at factors impacting adoption of interventions. Why is sensory integration therapy so widely used, given limited data, when other interventions with more data aren't used? And until we understand that, I think we are going to end up in this circle of doing research, research getting published and sitting on shelves, while the stuff that makes the nightly news makes it into classrooms.

So I think that needs to be part of this if we are really going to advance the practice agenda within the field.

DR. HANN: Comments from the panelists?

DR. HENDREN: I have decided to go back to Ellen Blackwell's idea to of, you didn't say it this way but the panels have been saying, doing kind of T-1, T-2, and T-3 research. So there is the translational in terms of bench to bedside or biologic mechanism. But then thinking about

effectiveness but then also dissemination research. So as we are thinking about treatments, we need to think about all three of those, I think. Some of what you are saying, how do things get out there and why don't they get out there.

DR. HANN: Okay. Just, I need to let you all know we have about five minutes left for this part and then I am going to open it up for public comment. So we will probably only have a chance for probably one or two more comments.

I think that next was David.

DR. MANDELL: So, I want to applaud Panel 3 in looking at the brain power and the thoughtfulness up there. I am sure there are many things that you discussed and what you present is really only sort of the global issues. But I worry that if some specific things don't make it into the report, then they don't get translated into RFAs. And certainly we don't want to handcuff

researchers but on the other hand, this is a chance to provide some direction. And so I was wondering about some specific things you may have thought about or not thought about or thought about and decided to exclude.

One is that there is this tradition of behavioral or psychosocial intervention and there is a tradition of pharmacologic intervention testing and those are very different traditions with very different sets of standards and measures.

And while there is nothing that you write that specifically precludes one or the other, there is not specific discussion of behavioral intervention, either, either talking about subgroup variation or which types of behavioral intervention work or combinations of behavioral and pharmacologic intervention.

The second things would be the use of treatment studies to elucidate mechanisms. There is discussion of translation, of what

happens in Panel 2 and 3 to Panel 4 but not that. And that that might be a good thing to include.

And the third thing to echo something Sue said is that this type of -- if you are going to study subgroup variation, then under our traditional analytic strategies, you need to be powered to test a three-way interaction. And what does that mean? Is that even feasible in a randomized trial design?

And either we have to dramatically blow up how we think, as Joyce said, as we think about recruiting or we need to think about different designs. And if they are not explicitly mentioned as acceptable design, then I worry that review committees are just going to trash them.

I will stop.

DR. HANN: Panel? Comments?

DR. KING: I will just jump in. So we didn't talk about specific behavioral

intervention approaches but you will see that there is, in the existing plan, a call for randomized controlled trials of behavioral interventions and across the age range.

There were lots of suggestions from the public comments about specific behavioral intervention strategies that deserve consideration and we didn't think that it was necessary to call those out specifically. I know that that was adequately covered already.

I will say that your point about learning from or using responses to trials as an opportunity to inform next steps is one that we did try to capture in the development of algorithms, although not explicitly. Stephen said earlier that he has been struck by how sensitive, how exquisitely sensitive some people with autism appear to be to psychopharmacologic treatments. And it does seem like there could be value in understanding whether someone who becomes

behaviorally activated on SSRI, for example, is going to go down a different treatment path, whether that is a window into the physiology there that could inform next steps in treatment.

So I think there absolutely is tremendous value in being able to learn from, you know, it is true on the behavioral side as well, learn from previous either response or lack of response to an intervention, as that keys up the next steps.

DR. HANN: Okay. It is now 10:15, so I am going to open it up for public comment. I note the two Cathys each had comment so if we have time, we will come back. And Lee. Okay. And Jerry.

So, I am opening up now for public comment.

MR. JOHNSON: Hi. My name is Chase Johnson. I am the Autistic Self-Advocacy Network intern. I was diagnosed with Asperger's when I was a young man, probably

around sixth grade. I have had sort of, as I mentioned yesterday during Panel 1, to have been a very fluid experience for me, as it sort of changed over time.

You and then someone else, I believe it was Stephen brought up the idea of sensory integration groups and so I have had very interesting experience with those. When I was going through those when I was probably in maybe first through maybe fourth grade, it was definitely very interesting because they sort of lumped all of the kids with any sort of mental disability in just one room and it was just like -- and sort of us made us do very, very strange bonding activities.

And it was sort of very interesting how the school system went about it because I was just a kid at that time and it was just sort of an experience of like what am I doing here? I don't belong here with everyone else. Probably because I was raised with the attitude that one, I knew I was

different very, very early on and society generally teaches that differences are bad. And once you see that in others, you tend to judge them right away. And so although I was a kid at the same time but not only that, I was a mind blind kid with Asperger's. And so ultimately it provided some degree of help in some way of figuring out how things went.

However, someone else, I don't know their exact name, also stressed the importance of expanding these to racial minorities and other people in like the lower classes. And I can't stress that enough because I was raised in white suburbia. And so all the kids were basically, like about 95 people in like my graduating class of maybe 400 were white. And it is just people are being denied so many of these opportunities that I had. And so I can't stress that enough that people should have the same opportunities in the classroom as I did.

Another thing that was interesting

to bring up is the idea of just appropriate treatments. I am on a few medications right now. In fact, I went off a very, very powerful medication called Trazodone, which is used as a sleep aid/antidepressant. Usually it was meant as both for me, just because like how Asperger's manifests itself in me is how my thoughts are processed and how they tend to race constantly to the point where I have insomnia at night because the thoughts can't stop. And so however, it did have a cost on my body, though. Like it caused, like one of the main side effects of Trazodone is vomiting. And so I lost maybe over the course of maybe three years I took it, the past three years that I have been taking it, I probably have lost realistically about a fourth of my meals due to vomiting.

And so although it worked wonders for me mentally, it is just at what cost, really, can we go about this. And so I can't stress importantly enough that we also have to

be very, very delicate in terms of how we approach things in the psychopharmacological sense.

And I guess that is it. Thank you.

DR. RING: Hi. Rob Ring, Wyeth Research. I guess, as you know, I am thinking here on the side, really have enjoyed the conversation today. It has been very enjoyable.

As I think and know of the pharmaceutical industry entering into this disease area and starting to tackle it, I have some genuine concerns about the potential for misalignment between what is clearly emerging as the research priorities for this community of research with the strategic direction of the pharmaceutical industry, as they contemplate novel therapeutics here.

And I guess my curiosity is whether or not there was much discussion about the prioritization of targets. Not the

targets that we develop agents for, but the symptom domains or outcomes that are of the greatest value or in the greatest need for the development of agents. Not knowing that makes our efforts a little, well, it is a gamble.

And I don't see a lot of interaction on this point and I am not, you know, saying, I think because of the absence of the activity in the area, that is why it is. But I am just curious whether or not there was a discussion about the prioritization. You know, if I was working in schizophrenia I would say cognitive impairments might be a priority for a research effort.

But in this area, given what limited information we have available, is there any particular target, symptom domain? Is it quality of life? Is it a particular thing that we need to be thinking about prioritizing as we develop our strategy for research moving forward? I am just wondering

if that came up in the conversation.

DR. COOK: Why is everybody looking at me?

(Laughter.)

DR. COOK: Oh, I did push the button. I'm sorry.

So, it is interesting what you say. And in many ways I shouldn't be the one speaking up because targets -- I think if you looked around the room, everybody would have a favorite target. I think it is an area that provides more opportunity in terms of development from pharmaceuticals because every area of disability, and I do want to reiterate if somebody enjoys flapping their hands, then that is cool and we shouldn't be treating that, but every area of distress or disability would be a good target.

So it almost frees up from the side of somebody sitting there. You know, and again, if you have got five things, one that will address overall cognition of

communication of reduction of distress, whether it is anxiety or other elements, if you have got all five of those and they all are going to be big hits, I am not sure why I wouldn't go after all five. If you had to make a choice, that would be pretty hard.

So you mentioned schizophrenia where there is not an emphasis on treatment of psychosis because we have pretty effective agents for that. So that is why you are focusing on what I would think of almost as a secondary but of course very important outcome.

DR. KING: I'm going to jump in as well. I think one of the other areas that I think can an impediment to drug development is finding the right outcome measures for the trials. And that was something that we discussed as a group, that there needs to be attention to how we identify and how we move forward with the right outcome measures. Outcome measures that would pass muster with

the FDA, in your case. Outcome measures that are valid for the field.

DR. RING: I think that is what we struggle with is on that pathway to registration. And ultimately, on the pathway to having drugs reimbursed. You know, is there an emergent consensus on what the outcomes would be and/or is on the of the priorities of this committee to begin assembling the conversation with pharmaceutical FDA insurance companies to make sure that we are all aligned and our efforts aren't wasted in any one of those pieces. Not wasted, but we have maximized the efforts that we are individually investing.

DR. INSEL: I just have a final comment on this. I think this is a great suggestion, one that we did not talk about. You heard from David Mandell the difference in the cultures between psychosocial treatment development and more pharmacological treatment development, the need to bring them together.

But Rob I think what you are suggesting is a great thing for us to communicate on to the IACC. That this may be the time to bring the different partners together for a discussion in just this area. It took us 25 years to do this for schizophrenia and to realize that we have been looking at only a part of the piece of the disorder and not the part that causes the most disability.

We don't want to make the same mistake here. And if Pharma is going to be now working in this area, we ought to be bring FDA and CSM and others to the table to decide what is the body of evidence that one would need and where should the focus be. And it may not be one. It may be three or four areas that we could begin to lay out and then figure out what the right metrics are.

So, it sounds like an agenda for a meeting that could happen this year.

DR. HANN: I believe the person

over here was next. Yes, you.

MS. SCHAAF: Me? Thank you. Roseann Schaaf from Philadelphia. I am an occupational therapist and a researcher in autism. I want to thank the panel for your work and your hard efforts in this area, which is a big area of need. And I am so pleased to hear terms like occupational therapy being mentioned, sensory integration, quality of life, functional outcomes, randomized clinical trials of these, of occupational therapy. So thank you for that.

And I want to just underscore the other theme that has been coming up about the need for training and mentoring of beginning researchers, especially occupational therapists.

I will just tell you a little story. About six or seven years ago, an occupational therapist got an R21 from NICHD to look at effectiveness of occupational therapy. Of course, it was only a two-year

project and of course we couldn't look at it. But from that funding came a national group of occupational therapy researchers who have been looking at ways to evaluate the effectiveness of occupational therapy, using a sensory integrative approach, now with kids with autism. And from that work, we have developed a fidelity to treatment measure, a quality of life measure, we have a way to measure functional outcomes in children. And these are all things that occupational therapists are concerned about.

And so I want to just let you know that there is an eager of cohort of therapists and emerging researchers who want to do this work. Autism speaks has funded a study. I want to thank them for that. We are working with Yvette's team at Tom's River, at children's specialized hospital, to do a randomized clinical control of occupational therapy using a sensory integrative approach. But it is just the beginning. And one of the

reasons that we are where we are now is because of the foundational work of this group and also because of the mentorship that I received from other researchers outside of occupational therapy who are doing clinical trials, who have helped me along the way to understand the rigor that is needed and the vastness of this type of research.

And another model that really helped me is the ARIS training workshops that are down at the University of Virginia, where they bring a cohort of funded, seasoned researchers together to mentor young investigators to help get their research funded. And there weren't a lot of clinical trial investigators there. There was a lot of basic mechanisms. And that was one thing that I thought was missing. And there was nobody with expertise in autism.

So when I got my grant reviews back, that was one of my big feedback is you need somebody with expertise on autism to

guide you in phenotypic assessment and things of that nature. And they were right.

So I think maybe something like along that model would be helpful to get this research jump started. So, thank you.

PARTICIPANT: Hi. My first statement is my son was also considered to develop PANDAS two years ago. And they found that by the doctor took a strep throat culture. It came back negative. The blood test came back positive for strep throat. And there were changes in his behaviors and he had this really weird Parkinson-type tic going on. And my doctor was smart enough, my pediatrician, to do the right test.

But I was amazed how many parents that I know with autistic kids had never head of PANDAS disease. And when I went online, it is an autoimmune disease, which makes you wonder how many children on the autism spectrum who have behaviors that are basically caused because they actually have PANDAS and

it is not diagnosed. And you wonder if there is a whole group of children who could be helped having the right diagnosis but he doctors don't know to do the test to see if they have strep. Because you know, one test comes back negative and then blood test comes back positive. That is big.

The other thing is, I think the school system impedes getting right services for children. They don't want to do anything that is out of the protocol. Three years ago, I was lucky enough to take our son to Soma, the lady who does the rapid prompt method who came to the United States because of Cure Autism Now. And it blew my mind away because I was lucky enough to watch, not by watching a show on TV like 20/20 a couple of weeks ago, but watching children who if you saw them walking down the street, you would say extremely autistic, low functioning kids, having a conversation with themselves by a letter board. And it was like, wow! There

are people there. They want to be able to communicate and they can't communicate because the school system is saying the only choice you have is a text symbol.

A lot of autistic kids cannot do text symbols. My son hates text symbols. He doesn't get text symbols but he understands the written word.

So, I go back to the school system and I say, I really would like to be able to have him work on a keyboard. I want to develop him being able to communicate using -- no. There has been no studies about it so we are not going to do it in the school system. So how are we supposed to progress with what kids can get and learn and do when all they are doing is ABA. But they are doing ABA and I say but I don't like strict ABA because all your teaching my son to do is the word no. And then you are teaching him how to do the wrong answer, instead of doing errorless discrete trials, which is teaching him the

right word. So why go and teach the wrong one and then you have to undue what he just got wrong.

So the only thing you teach with strict ABA is the word no. But you know, the school system doesn't want to do anything different than what they have been told they can do.

So and I absolutely believe that the future for children who, I won't say nonverbal. I will say they do not communicate with words. Because I understand my son very well but he can't tell me in words what he would like to be able to tell me. But I know as a 15 year old, when he is frustrated with me and he grabs my hand, and he is like this and I know he would really love to curse me out because he doesn't really have a way to communicate using a keyboard at this time. We are working at home but we don't have the support from the school system. So if not everybody has worked on it -- they are working

with my son more during the day than I am working with him. So, it impedes his ability to go forward.

So, I really hope that maybe some research can be done on kids learning at a younger age, kids who do not speak, how to communicate using a keyboard because I have seen it work for him and it is amazing. Because they just want to be able to talk and they don't really have a way. So thank you.

MS. DURBIN-WESTBY: Hi. This is Paula. I would like to address that. There has been research done by Joanne Cafiero using it was a picture exchange system but instead of whatever number of cells there usually are, I am not that familiar with it, say there are 25, they expanded it and made it twice as big or three times as big. And they did not expect that the children being studied would use that at all and they found that once they had access to that many different concepts and pictures, that they were even doing things

like taking two of the pictures and putting them together to come up with a concept that they wanted to explain. And Joanne Cafiero says the minute somebody gets a diagnosis, they should get some form of communication system. Of course, you don't know which one is going to work for which person, but it should start being addressed right away, not five years later when they haven't developed speaking language.

PARTICIPANT: Thank you. This is going to be real quick. My daughter is four and she is really a happy and healthy girl. I just wanted to add something real quick about the medical stuff.

One of my big problems and worries about her is she can't tell me when she doesn't feel well. I mean, she can sort of. She had eight ear infections in her life and at the end, she finally started to learn to say "ear." But I get worried because she can't express to me if her stomach doesn't

feel well, if her head hurts. And she has an extremely high threshold for pain, too. When she runs and plays, she can slam into the ground and get up and keep going and not cry.

So my ex-pediatrician now used to give me a hard time when I would call. I would think she would have an ear infection and they would say well, is she complaining about her ear and I would have to say no, she has PDD. She can't tell me. And they would cut me off. Is she warm? No but in her seven ear infections before this, she never got warm. And I felt like I had to appear before a judge before they let me bring my kid in.

And so I think that that is such an important thing. In the day-to-day life of parents like me who, you know, you don't know what is wrong with your kid. You don't know what they might be fighting off or if they don't feel well if you can't just say does your throat hurt or she can't tell me. And I think this is such a basic day-to-day thing

that a lot of parents like me go through. Just not only having to deal with your pediatrician in terms of telling you, oh, your kid doesn't have autism, when clearly she does, but just in terms of getting the good day-to-day, month-to-month healthcare that she will need from now until she is an adult.

So, that is all. Thank you.

DR. COOK: I would like to add something. Is that okay?

I just wanted to add that I very much agree with you and also make the comment that if a child presents to me, which often would be thinking about behavioral medication, my first statement is check the ears, if there is any behavior change, and definitely check other parts of the body.

And you said until she is an adult. And I must say I have to add one of my concerns now that I have followed patients who are older than I am now, I worry quite a bit about how we are going to recognize symptoms

of angina and prevent a whole host of medical complications.

MS. BOGIN: I am Jennifer Bogin. I am here from the Association of University Centers on Disabilities and a self-proclaimed IACC groupie, and also the older sister of an adult with developmental disabilities.

And my concern here is about the training. I want to echo some of what Peter was saying and I'm sorry, I don't know your name, but the occupational therapist was saying. You can have the best translational research. You can have the best treatments and interventions out there. And if you don't have someone to provide that service, it is just even more frustrating for the families.

As a behavior analyst, I get calls constantly, constantly, constantly, and emails, you know, can you come; and can you do this program; and can you look? I feel like we need to be doing more research into training professionals and interdisciplinary

professionals in how to provide these treatments.

I think it is great that we are starting to have the National Standards Report coming out and we are starting to have more and more research into evidence-based practices but no one is researching how to teach them to professionals.

In terms of the diversity issue, when we are talking about recruiting a diverse workforce, that is essential because who spends the most time with these children are their paraprofessionals or their one-to-one individual assistants. And we need to be recruiting from the communities that these children are in and we need to come up with evidence-based ways to train all of these professionals from all of these different places.

So I would really encourage. And I don't know, some of this might be more in the Panel 5 discussion, because I know that

sort of sticks between the two of them, but I really, really want the committee to encourage that and keeping that strongly in mind.

DR. SAMSTAD: Yes, that is a great point and I am wondering if there may be some things that the IACC can do to encourage residency programs to include discussions of autistic patients and include rotations and so forth.

MS. DAR: Marian Dar and I am a family member. My understanding is that we are here to update what is out there. And I wanted to suggest that we revisit some protocols and perspective.

The vaccine issue has been talked about over and over again and the causality issue. But what if it is really a real precipitant? And that is something, of course, that is so difficult to work with. But you know in Africa when they inoculate there, they pair the vaccinations with Vitamin A and they have been doing that for some time.

So, I am wondering if maybe there might be a better way and a different way to run the vaccine program that we have here.

Which leads me to my next perspective. We think of malnutrition and we think of a very severely ill person. We think of Africa. But let us also consider that there may be people here in the states that are very sub-clinically malnourished. And we each have different thresholds. And this can be totally asymptomatic. At the same time, there is a very real and subtle inflammation inside that over time is very harmful. And is this something that we can test as particularly harmful to developing children, different ages, different impact?

We talked about Dan and the types of medications or treatments that they use. Two that I know personally that have had intermittent benefit are something called DMG, dimethylglycine and methylcobalamin. They are both B vitamins. And there is a benefit from

taking these vitamins. Why is this B vitamin a problem? Is there a malabsorption? Is there a GI thing that is going on?

And another speaker talked about the focus on the brain. Well, this may be a chicken or egg phenomenon. Maybe there is something there that is upsetting the brain.

My final comment is we have talked about -- and back to perspectives. The brain is like, an autistic brain is a metronome that is gone awry and if we can get that synchrony back -- there is often comorbidity with depression. And deep brain stimulation has been very effective with depression. And maybe this is one way to possibly approach autism. They have done interesting work with software and with auditory discrimination. And so not just pharmacology but also radiology and also technology. There are many different avenues that we can look at.

Thank you.

MR. BELL: Good morning. Peter

Bell and I am going to use my "Dad" title this morning.

I think sometimes we, as a community, and particularly the parents, are looking for ways to treat our child's autism. And sometimes I think we have to take a step back and think about treating the issues, the symptoms, the comorbid medical issues that come up. And I think it is certainly from a clinical standpoint, important for physicians to also look at our children or adults that have autism in the same way and that sometimes we have to actually look at treating the biology and not just the symptoms.

And so I just want to share a brief story with you about my own son. Two and a half years ago, he developed catatonia. And for all that my wife and I know about autism, we didn't know anything about catatonia. And thanks to Sarah Spence here. She was the one that first suggested it. And we realized that about 15 to 20 percent of

adolescents that have autism develop catatonia.

And if you go to the medical literature, they tell you to treat it with lorazepam and ETC. And ETC is electric shock, basically. That wasn't a good solution in our mind. So we tried to look at the underlying biology and we were able to do a number of tests, including an MRI, a SPECT scan and a spinal tap. And the results of the spinal tap revealed that he had very low levels of folinic acid, as well as extremely low levels of the metabolites for both dopamine and serotonin. And fortunately, there are medications that can address both of those issues.

And so two and a half years ago, we had a child who looked like he was an 80 year old man with Parkinson's. He could not even walk up a set of stairs. And today I have a 16 year old son that has autism who I can run a 5K with and is going to homecoming

dances with his classmates.

So I share this story because I think it is important for us to look at the biology. It is important for us to look at personalized medicine. It is important for us to not just automatically go to what the literature says to do and that we have to push ourselves to really understand what is going on with our loved ones that have autism and not be so consumed with maybe trying to treat the autism but to focus on what can we do to improve the quality of life.

And I am thrilled to have my son with autism back today. Thanks.

MR. JOHNSON: I guess sort of just to summarize things, I think make sure we integrate as many possibilities as we can. Like see what works. Like you guys are really touching upon the idea of like making things an individually based treatment system. That is really, really good because we are truly like snowflakes. Really, like not one of us

is truly alike.

And so the other suggestion that could work is just sort of to foster the ways of communication, should we ever find appropriate ones for a given individuals. And then from there, see what skills we can find out from those communications. Like who knows, there could be untapped creative or scientific possibilities from the people who tried to find what the official term "pause" suggested for nonverbal was, but those people. See what kind of skills they have to bring to the table, once we get proper communication.

And then along that sort of ideology, I must respectfully disagree with the term of autism is like a metronome that had gone offbeat. Just one, as a musician, and just two, it is just --

(Laughter.)

MR. JOHNSON: And just as somebody with Asperger's in general, it is just that is kind of an unfair or not really a right

comparison because it is saying that all autism is essentially bad. And just for me it is not, at least. There are certainly a lot of differences and uphill battles I sometimes have to face but those uphill battles are really ultimately have proven to be worthwhile, for me at least.

It is just that they have brought me here. And so I have got to speak before you guys today and just sort of tell you about those in general. And so I guess that sort of summarizes my endpoints. Thank you.

MR. MOODY: Jim Moody with SafeMinds. First I have a question for Dr. Hann and her staff. Is NIH currently funding a trial of the GFCF diet or of hyperbaric oxygen? Or what of the items on, I guess it is page 21 in the plan, to identify three randomized trials of the comorbidities by 2010. Have those been identified or funded?

DR. HANN: I would have to go back and look at the analysis that has been done,

Jim. I don't have it directly at my fingertips.

MR. MOODY: Okay, good. Because at least on the first question, I am not remembering any. I know there was a small trial of the GFCF diet done a while ago. And I know there are some privately funded hyperbaric oxygen trials.

But what I would like to point to is an opportunity for IACC to think out of the box a bit on some process reengineering.

ARI maintains a list of I think some 30 different interventions that have been tried over the years. I know it is a little anecdotal but they are ranked according to parent feedback of what works and what doesn't work. And some have sort of fallen down toward the bottom of the list because they haven't been found to be particularly effective. And I guess you would call it sort of citizens' clinical trials but it probably wouldn't rise to level of evidence-based.

But because there appears to be a relatively narrow window at least of brain plasticity for some of the younger children, that the opportunity to bring onboard treatments that focus particularly on the biomedical issues, may be a relatively small window. And it may reopen at different times in life, as far as what we are learning about brain plasticity.

But in terms of the IACC core goal of urgency, I think there is a tremendous opportunity to think out of the box and do some process reengineering. And whether it involves closer collaboration with the DAN doctors and ATN doctors or it involves more aggressive identification, quicker identification of some of the work that is actually going on out there in the community and bringing to it the tools of evidence-based medicine or of the single baseline multiple outcome trial-type design, but to move with a greater sense of urgency to validate these

treatments because I have a sense, at least from the DAN conferences, that the parents who have some financial resources are able to take advantage of some of these treatments. But does 80 percent, 75 percent that would like to try some of these things, would like to try these treatments but just because of either insurance issues or translational issues or whatever, have not been able to access those.

And with respect to the comment I have heard a couple of years that it takes 11 years to 20 years to get information out in the field, given the relatively short window some of these kids have, frankly, that is just too long and IACC needs to be challenged to think out of the box to do sufficient process, reengineering, to move more quickly to validate and move some of these treatments from a bench to the field.

Thank you.

MS. BLACKWELL: I just wanted to respond to Peter's comments because I think

that this issue actually came up in our group and it does pertain to the work of this panel.

We talked a little bit about the difference between intervention and services, Peter. And I think, although we had a lot of discussion about it, one approach we took was that interventions are ways that can address a person's condition and improve it. And services and supports are a way to help a person live with the condition.

So I think you will see that but I think that was sort of the line between Panel 5 and are we Panel 6 now? We are Panel 5 and 6. You are Panel 4. So, that is how we decided to deal with the interventions and services.

DR. SPENCE: I just wanted to bring up Jim's point again, and I think a few other people have made it along the way, the idea of testing the commonly used therapies and kind of validating. And as somebody who has actually tried to do that a couple of

times, there is a barrier to that. And that is, the lack of preliminary data that is considered really viable data.

You know, Jim raised the point and I think it is a good one. The ARI has this lovely list but secretin was on that list for a long time. And I think it is important to kind of get out there that there were 13 negative studies on secretin. And I was one of them actually that was never published because I was part of the drug company sponsored one that, you know, they really believed it. They kept believing it and they sponsored a trial and their trial was negative and they actually didn't publish the results. It was a press release, not a paper. I think that, you know, when I went to our human subjects protections committee with this trial, they said, you know, this is an injection. This is more than minimal risk. How are you justifying the use of this medicine without any preliminary data? And my

point was well, people are going to their doctors' offices and doing it all the time and actually I feel like we have a very large ethical duty to be testing this so that parents can actually understand is this a good thing to do or is this not a good thing to do.

And so while I am a little surprised that there hasn't been the controversy tag put on this particular piece the way that there was the controversy tag put on the vaccine discussion, I think that there is controversy about testing commonly used but unproven therapies and I think that we probably need to have more discussion about how are people going to be able to -- which ones do we look at?

We talked about the diet. We talked about one woman raised the methyl-B12. You know, as a practitioner we certainly see lots and lots and lots of therapies getting used. And I think this may need, IACC may need to have a little more discussion on this.

DR. INSEL: This did come up in the meetings that we had last year. And one of the things that we heard was the fact that most of the secretin trials, use that as an example, secretin worked. It just didn't work as well as placebo.

(Laughter.)

DR. INSEL: And that is what -- no. I'm serious. That in terms, there is a fairly large effect size and it reminds us that the importance of doing RCTs. So when you look at the original document, we felt pretty strongly that the agenda going forward needed to look with placebo controlled trials because so many people do have that experience that something works. And they believe that or that their child gets better. They believe, therefore, that the drug must be helpful.

Sarah, I think in response to your question, where we struggled with this a little bit as a panel, the question comes up

how much time and resource do you put in to treatments that you actually don't think are that helpful but you feel that it is important to provide the public with data that demonstrates either value or lack thereof versus time and resource that you put in to developing something that you think really does have promise.

And I don't think we have come to a decision point there. I don't know what that balance ought to be. And we have talked about it a little bit. I think it is something that a number of research teams think about.

And I am not sure that the IACC can do more than say this is a dilemma that the field needs to think about because we need both. And yet limited workforce, limited patient base, limited resources, it may be that you have to make a choice.

DR. COOK: I have a follow-up. Because Sarah mentioned actually ethical

concerns about studying something without strong preliminary data, I have another issue that I want to raise, given the workforce issues, which is that I think that works two ways.

If you so strongly feel something works that you organize conferences around something, you make almost every parent feel like they should feel guilty if they don't try it, then I think then there is an obligation to become part of that workforce to develop those skills. I do think we need to support the mentorship of the people that want to test things that they are convinced are helpful.

But you have a limited workforce. We need to increase the workforce in general. And frankly, the workforce needs to include those who are so convinced something works that they are saying it works so strongly. And I think that is probably the workforce opportunity.

DR. HANN: All right. We are

reaching a five minute mark for this discussion. Are there any other further public comments?

Okay, from the list that I had prior to this, there was a list of four people on the panel who had questions who wanted to bring them to people's attention. Cathy Rice, Cathy Pratt, Lee, and Geri. Cathy Rice?

DR. RICE: All right. This will be brief because I think we went into the discussion a little bit earlier. We were talking about the importance of dissemination and translation. And I think this discussion we started having was talking about inputs and how do we prioritize what is important, given limited resources.

So my original question was just whether it was worth having an explicit goal that solicited feedback from the community from those individuals who are affected with autism directly from family members from a range of practitioners that help us get a

pulse on what is being used, what do they think works and why. You know, what are their needs and what are they trying to address in terms of that basic sort of process issue.

But then on the second side, in terms of how do we prioritize what may be of all the different symptoms we have and we are going after, what may be some novel ways of approaching intervention? We have heard here excellent ideas from individuals who have dealt with some of their own issues by using technology and have a lot to offer us but we don't have an explicit goal that helps us solicit that information and integrate it into our treatment research. So that was just my comment of maybe we need to be very explicit about how to solicit that.

DR. INSEL: Very quickly, that is a great idea, Cathy. IAN has done some of that. You heard ARI already has a wonderful site that pulls a bunch of those anecdotes together. We are developing a bridge between

IAN and NDAR. So hopefully, this will become even a broader framework.

DR. PRATT: The comment that I wanted to make was kind of in relation to Nancy and Lyn's comments. And I apologize for speaking for family members, since I am not one.

I think that what we hear repeatedly from families is that services are so siloed, that everything is so siloed. So you go to a gastrointestinal doctor and they look at the gut. You go to an allergist and they look at allergies. You go to somebody who is focused on neurology and they look at the neurology of autism. And oftentimes when parents who have children who have challenges, whether they are behavioral or health, the discussion is always well, your child is behaving and acting that way because they have autism. It becomes the circular discussion of, they have autism because they act that way and they act that way because they have

autism.

And I think the challenge for all of us, and we will be going into a lot of the implementation pieces, is that individuals on the spectrum are whole beings. And we have to realize that autism is a whole body condition. And you know, fortunately, I was very blessed to have been a classroom teacher. And many of my students went to Ed Cook and Cathy Lord who didn't look at the surface symptoms, but they looked and dug for the underlying conditions.

And I think that is what we need, is for people who will dig and not look at the obvious but to look beyond their specialty and to look at autism as this whole body condition.

MS. WISEMAN: Thank you, Cathy, for being so eloquent. I could not have said it better.

MR. GROSSMAN: Well, I'm going to defer to Geri, since she has been waiting so patiently and has had her hand up much longer

than I did.

DR. DAWSON: All right. I will be very quick. Just two quick comments. One, with regard to this whole issue of what do we do about investing and complementary and alternative treatment approaches. And I completely understand the challenge of do you invest in something that is high risk and potentially is not going to have an impact but on the other hand, you know, who knows. And we need to be listening to parents and people are telling us that this is useful.

So our solution to that problem at Autism Speaks is to make sure to invest in some pilot studies around these areas that are innovative and could potentially lead to new directions. So not to ignore them but to invest and to look at them in a pilot way. To invest a small amount of money to these more novel ideas. And then if they pan out, one can consider investing more.

But the larger point I wanted to

make has to do with the comparative effectiveness trials because I do think this is going to be a very important issue. It is going to be part of healthcare reform. They are going to be making decisions about what insurance is going to pay for, depending on what treatment is most effective.

One of the, I think, challenges in autism is the fact that there is such heterogeneity and that what we are going to find is that for any one treatment there is going to be a variability and response. And so Francis Collins brought this up as kind of a risk of comparative effectiveness research, that we can lose the individual when we start looking at these group designs where we compare, you know, how does a group respond to this treatment versus that.

So what I wanted to do is to remind folks that comparative effectiveness research can take many different forms. So for example, if you do a study where you look

at whether say a biological signature or a genetic marker or some other aspects that captures individual difference, whether people with that characteristic respond to a treatment better than people without that characteristic. That is a comparative effectiveness research design.

Similarly, I think that we might want to look at question that more have to do with mode or model of delivery. So one of the challenges that we have in hospitals and I certainly faced this when I oversaw the autism clinic at the University of Washington, is that we are not reimbursed for interdisciplinary teamwork. So you can pay for each of the individual practitioners but when you want to work together as a team to come up with an integrated program, none of that is paid for.

And so one example of a comparative effectiveness trial would be to look at the advantages for quality of life and

treatment planning, when you actually budget for that teamwork, versus when you work as individuals with no coordination.

So we really need to think creatively about these comparative effectiveness trials and to really step up to the plate now and make sure that we utilize that kind of research to have better outcomes for people with autism.

MR. GROSSMAN: Well, I am finally getting around to my second question that I was going to ask a couple of hours ago but it has really been beaten up quite a bit over the last period. It was a question that I was going to pose to Panel 4 regarding personalized medicine.

But in the discussion that we have had regarding these comorbid features and their treatment or lack thereof, we have pretty much covered it. But I want to put a different spin on it, since I do believe it is within the purview of the IACC to look at

public policy issues.

Unfortunately, we have had too much of an emphasis on the research aspects of it but in our duty and as we are authorized to make recommendations to the Secretary, I think that because of the urgency of the matter and of the chronic nature of this condition, that it is within the purview of the IACC to come forward in much stronger stance on this idea of treating this as a chronic medical condition. HRSA and others have come out to say that it is, indeed, a chronic medical condition and that we look at these comorbid factors and not look at it as Peter so eloquently stated, as the autism.

What we are finding and in deference to Yvette and all the other well qualified clinicians and researchers sitting around the table, the sad reality in the United States and I will say globally, is the fact that most individuals with autism are not being treated for their medical conditions.

We, in our office, receive, usually on a monthly basis, information of a child with autism that has died from untreated medical condition. And these are sad realities that are happening worldwide. And my question was going to be to the panel and has been answered, I was going to see if they had in their discussion on interventions, looked at ways that the medical community can be updated. And looking at this and analyzing it not by the autism but evaluating a patient when they come into the office for these obvious medical problems that they are having, and treat them based on that.

I think that the dialogue that we have had is very robust. And what it has shown me is that this issue of intervention is critical and it goes across all five of the panels that we are discussing today and fits so nicely into what is coming up next on Panel 5. You know, intervention medically is only one aspect. Where we see the greatest benefit

after that is through services and supports.

And but all three of those are so interconnected and interdisciplinary and needed to be addressed and none can be addressed in a vacuum.

But I would implore the IACC, going back, to my first statement, that we do look at this and we do address it for its public policy implications and move forcefully with a recommendation to the secretary that these issues be addressed.

DR. HANN: Okay. So with that, I will close this morning's session. We will go to lunch and we will be back at 12:30 to hear from Panel 5. Thank you.

(Whereupon, at 11:12 a.m., a lunch recess was taken.)

AFTERNOON SESSION

(12:37 p.m.)

DR. HANN: Okay. Well I see Panel 5 is now completely assembled. I will turn it over to you, Ellen, to do some introductions of the panel and to proceed through your panel's thoughts.

MS. BLACKWELL: Hi. Good afternoon. I am Ellen Blackwell, Centers for Medicare and Medicaid Services, also the parent of a 22 year old adult with autism. I facilitated Panel 5, along with my fellow IACC member, Christine McKee. And I just wanted to make a couple of clarifications and comments before the panel introduces themselves.

We are Panel 5 but in truth, we are really Panels 5 and 6 because we addressed two of the six questions in the strategic plan. So I think that this panel in particular deserves great accolades for the wonderful work and definitely the pressing sense of urgency that came not only with these

issues but in our discussions.

Second, we took a little bit different approach than some of the other panels. We felt that it was necessary to focus some of the present objectives in the plan a little bit more. So you will see that in our slides. And then we defined new objectives that we are proposing.

So I am going to let the panel introduce themselves.

MS. McKEE: I am Christine McKee. I am the mother of a nine year old girl with autism and I am a public member of the IACC.

MS. GIBBONS: My name is Ann Gibbons. I run the local office of Autism Speaks and I am serving on the panel in my role as mother of a 21 year old son with autism.

DR. SOLOMON: Hi. I'm Marjorie Solomon. I am an assistant professor at the UC Davis at the M.I.N.D. Institute and I am serving on the panel as a representative of

the families who participate in my intervention program.

DR. MANDELL: My name is David Mandell. I am at the University of Pennsylvania School of Medicine and the Center for Autism Research at the Children's Hospital Philadelphia.

DR. PRATT: My name is Cathy Pratt. I direct the Indiana Resource Center for Autism and I am Chair of the Board for the National Autism Society of America.

DR. GERHARDT: I am Peter Gerhardt. I am president of the Organization for Autism Research.

MR. CHAPMAN: Good afternoon. My name is Tec Chapman. I am the Deputy Director for the Division of Developmental Disabilities in the State of Missouri.

MS. BLACKWELL: And Tec is going to be presenting our first question, which is where can I turn for services.

MR. CHAPMAN: We have kind of done

our introductions and I am going to kind of talk you through a little bit and I appreciate the work of the panel. I think you have heard throughout the day yesterday and today just about the work that each group has done and how much I think we have all learned. And I have got to tell you with the panel, some of the people, the networking and the opportunity that has come through this today and yesterday I think has been pretty strong and remarkable.

But in our work and our discussions through the conference calls, obviously we reviewed the materials that all of you have in those big binders and that we had gone through that. But we also took a look at some other material that was outside those materials in the binders. Specifically, we looked at needs survey that was one in 2009 in Indiana that was conducted, as well as the document in the strategic plan that talked about the need that families and individuals along the spectrum had had for finding valid

and reliable information about how to navigate the adult service delivery system.

And so we specifically looked at what we have developed in Missouri, along with several family advocacy organizations and individuals with ASD. So, we have looked at a pretty broad amount of information.

When we look at where we can turn for services, some of the key things that came up which are not uncommon to what we have heard over the last couple of days is this lag between development of efficacious interventions and services and supports from research to community settings. And that was really a disconnect sometimes for folks and people were saying well the research has shown. But some of the things that we struggled with that we talked about earlier this morning were the issues around workforce development, which I will talk about here shortly.

The second piece was increased

emphasis on quality of life and across the Autism Spectrum Disorders, across that spectrum and also making sure that we are looking at that across the life span for individuals.

The fourth point was really around systems collaboration and new models of service coordination, as well as the principles of self-determination and self-direction were some of the key findings that we had.

We modified, as I think the term I am going to try to use is our aspirational goal. And you may be able to see here on the slides that you have in front of you. The tings that we are bolded are the things that we have added in to this process.

And our aspirational goal has been modified to say communities will access and implement necessary high quality evidence-based services and supports that maximize quality of life and health across the life

span for all people with ASD.

The next several slides talk about some of our research opportunities. Obviously this is the state of the state and its implementation at this point. We also then modified the research opportunities to talk about the development and affective dissemination of evidence-based community practices for people with ASD across the spectrum and the life span. We did talk a little bit this morning. I think there is a panel looking at this issue of dissemination that needs to get out there.

We also talked about comparative effectiveness studies of interventions. And again, you will notice that we talked about across the spectrum, as well as the life span.

The next one was looking at studies that characterize current ASD diagnostic and service utilization, patterns and community settings and examining the relationship between the likelihood of

diagnosis and services availability for ASD and evaluate services and intervention outcomes across the spectrum. Again, making sure that we are looking at adults and what their needs are as well as transitioning its youth and younger children.

We have several new proposals that we have put in here that we would like for people to discuss and consider. And first is looking at a comprehensive descriptions of creative and innovative community-based services and supports and stimulate systems change, generate ideas, and inspire the next generation of service innovations across the spectrum.

Second is the development and evaluation of effectiveness of a coordinated, integrated, and comprehensive community based services and supports; a delivery system that is designed to enhance access to services, self-determination, economic self-sufficiency, and quality of life for people with ASD across

the spectrum and life span and their families.

I think one of the things maybe to expand upon that one a little bit is talking about better integration and coordination not only at the federal level but equally maybe more importantly at the state and the local level around service delivery. And specifically, thinking about elementary and secondary education, state DD systems. You also can look at vocational rehabilitation, housing, etcetera, and how we have better integration, and coordination, and collaboration across those entities, so that families and individuals aren't feeling fragmented and for the lack of a better term, dissected in their lives.

The third is about support. A demonstration project to evaluate the effectiveness and outcomes of models for single case management across service delivery systems.

Fourth, to conduct a study to

examine who self-directed services and supports impact children, youth, and adults with ASD across the spectrum.

And fifth, is the researchers. People with autism across the spectrum and the practitioners who work with them to partner in developing and testing innovations, services, and supports, and using community-based participatory research models in that process.

And I think we have heard very eloquently, you know, not only today but in other venues, I mean Paul and Chase specifically talking about the importance that individuals across the spectrum being included in the design and implementation not only of research but also of service delivery systems and that clearly we have to make sure that they are responsive to those needs and that they are incorporated.

I think sometimes, as somebody as a state DD system, involved in that, that sometimes it is the research and then getting

that involved and implemented at the state and local levels sometimes is difficult because of the environment in which a lot of the research is conducted and not always being demonstrated and field based.

We had the short-term objective summary which are going to obviously mirror the research opportunities. You have the state of the states. We also have the supporting studies that assist the variations and access to services. And specifically looking at underserved populations and our fellow panelists may extend comment here a little bit later on this, but I think specifically we are looking at obviously people fully across the spectrum but also looking at the issues that individuals who live in urban and rural areas and the differences, and the subtle needs that may be different there for folks. And we need to make sure that the research is addressing those types of activities in rural and urban

settings.

New proposed short-term objectives. We talked about supporting promising practice briefs that describe innovation and successful services and supports being implemented in communities that benefit the full spectrum of people with ASD. There is numerous examples already that are done at the federal level around promising practices. And sometimes it is getting out thing that we are finding that have been shown to be effective and some local areas or state and regional. But how do we get that information out so other people are knowledgeable and they can replicate that in their local community or in their state.

Support a demonstration project to evaluate the effectiveness and outcomes of models for single case management across the service delivery systems; conduct a study to examine how self-directed services and supports impact children and youth, and adults

with ASD.

The fourth is looking specifically at initiating demonstration projects that evaluate models of policy and practice level coordination. Again, this issue here is looking at how do we have better integration, coordination, and collaboration, around the service delivery system from K-12 education to higher education, to state DD systems, to vocational rehabilitation, etcetera, that supports self-determination and economic self-sufficiency and quality of life for folks. But that is critical that we have an integrated and seamless service delivery system.

The other piece here on these long-term objectives, these next two, you will see again in bold where we have just added in some additional clarifying language on these objectives, specifically looking at not only services but also support for people again across the spectrum. And then testing methods

to improve dissemination, implementation, and sustainability of evidence-based interventions, services, and supports in diverse communities.

The next two bullets specifically get into looking at workforce development issues. The first one about developing and if necessary testing and service-training strategies to increase skill levels in service providers, including direct service workers, or support professionals, educational staff, and other public service workers.

And we talked about other public service workers. We are oftentimes looking at people who are first responders and other folks such as that. But it is critical that we have a, you all talked about it this morning, about this workforce from the very front line level folks who are doing the direct implementation all the way up to researchers. And I think one of the challenges that we continue to see is that

people are knowledgeable about effective practice but then also feel efficacious in their ability to provide and to deliver those types of supports and services. And ones that are consistent with what the individual in a family is seeking that is individualized and recognized as their needs across the spectrum.

The next bullet specifically goes into demonstrating projects that evaluates the effectiveness and outcomes of person-centered models of single case management on self-advocacy, self-determination, economic self-sufficiency, and quality of life for persons across the spectrum of ASD and their families.

That was my portion. And Peter is now going to take us into question six.

DR. GERHARDT: Before I start, I again just want to thank the rest of the panel for what was truly a collaborative and I think very productive endeavor and experience. I mean, everybody really sort of checked their egos at the door and, well, okay, it was me.

They didn't really have to worry about it but that was my problem.

But I really, I just want to thank everybody because it really, I think this is very worthwhile.

So, question six. What does the future hold? The key issues that we identified is, as we pursue a research agenda, it does need to include the full spectrum of adults with Autism Spectrum Disorder. I think if you look over the last ten years, we have increasingly sort of focused on this more competent, more able, more verbal component. And we really need to look at how do we best support individuals with more significant challenges, and more significant behavior challenges across the life span.

We need to focus on principles of self-direction and self-determination. Integrate programs for transitioning youth. Cathy said before we tend to have silos of services and information and how do we now

bring this into one collaborative hole in support of a person.

Focus on training. Where are we going to get new staff from? How do we train staff in evidence-based practices? One of the things that we do know about training is that didactic lecture-based training tends to result just in lecture-based responses. It doesn't give you actual hands-on behavioral responses. So how do we now address this issue?

Issues related to community integration. And what we saw is a potentially significant challenge. The use of medication with adults oftentimes for behavior suppression reasons, not for any real significant secondary psychiatric conditions or true behavioral reasons; issues related to access to adult services; and then lastly, sort of overarching concern if the individualized quality of care for individuals.

The aspirational goal for question six. All adults on the autism spectrum will have the opportunity to lead self-determined lives in the community of their choice through work, community participation, satisfying relationships, and access to necessary and individualized services and supports.

As Tec had said, our new language is in bold, to make it somewhat more inclusive. Longitudinal studies of adults across the spectrum with ASD in their families to track factors that account for improved quality of life outcomes across the spectrum, including medical issues, vocational, community, and life span issues. So we just sort of expanded our global, our reach in terms of where our research goals should go.

Our research opportunities also include studies of the scope and impact of the spectrum of ASD in adults, including diagnosis of Autism Spectrum Disorders in adulthood and needs during critical life transitions, and an

overall assessment of quality of life.

Use of existing administrative data bases for information relevant to diagnosis, cure, interventions, and long-term outcomes for adults on the ASD spectrum. Again, we are not coordinating our efforts. We are not looking into how do we best support people. What works? What doesn't work? What do we know that is out there that seems to be effective?

Our new proposed research opportunities. Longitudinal studies that follow carefully characterized cohorts, that is an important consideration, that we really want to look at who we are looking at of the broad spectrum of adults with Autism Spectrum Disorder and their families into adulthood, in order to better understand their needs during critical life transitions, and to identify and track risk and protective factors that account for improved quality of life and health outcomes.

So how do we look at this as a longitudinal study, in terms of what really worked. How did this get this point? What services were necessary? What interventions were necessary? And not just for the person, but for their family.

New proposed research opportunities continued. Support a series of promising practices briefs that describes innovative services, and supports being implemented in communities that benefit the spectrum of adults with Autism Spectrum Disorders, optimize the use of existing state and federal data to report information relevant to diagnosis, course, services, and intervention utilization, medical and pharmaceutical utilization, and other factors that describe long-term outcome with a spectrum of adults with ASD.

Support the evaluations of projects that increase coordination across state and local delivery systems, to improve

access to services and supports, particularly projects that focus on transitioning youth and adults on the ASD spectrum.

For those of you not necessarily familiar, there is that sort of cliff that happens at the end of your 21st year. And there is this very distinct lack of service coordination for individuals across the spectrum and their families. So how do we sort of address that issue in a way that is cost-effective and effective?

Report on and develop, if necessary, accessible, affordable, and integrated housing options for adults with autism spectrum disorders, that promote independence, choice, control, and privacy.

The database objectives subsumed a new long-term objective. Develop and have available to the research community means by which to merge or link databases that allow for tracking the involvement of people in ASD research by 2010. How do we get people who

are with adults to actually coordinate within the context of the research agendas.

Conduct a needs assessment to determine how to merge or link administrative and/or surveillance databases that allow for tracking the involvement of people with ASD in healthcare, education, and social services by 2009.

What? These our out.

MS. BLACKWELL: We had several objectives on data that were in chapter six that we weren't quite clear on. So what we did was we tossed three of them out. These are two of them and then I think there is one coming up. And then we wrote them as a new long-term objective that Peter is going to get to in a second.

DR. GERHARDT: Okay, but they are still here, though.

MS. BLACKWELL: Well, they are in the plan that people have in front of them now. But we are proposing that they go out.

DR. GERHARDT: So forget about that, what I just said. Is this one in?

MS. BLACKWELL: This one is out.

DR. GERHARDT: What? I say goodbye. Goodbye, Gracie.

Our short-term objectives. Launch studies to assess and calculate the variation the quality of life for adults on the autism spectrum, integrative employment, community inclusion, self-determination, relationships, and access to health services in community based services by 2011.

This is all in here, right?

MS. BLACKWELL: Yes. Oh, yes.

DR. GERHARDT: Just checking.

Our short-term objectives. Conduct comparative effectiveness research that includes a cost effectiveness component to examine interventions, services, and supports, to improve health outcomes, and quality of life for adults on the autism

spectrum over the age of 21 by 2012. Cost effectiveness issues related to adults are of critical importance when you look compared to educational systems. When you do get funded, you get funded at about 20 to 25 percent of the cost of education. So we need to actively consider cost effectiveness in terms of how do we support adults.

New proposed short-term objectives. Develop a method to identify adults across the ASD spectrum who may not be diagnosed or misdiagnosed. So looking at older individuals who may never have been diagnosed or may have different diagnoses and find out where they are and how do we best serve them. Conduct a study to measure and improve the quality of care being delivered in community settings to adults across the spectrum of ASD through provision of specialized training of direct care staff, including assessment and development of ASD-specific training, if necessary.

Initiate demonstration projects at the state and local level that evaluate models in which existing programs to assist people with disabilities, for example, Social Security Administration, Rehab Services Administration, are tailored to the needs of transitioning youth and adults with ASD.

And the long-term objectives. Develop individualized community-based interventions that improve quality of life for health outcomes for the spectrum of adult with ASD by 2015.

The following proposed long-term initiative encompasses the three short and long-term data objectives referenced earlier. That is what I referenced earlier. Develop and have available to the research community means by which to merge or link administrative databases that allow for tracking adults with ASD involved in various service systems.

For example, state developmental disability agencies, voc rehab, state

insurance commission, state offices of children and family services, state educational agencies, state mental health agencies, state early intervention agencies, Social Security Administration, local jurisdictions, state Medicaid agencies, state and local criminal justice systems, and other relevant entities.

Conduct a study that builds on carefully characterized cohorts of children and youth with ASD to determine how interventions, services, and supports delivered during childhood impact adult health and quality of life outcomes. Again, we are looking at this carefully characterized cohort because again, with the assumption that one size does not fit all. So we need to know what works for who at different times in their lives.

New proposed long-term objectives. Develop a community-centered intervention that improves understanding of the strengths

and challenges of the spectrum of adults with ASD and increases opportunities for full community inclusion, including an assessment of benefits to communities and adults with Autism Spectrum Disorder. So this is, in effect, changing the perceptions of Autism Spectrum Disorder.

Conduct a study to evaluate current practices leading to the use of psychopharmaceutical medications and their effectiveness in the treatment of comorbid conditions or specific behavioral issue with adults across the autism spectrum.

And implement a demonstration to test the effective services and supports resulting from comparative effectiveness research that include a cost-effectiveness component to improve health outcomes and quality of life for adults on the ASD spectrum over the age of 21.

Other comments from Panel 5. The panel recommends in the future convening

separate workgroups for questions five and six. The panel could have used additional discussion time; for example, more than six hours. The panel appreciates OARC's work coordinating telephone meetings, sending emails and providing materials and overall the process was a great experience.

Thank you very much.

MS. BLACKWELL: Thanks so much to Peter and Tec for presenting our work to the group. And I just have one further clarification that I am not sure we focused on a whole lot at the very beginning but the panel also made a suggestion. The title presently of chapter six is "What Does the Future Hold?" And we actually started out struggling with that immediately because we weren't sure what it meant. So we decided that we would propose a new title for chapter six. "What Does the Future Hold for Spectrum of Adults with Autism Spectrum Disorders?" Because we really felt like it was indeed the

IACC's intent to focus chapter six on adults. So that is kind of where we went with your revised objectives.

So would the panel like to discuss our work?

DR. PRATT: I will go ahead, first.

First of all, I have to tell you this is very exciting to be in a room of professionals that I know, have known for so many years. And I look around the room and such wonderful names and people who have such tremendous passion. And Tom Insel and to IACC, thank you for putting this together and for the transparency of this organization.

It is also heartwarming to see advocates sitting at the table with us having a voice and family members also adding to this process.

It seems like during the last day and a half we keep creeping into the area of implementation because I think that is always

an issue for always is this is great that we are doing this but how do we actually implement it.

And for those of us who are practitioners on this stage, we realize that much of our work is not about group studies or about finding individuals that we can do single subject research design with but it is really about looking at individuals and providing individualized supports and individualized systems, and individualized families, and individual preferences, and individual strengths.

So many of us are really about creating stories, which I think is incredibly important. We also can't think in terms of two year grants. But what we are really talking about is long-term capacity building and how we take what we know that we have learned in the field for many years. And I think one of the invitations that I would give to all of us is that while we work in the

field of autism, we shouldn't be autistic in our approach.

And by that I mean that there is a lot of research in other disciplines. For example, when we look at implementation research, looking at the work of George Sugai and Rob Horner and their implementation research around school-wide discipline, looking at the work of Dean Fixsen around change and also about scaling up, look into the dissemination sciences that come from other fields. Look into the severe disabilities field and, as Peter made the comment earlier, is that we seem to have a 20 year lag time.

I think the real issue that we have in terms of implementation is that we forget lessons that we have learned in other fields and lessons that we have learned earlier. And so we kind of go back to the same mistakes.

For example, we have learned in

the severe disabilities field, which included people with autism, that if you put them in segregated settings, they often times end up being employed in segregated work options.

And so not making those same mistakes but looking at our history and reliving that history is incredibly important. If we are talking about reading for children on the autism spectrum, look into the science of literacy and people who are engaged in literacy. If we are going to be talking about employment, some of the people that need to be sitting around this table now represent corporations. And folks who have done employment who have looked at that in terms of project search and other national initiatives.

There is not a transition process for autism. There is a transition process that has been very well researched and documented in the disability community. And so not relearning those lessons but going to those folks who understand that.

And I think that is going to be the real challenge for us is that we have to kind of extend our boundaries and look to other professions.

In terms of healthcare, we are really talking about healthcare reform that impacts not only the folks on the spectrum but my mom who is 86 and many people in the aging community. And how do we look at these common issues and come together around these common issues?

I think that and professional development, Jen, you brought up a question about professional development. We know, as Peter said, a lot about professional development. We know that if you lecture to people that a very small percentage of people walk away with knowledge. I think it is less than ten percent. And we also know from the professional development literature that coaching is really the best way to help people. And so how you build those systems in

states to really build that coaching network.

And Gail Houle, I have to applaud you and Education for funding the two grants that have really looked at statewide systems capacity building. And I think what we have come to understand from that is the complexity of these issues and how important it is to look at those systems in various states and how you build on those. And not only look at good practices because I think that we know a lot about what interventions work. I think the problems is that we oftentimes don't have that fidelity of implementation. How to make others in the field to have the ability to implement those interventions that we know are effective and then to measure outcomes that are really useful outcomes. And I think this grant does a nice job of looking at IEP goals as a way of measuring progress.

So I think that what is difficult, as I sit on this and having been doing this for a lot of years is that what we do is very

messy. It is not easy. It is not simple. It doesn't happen in a clinic. It doesn't happen in a lab. It happens in people's lives. And I think for all of us to think about that, it is a very overwhelming process.

But I am very honored to have been with this panel of folks who have a like-minded spirit about this and are really looking to improve the quality of life for all those on the autism spectrum.

DR. MANDELL: We have fun.

We disagreed about so little that I feel like I have to bring up the one thing that Ellen and I did disagree a little bit about was the definition of services.

And for me, the issues of services is more than those things that help people live in a community but don't necessarily address the core symptoms. For me, services are the delivery mechanism. To use an unfortunate example, they are the syringe. They are not the vaccine. But without it, you

are not getting into the person. Right?

So thinking about it that way, I think you could take many of our recommendations and the challenges we identified as falling into, addressing two questions. One was why don't community services deliver the interventions that the literature says work? How come when I am looking for stuff in the community that my experts that I am going to say I should get for my child or for myself, I can't find it. And the second is what I do I do when I have a need and there is no evidence about the best approach to address it?

And we know that there are many needs that aren't addressed in the literature but people are doing stuff in the community anyway to try and address those needs. And so our objectives and our gaps fell into those two camps.

And our answers, I think, also fell into two related camps. The first is

that there has been a really fundamental disconnect between intervention and services research. In intervention research that primarily takes place in university-based research settings and the services that primarily take place in the communities where people live.

And we need to bring them together. We need to understand, even as interventions are being developed, how it is that they would ultimately be implemented. And we also need to think very carefully about as we start to do that kind of research in the community, how we make sure that we don't do what a mentor of mine calls drive-by research. That we don't establish, we don't do studies in the community, develop a community that depends on those services, and then the grant funding ends and those services are no longer available.

And so from moment one, we have a responsibility as people who do that

intervention research to think about what the transition is going to be from the research study to the community practice. And that is a little bit of a change because normally we want to see if the intervention works first. But even in the absence of those data, we still need to be thinking about what we are going to do if it works. And so that is a slightly different model thinking about those kinds of studies.

And the second set of gaps and our responses to them fell into the category of the fact that science has to catch up with practice. And that is not just about treatment. It is not just about whether different diets work or different behavioral interventions work. It is about whether the systems that are delivering those interventions work.

So we have a giant 50 state 3,142 county natural experiment going on in the United States, as each local system and state

system struggles to think about how to address these needs. And there are real models of excellence out there. And there are some not so models of excellence. And we need to be taking advantage of that. And I think that that was evident in a number of our objectives that we identified those examples that we evaluate them in some rigorous way and that we quickly think about dissemination. And I will tell you, dissemination happens no faster than when one state official talks to another state official, as opposed to a researcher talking to a state official.

So those are our natural allies, as well, those of us in the research community, that we need to be taking advantage of.

MS. GIBBONS: First of all, I wanted to apologize to the drafters of the original strategic plan for ripping it up so much. But it is so much easier to do version 2.0. So we greatly appreciate what you gave

us to work with. And I think the clarification of question six, I believe, if I have understood it correctly mirrors what you all had in mind. But it also helps with the public comment, which we took very seriously. And we read all of the public comments.

And I think that it can boil down to me sounding like a little old lady saying what terrible food and what small portions, when it comes to services, because particularly families that are dealing with the system and particularly for big-hearted people like Tec who work in the system, it is very difficult to deliver services in a cost effective and efficacious manner.

It is also very difficulty to see how the Combating Autism Act is solely going to solve this problem. We understand that a lot of what has to happen in the improvement and delivery of services falls outside of the strategic plan and falls outside of what the Combating Autism Act has asked you all to do.

Nevertheless, we have tried to look at the materials and come up with ways that can best implement and use the research dollars that you do have at your discretion.

One thing that we took very seriously and again falling in line with it is easier to do version 2.0 than 1.0, is we did take issue with words that put us a little bit cold in our tracks. Those would be productive and a contributing member to society. I am glad to say that the only person that holds me to that standard is my boss because I think that that is not always a realistic standard. I think we look more in terms of satisfaction, quality of life, and happiness. And if that seems a little prosaic, I apologize but that was kind of the emphasis we took.

We did speak in terms of self-direction and that was fully cognizant of individuals that may not be able to speak for themselves. And I think Paula put it quite

well. If somebody finds happiness in flicking their fingers, we would respectfully suggest you think twice about extinguishing that behavior if you can't replace it with something that is meaningful to the individual, whether or not it is appropriate to society.

And lastly, I did want to way that a lot of what we are asking in our aspirational goal will require cultural changes that cannot be funded by research. And we are so pleased to be able to participate and talk to all of you. I really do believe that all of you in this room are dedicated to alleviating human misery. Whether or not we can do that today by the end of the day is not entirely clear but I am very happy to be able to work with such a group of people.

DR. SOLOMON: Well first I wanted to thank the IACC for giving us all an opportunity to serve in this role.

Second, I want to say that it was a wonderful experience to work with this great group of people and actually very gratifying to sit and listen to two days of talks that led to a lot of the same themes. In a way, I felt like we were batting cleanup for the symposium. And it was very gratifying to see a lot of the themes coming up again and again.

Some of those included a focus on quality of life, the focus on life span research that really looks to examine carefully the development trajectories of all individuals with autism. Issues that are particularly important to me that I think merit further review would include an understanding of how to diagnose adults with autism, adults that haven't been diagnosed before, a better understanding of how to measure and define quality of life, more study of vocational training and college for individuals on the autism spectrum, and as we stressed a lot in our points, emphasis on the

coordination of systems of communication and existing data sources that are out there in the community.

So, thank you.

MS. McKEE: I know we took the plan and expanded it quite a bit but that was actually my hope sitting on this panel as a co-liaison. We have spoken a lot in our IACC meetings about the pie charts for the summary of advances and even research portfolios, where services always has this teeny tiny piece of the pie. And I don' think that that is a place any of us wants to be. I think that we want to start to even out the pie and that is why we have taken a good look at the plan and really expanded the research opportunities as well as the objectives so that we start to take up a little bit more of the pie.

I also wanted to say one other thing that we have talked about in our meetings that I don't think came through here.

And it is the idea, I guess the goal, that inclusion isn't enough. When we talk about inclusion, we sit down next to a person on the spectrum. And what we really need to be looking at is participation. And if that person is able to participate in the community, then that is a more reasonable goal than simply having them included.

MS. BLACKWELL: The only thing I could add to the great comments from this wonderful panel is that Tec mentioned at the beginning of this discussion that we did consider a lot of other materials. And I would like to stress that this group in particular really focused on public comment and tried to integrate it into our work.

I co-chair the Services Subcommittee of the IACC with my colleague Lee Grossman from Autism Society. And IACC had solicited a separate RFI on services last year. So we reviewed all of those materials, as well as the Services Subcommittee convened

a town hall meeting in June in Chicago and we also had the benefit of all of the comments from the town hall meeting and the RFI comments that the rest of you folks had.

So, I would just like to say that this group did a really good job, not just thinking about what is the right thing to do and what is needed but what does the public want to see.

So, thank you so much. I think we -- oh, go ahead.

DR. GERHARDT: I just wanted to add two very quick last things. First of all, I wanted to thank both our co-chairs for shepherding us through this whole process because it was, you know, difficult and challenging but a whole lot of fun and it really was due to you.

So, -- I said both our co-chairs. I said two. Two questions. Oh, I should have read through questions. Exactly. Phenomenal. Phenomenal.

The other thing I just want to point out is these issues up here for everybody here and outside, these should be your outcome data. You know, as we look, and we do, we look at drawing attention and we look at all these other issues of functioning and life. At the end of the road, this is where everything should be leading.

So I think if we tie everything into well where does this bring us closer to these outcomes, then I think as a system, then the plan really works together. And that is that integrated hole that I think we were all hoping to achieve today.

MS. BLACKWELL: Okay. I see that our light is not flashing yellow but it is yellow so I am going to ask our panel if we could go take our seats again and then answer questions from the rest of the workgroups.

DR. HANN: Okay, thank you, Panel 5. That was quite impressive.

DR. SHORE: I have got a comment.

DR. HANN: Go ahead.

DR. SHORE: I was real encouraged by what I saw, especially Peter's parting remark about what we have been talking about are actually outcome variables. So I thought that was really good. I also think that it can't be over emphasized the need for considered involvement of those of us on the autism spectrum. And as we think about involvement in the community, as we think about community involvement, that includes us as well. And that is all of us who are all over the spectrum. So, I thank you for that.

MS. DURBIN-WESTBY: Do we have figures for 2008 or do we still have those embarrassingly inadequate figures of 1.6 million dollars devoted to services research out of the, what was it, 127 million dollar budget? It was less than one percent. Because for all of this to happen there is going to need to be funding. So I strongly suggest that the IACC committee look at how

you are suggesting that the funding be allocated.

Because last night and this morning, I was thinking we have done a lot of good work but if it doesn't translate from the research on interventions and treatments and even research on services and delivery, it is not going to happen and more money needs to be diverted over to that.

DR. INSEL: So just in response to that, it is probably important to clarify that the IACC has no money. The money is at the level of the various agencies, both public and private. But in reference to this question about the pie chart and the funds that are apportioned to different areas within the strategic plan, we took the IACC's strategic plan to heart with the RFAs that we put out for the use of the stimulus money, the error money.

And what is really interesting as I said yesterday, we had 590 applications come

in for all six questions. But there are very, very few at this end. I mean a handful. So it is not that we don't want to invest in this. We don't get the applications, even when we say here is the money for this kind of work to get done.

So, I would love to hear from the panel about ideas on how to respond to that. It is easy to point your finger and say well NIH needs to spend money on this but it is not for lack of trying that we don't have some of these answers.

DR. GERHARDT: Well, I mean, one, just to give you some more concrete data on how that works. I mean, if you go to American Psychological Association, if you have gone to PsycSCAN and to the database that has all the peer reviewed psychological educational research and you type in "autism 2008" into the search engine, you get 1,487 hits. You type in "autism and adolescent or adult" you get 37. And half of those are discussion

articles. They are not actually research articles.

So there is a significant challenge in how do we now get researchers interested and involved. And I think part of that is we have to start talking about what we perceive as better outcomes. One of the points that I make is that if we are spending $50,000 a year to educate a child with autism and he goes to, and sort of a very old day hab, and I am not knocking day hab adult programs, he could go to a day hab program for $10,000 a year of education. He could end up there.

We need to come out with better outcomes and better outcomes will interest researchers into saying, you know, what else is possible. Where do we go from here? You know, if we say our best outcome is that he is going to be in a day program doing ceramics, how do you get people interested in that? We need to point out that people can work and be

contributing members of the community and be involved, and you know, have friends and be your neighbor, and go to church, or go to temple, or go to mosque or whatever it is.

You know, the way the system looks now, as a researcher I am thinking well our own intervention research is much more interesting and joint attention research is much more interesting. And I get to see more significant changes with little kids in the context of this classroom, as opposed to saying wow, I have got to do this for three years out in the community and the change is going to be like identified in very different variables.

So it is much more difficult but I think even more important that we start looking at these variables because otherwise, it sort of diminishes the impact of the other research that is going on. If we can't end up with the knowledge and servicing systems that actually support lines of competence, quality,

and dignity. I think that is where the problem is. That needs to be the focus.

DR. HANN: Other panel members? Cathy?

DR. PRATT: I think part of it is also the issue about research design. And oftentimes the traditional kind of single subject or clinical trials doesn't work for the kind of things that we are talking about.

I mean if you look at the literature around literacy, what they basically did related to literacy is that they did a meta-analysis of all that was out there in terms of literacy and said, okay, if you want to teach people to read, these are the five things that you need to do.

And in many ways, that is almost what we need to do is to say -- and the issue is even more complicated because we are not talking about doing research in a clinical setting. We are talking about doing it in the real world with all the complexities. So it

almost is that we need to look at way to gather that information so that we can make some generalizations that won't apply to everybody but can enough generalizations that we can build on and say these are truths.

For example, in schools we know that when people go in to look at kids with autism in schools who are having behavior difficulties, oftentimes people want to look at just that child's behavior. And we realize that behavior is really going to be also impacted by school-wide culture, by discipline practices. We realize that it is a bigger picture than that and then trying to capture that.

So it almost is we have to start thinking in terms of implementation research, instead of, you know, looking at the technology. Because I would say, Peter I don't know if you agree with this, but I would say that we actually know the technology. The problem is is that when people, and I think

David when you framed the question, when you travel around the country what you see is that people aren't utilizing that technology very well.

So it is how to take the technology we have learned and think about what are the components of a system or culture that are going to accommodate.

DR. HANN: Okay, Craig? All right.

DR. NEWSCHAFFER: I will be quick. And Dave is probably more qualified to comment on this than me but I think there is a research labor force, big research labor force issue here. I can think lots of places that have very well developed health services research programs and very well developed basic or clinical autism research programs but nobody doing health services research around this. I mean, you have got Dave, and I don't know, you probably have a few others but not very many.

So I think this would be an area where special RFAs that were focused around bridging that gap, dissertation research funding so that, you know, those kinds of incentive and research workforce building programs would be very appropriate here.

Hello David.

DR. HANN: Response?

DR. MANDELL: Thank you for funding my research and you should fund more of it.

(Laughter.)

DR. MANDELL: But so when I was looking through the services, I looked through all of the funded programs. And I looked at the services one. I thought, man, they are calling some of this services? This is not services. And so then I thought well maybe the same thing is going on in some of the other areas.

So I especially looked in question one and question four. Anytime you talked

about an effectiveness trial, that is you are testing it with real school teachers and not your post docs who aren't going to make it through if they don't do it exactly the way you say. Or anytime you are talking about testing a screening protocol in a pediatric practice. You are doing services research but those aren't counted as services research.

And perhaps more importantly than where they are in the pie chart is the link of the people doing the screening to the people who know about how to work in those systems.

So there is sort of a fuzzy boundary here. Maybe sort of in line with Craig's thoughts, which I certainly applaud for all sorts of reasons, that we should be thinking about how to connect those people who are developing the screening instruments with the people who are studying the places where they are going to be implemented or who are studying the interventions with the places they are going to be implemented. But also

you could also redraw the pie chart. I don't think the number is as dismal as that evidence would suggest.

DR. COOK: Yes, I want to bring up something I brought up yesterday and emphasize it again because I almost questions about why isn't more NIH funding going to this.

And in my experience at my institution, which has extensive services research in psychiatry, I was surprised at my colleague who is extremely well funded just got her first NIH grant in 20 years. Of course, she has SAMHSA funding. And so I would like to know how much of this fits within portfolio outside of narrow NIH. In a sense, turn that around. How much SAMHSA funding is autism funding?

DR. HUANG: Well, I guess that question is addressed to me. We don't have any SAMHSA funding that is specifically dedicated to autism. We actually have a small unit within our agency that is a statistical

unit, Office of Applied Studies, that is allowed to do research. Technically, the research piece of our portfolio was taken out of SAMHSA with the reorganization.

So when we used to do sort of what was on the interface of services research, that is no longer necessarily what we can do. What we do do, however, is fairly extensive evaluation. We can't even really call it research. But we do evaluation of our grant programs, our primarily discretionary grant programs.

So but it doesn't mean that we can't partner. In fact, we do have a large well funded over the last 14 years a system of care initiative for primarily focused on children with serious emotional disorders and their families. And that is, it almost looks identical to this new proposed short-term objective here. When I looked at this, this looks very much, this initiation of demonstration projects, looks very similar to

what we have in what is called our system of care or Children's Mental Health Initiative.

Very similar concepts around demonstration projects. A set of clear principles since -- It has been in existence since 1993, initially funded at like 37 million dollars. It is now funded at about 125 million. It is one of our programs that continues to grow with this concept of a system of care, which I think David was saying is kind of like the syringe. And then the evidence-based interventions are kind of within. We don't think about syringes at SAMHSA like that.

But what has happened to that program is it has generated a tremendous amount of data, primarily evaluation data, over every state has one of these grants. There have been over 125 communities funded. And we did do a shared funding announcement with NIMH for secondary analyses of that large database of information from systems level

data, financing data, specific services interventions data, and a lot of family and child characteristics.

So that is sort of the closest and we put that, at SAMHSA we have put that funding announcement out regularly. We get, you know, a minimal amount of response for it. But I think it also speaks to how our research and our price is crafted, in a sense. I think listening to the research that was presented yesterday, I was trying to think how do we use a lot of the genetic or the biomedical pathways research. How do we really move that into things that might be informative of what is going to work and what is not going to work in terms of helping promote quality of life for people along ASD?

Health services, health interventions, the basic biological genetic research. They are such in different camps I don't see that translation which I think needs

to go from multiple bodies of research. We just don't see that happening.

Now the other thing I just wanted to mention around these, I am really pleased that this panel also addressed the transition youth. That is something that we see in our work at SAMHSA that has really been falling through the cracks. We have a lot of investments in child and then adult but we have had very little in terms of transition models, although we recently funded a grant program based on a significant GAO report, talking about these transition youth who don't fit, they don't make the connection over to adult services. Ideally, we would like to get them out of adult services. So I am pleased to see that piece.

I would suggest to this panel that, as somebody mentioned, we need to learn from other systems. We have learned recently, for example, a lot from the employment system and partner with the Department of Labor. And

that they have a whole infrastructure set up for getting people into a sustained employment with our supportive employment services. And also they do the business development for a range of people with different kinds of challenges. So, rather than we take that on as a service industry, we are partnering with HUD and with Department of Labor on those other kinds of services that are critical when you are looking at a quality of life paradigm.

DR. INSEL: So, Ed, SAMHSA may not -- so SAMHSA deals with serious emotional disturbance in children but not with developmental disabilities. So ASD usually ends up at HRSA. And HRSA does have a fairly serious commitment to autism, which is just announced, I think, by the Department and the White House is going to bump up very significantly from, I believe the numbers are 42 to 48 million dollars in 2010. That number has now been supported as well by both houses of Congress.

So, that is probably where you and your colleagues ought to be looking if you are trying to find the funding for services.

DR. COOK: I am not sure I like that. I mean, I am glad to hear about HRSA but I am not so sure I like the idea of SAMHSA not being involved. Because from where I sit as a psychiatrist, I see more severely emotionally disturbed people who also have ASD. Let's talk about it as a comorbidity.

So I don't want to see them missing from some integration of what is offered by SAMHSA.

DR. HUANG: We don't not serve youth. They do show up in our portfolio of children's services. Probably less so in our adult portfolios. But my answer was do we have dedicated funding, no, but we do have children primarily in children and adolescents in our portfolio.

I just wanted to mention one other thing that we do around this translation piece

is we have a concept that we do with National Institute on Drug Abuse, which we call a blending initiatives, which is really trying to get at this translation piece, where we participate with them in their clinical trials network and really pair that together with some of our service centers, our grantee centers, and also with our technical assistance centers.

So in substance abuse, we have 14 addiction technology transfer centers around the country who are paired up with the clinical trials network team at NIDA and with our grantees. So that the idea around it is getting what was discussed yesterday about accelerating research into practice. This idea to really accelerate the movement of interventions, you know, into communities, into services settings.

So that is another model we haven't not focused on this population but another model that has been working pretty

well.

DR. HANN: Alison?

MS. SINGER: A lot of the studies that are currently in this section of the plan and a lot of the studies that the panel proposed are studies that look at individuals with autism and cohorts in subtypes. I am wondering if the panel considered studies that looked at sources of community barriers to self-determination and quality of life.

So studies that really helped us to get at really removing the boulders that are on the road. Because that is really a big source of some of the issues for individuals with autism, at least in our community.

DR. PRATT: Alison, I would suggest that some of that literature is out there but it is not in the autism community. I think that that literature is out there in other communities and we have to look a that. I know it is in the global disabilities community. I think it is also in the aging

community as well. So we are going to have to kind of look outside of ourselves and not recreate the wheel in terms of looking at some of this research.

George Jesien, I want to kind of pick on you for a second and as a way of kind of answering this question. One of the issues that has been coming up continually is looking at communities and the capacity of communities and also about training of individuals and also about the science of dissemination. And I think that the AUCD is a really under utilized network to look at both training of physicians, training of practitioners involving, they have a very strong, I guess I should say we do, because I am part of your network, have a very strong bias towards consumer and family involvement and really looking at those community issues. And that is really a lot of the work that we do.

So I think, Alison, it may be there. I think that we just have to help

people generalize it to the autism community.

MS. SINGER: I think what I am trying to get at is that the definition of community needs to be broader. It has to be bigger than just the community of individuals with autism and the people who provide services to them and their families. It has to include the community of all citizens on earth and how we can reduce stigma and remove barriers that cause people to protest and we want to build new service providing organizations in our communities and things like that. And how we can get parents of mainstream children in issues with regard to seclusion and restraints and a lot of the bigger issues that I think that is an area that is under researched.

DR. PRATT: Alison, that also speaks to the importance of us getting outside of our community and that, you know, I know that we do things, we go and talk to different organizations, service organizations, the

Kiwanis. I am going to go speak to an organization of Greek women. But I think that if we only have these discussions in the midst of the autism community, we are really alternately not helping folks. We have got to be talking to employers. We have to be talking to physicians. We have to talk to those people who don't have any definite interest. But our job is really to make community a common place for individuals and that everyone has the same opportunities for access.

And I don't think that any of us on this committee defined community narrowly. I think that we all defined community very broadly, realizing that is not about just respite care but it is about daycare. You know, it is not about creating good autism classrooms but it is about creating good schools. It is not about just insurance coverage for children with autism but healthcare for everyone.

So we realize that in order to really make these changes, we are going to have to extend our arms and include community members that traditionally wouldn't line up with us absolutely. So that is a great point. Thank you.

DR. HANN: Okay, I have Lee, Lars, and Peter.

MS. BLACKWELL: Can I just go to Alison's question for one second?

DR. HANN: Sure.

MS. BLACKWELL: We actually, actually Alison, we did talk about this a lot and how that would play out if we wrote it as a goal. And we have it as a proposed long-term objective. And it is in chapter 6 in terms of adults. I wouldn't say that it was necessarily limited to adults but I think that we felt, I don't know, maybe we felt that children had more opportunities for community inclusion, simply because of the way their lives are structured. They have some sort of

school life and that it is harder, perhaps to integrate adults with autism in the community.

So the goal was written very broadly because we weren't exactly sure what that would look like but this was an issue that we took off at some length and have expressed concern about.

DR. GERHARDT: I really was just going to agree with you because I think that is the last major barrier. I think there are not necessarily bias as in the community as a whole but like misunderstanding by the community about people on the spectrum and their capabilities and their potential and all of this sort of stuff.

One of the real challenges, though, in terms of researching those issues is, at least it seems to me, is that research tends to go in cycles. And if you went back into the '70s and '80s, there was a fair amount of attitudinal research looking at people with mental retardation/intellectual

disabilities. And there is a sort of sense that well, we did that. Just like in the '80s there was a lot of family research that was done. You know, going into the '90s and 2000, there is not a whole lot of family. It sort of gets into this sort of cycle. So I think it is time to sort of revisit that because we are looking.

And it is not just inclusion in the community, it is really inclusion in multiple communities. You know, we are finding out stuff that like if you take the bus every Tuesday, you know, what, the same people are on that bus with you. And that is a community. And you have to sort of look across all those different dimensions when you do this. So it is time to revisit the whole issue about how we do this most effectively.

DR. SOLOMON: Alison, we definitely did discuss it. We talked a lot about stigma prevention. And in long-term objective, new and proposed, the first one we

say that we wanted increases in opportunities for full community inclusion and including an assessment of benefits to the communities and to the adults with ASD. So, I think you are right, we should break it out more clearly than we did but it definitely was discussed in our panel.

MR. CHAPMAN: Just one thing to add on to this. I think sometimes the field of disability needs to know when it needs to leave and when it needs to step aside and be a support to that. Because I think there is many communities where there is excellent work going on and it is being led by the business community or it is being led by other nontraditional partners. And I think sometimes we need to know what our role is and how we can be a conduit and a support mechanism to that, instead of oftentimes I think we end up taking things over. And then when it gets taken over, you find some of those other partners slowly drop off. And I

think that is just a natural occurrence because they don't have buy-in because it is something that we are imposing.

DR. GERHARDT: Just one last thing. I should have said this before. You might be interested in looking at the work of John Campbell of the University of Georgia. He has done a really lot of innovative stuff in schools, where he doesn't look at all the kids on the spectrum. He looks at their peers. And what information and in what form do you give their peers in order to promote social inclusion. So he says, you know, this kid in the spectrum is this kid in the spectrum. Let me change these kids.

You know, and he is coming up with some very interesting findings and his initial study was funded by OAR, so I will say that. But you really -- he has done some very interesting work.

DR. HANN: Okay, Lee.

MR. GROSSMAN: Thank you, Della.

I do have a question for the panel. And but before that, I wanted to respond to Tom's comment regarding the ARRA funds. We disseminated the information on the grant proposal as far as we could and we actually did an outreach to many of the coalitions and collaborative partners that we have asking them to find ways to apply and most of them were in the applied fields of research. And they looked at the grant proposal and said that there was just no way that they could find a way to fit in.

And I guess with that said, at some point maybe we should get into a discussion, but not here, about how NIH might go about funding more of the applied types of research as what has been described by this panel.

And the question that I have for the panel is did you consider this question about funding and other departments, such as SAMHSA, HRSA, DOE, I can think of Department

of Labor, OSERS, OSEP, RSA, and a whole host of other acronyms that should be getting significant funding to look at the service and intervention side. Is this part of one of the questions that you looked at?

MS. BLACKWELL: No, actually, Lee. I think we felt our charge was a little bit more narrow, to go look at the strategic plan and try to identify the gaps, the new opportunities. And as an IACC member, I guess, I mean, to me the plan is, as Tom said, the plan isn't really funded. It is sort of a road map for opportunities for research.

I mean, what I have heard over the past couple of days is that although what we know has expanded a little bit. I mean, I think we have heard what we need, you know, exponentially. So I guess in our further, in our upcoming discussions, we will have to try to stratify that so we can make it clear for the entire research community what research is important.

MR. GROSSMAN: And I guess to that end, would you think that could be a gap that you can identify as putting into the strategic plan that other agencies should be considered for funding mechanisms, and that they are funded so that they can put out the grants to handle this aspect of the strategic plan?

MS. GIBBONS: Actually, Lee, I just want to correct Ellen. Because we did initially ask her should we worry about where the money could come from and who could implement this and she said no. I want you to think broader than that. I want you to be aspirational. And we were actually encouraged by that to think about what was needed as opposed to what the system can currently pay for, which is so limiting.

So in that sense, I think the answer no is a good answer.

DR. HANN: Wait a minute. So wait a minute. Okay. So, I saw Cathy had her hand up and I saw Eric, you had your hand up as

well.

DR. SAMSTAD: Okay, I have a concern about ASD adults that may have yet to be diagnosed or who may be misdiagnosed out in the community. And I am wondering if the panel had any discussion about this and how to identify them and bring them into appropriate services.

DR. SOLOMON: Well that is definitely an issue for the research community and for the clinical community that there aren't, you know, there are wonderful ways to diagnose adults with autism but they may need to be reviewed a little bit and be made a little bit stronger, because that is an area that a lot of people are looking at as being possibly one that needs to be beefed up and thought about. So we did put that in as an objective to look again at that issue and revisit it.

DR. HANN: Any other panelists want to comment?

MR. CHAPMAN: You know, Eric, I mean, just to expand upon that. And I think while there is probably folks who are misdiagnosed that are out there that may be on the spectrum but not have that diagnosis. I think from a state DD delivery system, we are looking at what are the needs of the individual and how do we individualize and tailor the supports and services to meet their needs and, oftentimes, irrespective of what their diagnosis is.

So, it is really looking at individualizing that and not simply saying hey, all of a sudden now you have autism so now we are going to move you over into this program or into this service delivery package. But it is typically looking to what those needs are related to their quality of life outcomes and goals that they have.

DR. HANN: Panelists?

DR. PRATT: I think the other issue that is very hard, whether you are

talking about education or you are talking about diagnosis or whatever you are talking about is is that a lot of it is people developing the clinical tools and ease to be able to do some of these things. And I know that in our state we have individuals who are professionals who are happy to work with children but they don't have that comfort yet with the adult service delivery system.

And I think, you know, having been in autism for many, many years, the kids that we are seeing and now the adults that we are seeing really do come to us with really complex issues and complex needs. And so I think again that goes back to a training and information dissemination issue is for us to help individuals in the field.

You know, we spent a lot of time working with physicians and dentists and you know, parents can't find obstetricians or a gynecologist for their children. And you know, working with people to understand this

community so that they can support them in a more appropriate fashion.

DR. HANN: On this topic.

MS. GIBBONS: Yes. One of the really cool things about this panel is that they embrace adults with autism and they didn't give me, as a mother, the feeling that I had failed autism as well as failing regular school. And I think they are very sensitive to whether is this the last shot an individual has in the healthcare system to get a proper diagnosis. I mean, we actually had conversations about whether that was beneficial, where it was not beneficial, are they on drugs that are inappropriate and causing terrible things to them that shouldn't be happening.

I mean, one would hope that best practices, when you do go through transition, include a new psychological and one would hope that that person would be the best doctor you had ever met. But until we have better

dissemination of best practices, like for example, what they do in Missouri, then it is really kind of difficult to implement.

But Peter, in particular, has always been very respectful about thinking about what the needs of the individual are, regardless of their ability to communicate them themselves, and he helped us a lot with that.

DR. HANN: Peter.

DR. GERHARDT: I mean, it wasn't a specific objective but I would also add to it that I think it would important to look at what really is sort of a splinter population within the ASD population and that is the prevalence of the people on the spectrum in the correctional systems.

We know historically that there is a large percentage of individuals with an intellectual disability, learning disability, but we have never looked at the issue of people with an Autism Spectrum Disorder in the

criminal justice system. And unfortunately, a large part of my private practice is working with people who are accused of crimes who have a spectrum disorder label and how they are just -- we have no data. And the system doesn't know what to do with these people and they usually end up in isolation to protect them from themselves because they tell on people when they break the rules, which doesn't really help you in prison.

So there is a lot of things that we can look at in terms of these later diagnoses.

MS. BLACKWELL: And we did try to get to that, those three data tracking goals that Peter talked about that we collapsed into the one big long-term goal in the six chapter. We did talk about tracking people's involvement in the criminal justice system because we felt that it is one system that needs to be looked at more closely.

DR. HANN: Okay, new question.

Cathy.

DR. LORD: I mostly wanted to comment about longitudinal studies. So not so much services, although I am having guilt attacks that we should be hooking up with services researchers. But just first of all I think I wanted to give NIMH credit for we have been doing longitudinal studies for a long time and it is really tough getting through the review system. Because even though people say you have an incredible sample and no one else will ever have a sample like this, everyone who reviews it has ideas of what you really should be doing, instead of what you are doing.

And so it is a very, it is just very difficult to get funded. And we have been funded four times. So we have 200 male adults who we have followed since they are two. But it has been only really sometimes with the help of NIMH where we come out on these borderline edges in Autism Speaks and in

ICHD to rescue us that we have been able to maintain this.

Because the other thing is if you lose touch with your families, you lose people. And so if you are going through a standard review process and it takes three years and three submissions, then you have three years where you are not in contact with people. And with cell phones now where you can't necessarily track people down as easily, it gets very difficult.

So I think it is, I think first of all, I wanted to just acknowledge that I do think that NIMH in particular and also Autism Speaks is conscious for the need for this. But it is hard because it doesn't fit into, you know, it is much easier to get funded for a genetics project or something you are going to do quickly that someone things is going to find the cause of autism than to follow people.

And you do get criticized, for

example by we have 200 consecutive referrals in North Carolina and Chicago referred for possible autism that range from everybody, you know, from individuals who have never spoken and don't speak and can do very minimal adaptive skills all the way up to people who are in university now. And then you get criticized because this is too broad a sample. Or it is not representative of what you would get today, which is true. It is not the same thing as two year olds that you meet today.

So I think, trying to think about it, I am sure this has come up in millions of other topics. How do you help other people do this? I mean, I feel like we have done okay but I think a lot of other people give up.

Another thing that happens is if you are going to do longitudinal research, you really need to know in advance that you are going to do this. I mean, we discovered with CPA trying to go backwards to people that you saw before and say guess what, we got money to

follow you up is not easy because you don't necessarily know where they are. It is just more complicated than starting and knowing in advance that these are going to be people who are followed, regardless of when you start. I mean, you could start with 20 year olds or start with 30 year olds or start with four year olds but to do that backwards is tough.

And the way that the funding mean the way that the funding mechanisms work, I mean, even with the say two year grants from the ARRA, is, you know, two years is not enough. You would barely get started.

So I think that this is a thing where everybody always says boy we need more longitudinal studies but having lived in the middle of this, it is very difficult to get from people saying it, even reviewers say it but then it is just too easy to say, you know, please do something different.

I mean, the last thing which has been very interesting for me to hear here is

we are studying now, which is with 17 to 22 year olds, so kids we have known, I shouldn't be calling them kids, young adults we have known since they were two that we are emphasizing, we are trying to look at quality of life. We are trying to look at where are they and are they happy where they are. And how do their families feel about where they are? And that was greeted with a lot of concern because that is, that is much softer science than looking at other things.

And we can do IQs and ADOSes and achievement tasks. I mean, we are doing all of that. But really we do want to know just where are these individuals and how are they doing. And how do they think they are doing?

And just one quick final comment. It has been very interesting because these are families we have known now for 18 years, when we started sending them questionnaires and doing interviews, they were like why are you asking us these questions. You know, this

is personal information. Do you really want to know this? Which was surprising to us because we felt like people often tell us these things but not as part of the research. And they were so astounded that someone was actually going to code what they said about what their lives were like.

So I think it is, to the sort of science of autism, it is sometimes quite uncomfortable and doesn't fit in easily with hypotheses about genetics or toxins or something that is going to cause a disorder. It is quite different.

So and finally, I think we will, out of having to do this, we have modified the diagnostic instruments so that they work better with these older teenagers and young adults. So we feel like we have also done something practical that hopefully will be of use to other people. But we could only do something practical because we had funding to do something else. So no one would have ever

given us money to modify the ADOS for nonverbal 17 year olds. I mean that would have not gotten past any committee anywhere.

So and that is not something that will make money. So the publisher is not interested in that because they don't think this is going to sell. So I think we somehow have to think about just realistically how do we support, not just how you support my research, but how do you support things that will have practical benefit that everyone says is important but often just go right to the bottom when you are within the scientific community.

DR. HANN: I want to tell people we are at the yellow light, which means we only have about four minutes left to this part of the session. So certainly if the panelists want to respond to that, that is fine.

DR. MANDELL: I will respond quickly. Come over to this side. So there are two sets of issues. Right?

(Laughter.)

DR. HANN: Red rover, cross over.

DR. MANDELL: So, one set of issues are the dependent variables. That is, there is this assumption that you are studying the natural course of the disorder. Which of course is a myth because there is no such thing as the natural course of the disorder. Right?

So then you have all these independent variables, which are the context. And that I think is what we study is the context. And so the question is not are you happy but why are you happy or why are you not happy.

And so I think what we were thinking about in our longitudinal studies was that there are wonderful careful studies like yours that are increasingly challenged to get refunded to address the same types of questions. But now we can add on this additional element of the context. What is

the community? What are the services? What is the intervention? What is the family support like and the family dynamic? And by treating those as the independent variables, we have a whole new study. And because we have such wonderful baseline data, we can then begin to look at the interaction, the heterogeneity so that variability that you have becomes the selling point, rather than the fatal flaw for the review committee.

I will stop.

DR. PRATT: I will just make one quick comment. I would also say that we don't have one dependent variable. You know, when we talk about quality of life for one person, it may be a volunteer position. The other person it may be living in a group home. The other person it may be a home of their own. The other person it may be a college degree.

And so it doesn't kind of fit so nicely into the package of the traditional research design.

DR. GERHARDT: And just because this is part of one of my workshops so I have it memorized, the quote is "Happiness among people with severe profound multiple disabilities can be increased significantly improved and measured supporting the fact that behavioral analysis has yet to realize its full impact and improvement of quality of life for people with disabilities." Denny Reid wrote that in an article where he looked at if we do these two interventions, which intervention results in greater happiness.

So, if we can do that in applied behavioral analysis, which let's face it, has the biggest stick up its butt of any of our fields, we can look at happiness in other fields. I mean, it is not -- yes, I am getting drummed out of the union on that one.

And to date, to my knowledge, Denny, Dr. Reid is the only researcher who has published in JAVA. He has got five studies with happiness as an outcome variable. So I

think we can look at this sort of stuff. Not easily but relatively easily.

DR. HANN: Any other comments from the panelists on this particular topic?

Okay, so Ed you had your hand up a little while ago, do you still have a question? Oh, okay. Lars?

DR. PERNER: I think that one of the more important things when we talk about quality of life and the autism spectrum ultimately comes down to individual interests which very dramatically and often take on quite obsessive qualities.

A few years ago I was rather struck. I got a question from parent about aptitude tests adapted for individuals on the autism spectrum. And I was sort of embarrassed I hadn't thought about it before and started looking around and there weren't really any. And it also seems in the population in general that aptitude tests have decreased in popularity. But I think this is

an area that we need to pursue to match people with potential employment and other life opportunities.

One time a mother of a young man who had been out of college for a while called me. Basically, he had needed to move on. After college he had been working in a university research setting and the funding was discontinued. After speaking with the mother of this young man for a few moments, it became very obviously to me that this gentleman should be, assuming he could work the social of this, he would really would have been rather be an actuary in the insurance industry.

Now that raises another question of having the background. If you rely on people in a local setting, they may not have the full knowledge of different opportunities that may exist. I think it is important to have some instruments that can be used nationally to identify different opportunities

for individuals on the spectrum, given interest which we also know are highly important in motivation.

I will also briefly emphasize that we also know from research that shared interest with others can be a strong social motivator. So I think we need to think of that from the point of view of quality of life as well.

DR. HANN: Okay, thank you. The red light is flashing. So we need to move to the next part of our discussions, which is open for public comment.

PARTICIPANT: Not liking silence, I just had to first of all say, all of you folks look great on the computer. I had a couple of conference calls and was watching this whole session on the web. So I just have to compliment whoever has set up the technology. You are bright, vivid, in great color, and subtext works great. So you can be listening to a conference call and still be

participating. So hats off to those of you who set up the technology.

I would just like to make comment about two areas. One is this movement to adults. And what we have heard from parents is discussions about the cliff that happens at either 18 or 21. And we think of transition as a handoff of the baton from one service to another. The problem is, there is a baton to be handed. There is somebody handing it off. There is just nobody on the other side of the relay to pick it up. And that is true in medicine and healthcare. We have a lot of folks who are still seeing their pediatricians when they are 30, 35, 38 years old because it is the pediatrician who understands what has been going on and has the life history.

But the same is true in education. We haven't prepared our community colleges. We don't have faculty at our universities. We don't have curriculum. We don't have the kinds of supports and services that have spent

the last 30 years developing in K-12 education. So folks go through with all kinds of adaptations and accommodations and then hit a system that really is unprepared for them.

So one of the answers is clearly the training that we need to provide for folks to be dealing with adults with developmental disabilities, including autism.

The other is really a systems issue. And that is, there is nobody accountable. We have spent a long time and God knows we have a lot more to do but at least there are folks who have responsibilities for children. You can go to MCH. You can go to Title V. You can go to your special education system. And there are folks that have legal mandates on what they are supposed to do. That cliff also happens at the systems level. There really is no entity at the federal level that says adults are my responsibility.

I am not sure it belongs in one

agency. We certainly have CMS, and Social Security, and Department of Labor but there really isn't a coordinating entity at this point that says here is what we all need to do together.

I brought this up yesterday and I would like to just re-mention it today because I think there is so much that we have learned from this. And the idea was to pull together summits around early identification and assessment and diagnosis of kids. And we brought together the Early Intervention Part C folks, Early Childhood, Head Start, childcare, the Academy of Pediatrics, the DD Council, a legislator if we could get them, CMS folks, Title V, children with special healthcare needs, providers like Easter Seals, advocacy groups like the Autism Society and put them in a room for two days. And we said what are the barriers? What are the resources? And where can we go from here?

And the impact was, in some ways,

pretty astounding. Everything from a coordinated, concerted outreach effort throughout the entire state, to legislation, to some agreements about the kinds of training that folks were going to provide. But in some ways, it was a mini-IACC meeting and focusing on the areas of early identification.

I really wonder if we don't need to do the same thing around transition and adults because in some ways the action for services and support is at the state level. That is where folks lay their hands on human beings and that is where they develop the systems. And I almost wonder if we couldn't have a recommendation that would push down to the states the same kinds of discussions that you are having across agencies to really look at the needs of adults with autism and I would push for including other development disabilities. Because in some ways, there really is some overlap when you look at employment, transportation, post-secondary

education, health benefits, etcetera.

And I will just say this. I have been in Washington now about 12 years. Federal government is really good at telling others to collaborate. And saying, you folks should partner with all of these other folks. What we don't see an awful lot is the demonstration of that collaboration.

And one of the biggest messages I think that these summits and why they were so successful is that we used the UCEDDs and the LEND programs that were funded by ADD and MCH with additional funding from CDC and proponents from education grantees, as well as the Maternal and Child Health Bureau, which demonstrated to the folks in the states that we at the federal level are on the same page of wanting to support what you want to do in the state.

So the second sort of systems recommendation is I think what NIH has been doing are these cross-institute research

efforts which demonstrates that nobody owns a particular issue or a problem. I think the same would be very effective to have Education, CMS, HRSA, NIH demonstrate some collaborative efforts that would focus or encourage or incentivize states to get together to deal with some of these services issues.

So, I will stop there. Thank you.

DR. HANN: Additional public comment?

MR. BELL: Hello. Peter Bell from Autism Speaks again. I am going to put my Autism Speaks hat back on and I am also going to do a very shameless promotion of an initiative that we are involved with called the Advancing Futures for Adults with Autism. And this is a national consortium of about 41 different organizations that are going to be coming together on November 13th to hold a national town hall to discuss the future agenda for how we, as a society, prepare for

those people or children who are on the spectrum today and will become adults in the next decade or so. And also how we can better serve those people who are on the spectrum as adults today.

This national town hall follows from a think tank that we held in New York City in January of this year where we brought together 60 thought leaders. And attending this and being a part of this whole initiative are people who have autism, family members, service providers, members of the community at large, potential employers, and so forth. It really contains the full gamut because we believe that this is something that we as a society have to address and not just the autism community itself.

We think it is important that as many people in the community participate in this. The national town hall will have over 1,000 people participating at 15 different satellite sites across the country. There

will be one major site in Chicago and they will all be connected through a webcast. And we have a system where we can actually do polling and live voting so that we come up with an agenda that represents the collective voice from our community. And I think one of the things we have learned in the autism community over the last decade or two is as much as we can have a unified voice as possible, the better we are going to be in the long run. So I just would encourage all of you, there is a good chance that one of those 15 sites is going to be, hopefully near you, and if you are able to participate, we would love to have you involved.

We are going to be putting a press release out. Tonight in our e-Speaks and also will be available on our website if you want more information.

Where this will then go is in 2010 our goal is to start working with legislators and policy makers and the different divisions,

both at a federal and a state level and talk to them about what we believe are the needs. And one of the things we have heard today is there are a lot of needs and while it is good to have good research behind it, we need to go beyond what the Combating Autism Act was provided for and actually increase the number and quality of services that are available for those people that are on the spectrum and particularly in the adult end.

We have come a long way. When I was first at one of these meetings, I don't think we ever talked about someone that was older than ten years old. It was very much focused on the young child with autism. And here we are spending a considerable amount of time and across every domain. Across every panel question from even the early identification, early diagnosis, we are now talking about adults in that realm.

So, this is very encouraging and I hope as many of you as possible are able to

join as we try to create a better future for our loved ones that have autism.

MS. REDWOOD: Peter, what was the date again?

MR. BELL: It is Friday, November 13th.

DR. HANN: Additional public comment?

(No audible response.)

DR. HANN: Okay. I will take that as we can turn it back now to discussion with the panel members. Lee?

MR. GROSSMAN: I wanted to ask the panel their thinking on this. At the Autism Society, we have kind of taken the approach that to address issues related to autism in adults that we needed to actively engage with the rest of the disability community. We have been impressed by them that if we don't work collaboratively together, then we probably won't be able to get any of our efforts forward.

So I wanted to get the panel's impression on that. In that light, we have been working quite aggressively with a number of other national disability organizations in moving forward on adult issues to draw up some legislation and some other activities which will be introduced in the near future. And I guess with that said, we have kind of taken the approach that we feel like there is a great sense that we know what do with adults. It is just that we don't have the systems in place to implement what we know.

So again, I wanted to get the comments from the panel on that line of thinking.

DR. HANN: Panel? David.

DR. MANDELL: We did talk a lot about the idea of using existing systems and working with other groups that use those systems in efforts to improve the quality of care and quality of life for adults with autism. I think we have thought about it more

from the system perspective, like the rehabilitation services administration or the Social Security Administration than we did from the perspective of other advocacy groups.

I would -- I am not sure. I am not even sure I like the phrasing of we know what to do with adults. But I don't know that we have a lot of evidence about what the most effective ways are to support adults with autism. We may know the service vehicles that we think are going to be the conduits for that intervention but I don't know that we have good data on what those supports and those interventions should be. And so I wouldn't want to -- I think there are things that we know that we could be doing better and that we have ways to do better and that we should focus on.

But I don't want to jump the gun on saying that we already have a body of evidence and now all we need to do is put it into practice. I think there needs to be

equal attention paid there.

MS. BLACKWELL: Lee, we did talk about this issue of the fact that there are certain challenges across all disability populations. And I mean, we weren't quite sure. You know, we talked. A lot of these issues came up in all of the RFIs. So, our approach was to look at it through the prism of is this problem different for people with autism and we didn't know the answer to that.

So for example, in our proposed housing objective and in our proposed objective that deals with training providers and other professionals, I mean, we put those in there because we felt they were important issues for people with autism. But in the context of we know these are important issues for all people with disabilities.

So I guess were weren't, that is kind of the approach that we took.

MS. DURBIN-WESTBY: Is anybody else talking right now? I want to talk about

one initiative that is a research project. It is the Academic Autistic Spectrum Partnership in Research and Education. And currently we have a gateway project going and it is a gateway for research that is committed to inclusion, respect, accessibility, and relevance to the community of autistic adults.

And so the AASPIRE Gateway Project includes a series of online studies on topics such as healthcare access and quality, which we are doing right now. And then there will also be projects on online sense of community and identity, problem solving and perspective taking. And after the research is completed -- and there is a team of people that include people on the autism spectrum, researchers who aren't on the autism spectrum. And after the research is completed, and we are participating in every aspect of developing it, and doing online surveys, and even how you access the gateway, just every detail of it, then there is going to be a dissemination

piece to disseminate the results and information to practitioners. Because access to healthcare is one area that autistic adults traditionally, it is a difficult, it is just a difficult area. So there will be a part of disseminating both to adults for their use and also to practitioners and others involved in the healthcare system.

MR. GROSSMAN: Yes, I just wanted to clarify to David's point. David, I totally agree with you. And to clarify what I was saying was that yes, we do need to know what is best to do and we need to study that.

The point that I would like to emphasize is that we shouldn't wait until we know what the best is. We do know that adults need more housing options. They need residential programs, vocational services, supportive employment, proper medical attention, a whole host of things that we already know exist. And we should be working towards getting those provided now versus

waiting to know what the best is.

And I think by doing what we are not doing now and not doing effectively now, we will learn a lot and that will add to our body of evidence of what is best practice.

DR. MANDELL: I agree. I mean, I think was it Walter F. Dearborn said if you want to understand something, try to change it. So kind of prosaic but I think this idea of learning by doing if we know things could be better for adults with autism, we know there are opportunities we can make available to them, let's at least try what is available to other adults and then learn what works and what doesn't work.

I also wanted to speak to Paula's point about using this sort of online strategy to collect data from adults with autism, at least those that are identified as having autism, to have a better understanding of what the range of experiences of adults with autism is like is a great one and probably worthy of

further exploration.

MS. DURBIN-WESTBY: I think it also the study is not limited to adults on the spectrum it is also people with other disabilities and people who just want to participate in the survey. So hopefully, it will reach a broader array of people that can use the information.

MS. GIBBONS: And I think part of achieving our aspiration goal relating to the sharing of data and the collecting of data, IAN has recently opened up taking data on adult subjects. So I would encourage advocacy organizations to have their members file with IAN so that we can begin to build the data in a way that is very cost effective.

DR. GERHARDT: The only thing, just to sort of follow up on what Lee said and David, I think we do know a lot about models but what we don't much about are practices. You know, we tend to say well we need residences but we don't know -- what do you do

in the context of the residence. What is the best way to get someone with challenging behavior and autism and who doesn't use his voice to communicate, a job? Those things we don't know. We could say we need employment programs, we need residential programs, we need this. But the services that occur within the context of those currently now are so variable to be almost meaningless in terms of understanding best practices.

So we need to come some practice understanding about what we are doing and then we can, I think, move forward in terms of what best practice really is.

DR. HANN: Other questions, comments from panelists? Fourth panel, I should say.

DR. PRATT: Well, let me make one more comment. In Indiana every year, and Tec alluded to this, we do a needs assessment survey to find out things around, actually, I am sorry, every three years around if

individuals are employed or not, what their average annual earnings are. We find out about how pleased parents are with educational services, how many individuals have been in trouble with the criminal justice system. We ask a whole host of questions. We ask about insurance coverage and a lot of things. And we use that to kind of inform policy work.

And I think that for all of us, there are questions or outcomes that drive us. There are a couple of questions on our needs assessment survey that drive me, and I think drive all of us on the panel, and those questions are around employment and the income level. A few years ago we found out that, and I am not going to have these exactly right, that we found out that about 26, 27 percent of our folks were employed. And that is individuals all across the spectrum from those with the most significant disabilities to those who are now professors in colleges. And I can say that, as being one of them not on

the spectrum.

This year we found out that it was more like 20 percent of our folks were employed and that probably is an impact of the economy.

We also found out that the average annual income for individuals on the spectrum is $7,200 a year. And so I think you know when we look at measuring outcome, I hope that we will always keep that in mind is that what we are really gearing for and I am not saying that job means a high paying job is the measure of a successful life but I think it is an indicator of some success.

And I hope that is the question, the first question that I always look at in our needs assessment survey and probably the question that drives me more than anything.

And I think we have to look at in terms of coordinating systems. We oftentimes look at even service delivery systems as being fragmented. From the moment a child is born

the transition process to adulthood begins. And you know, we all have to line up all of our supports and all of our energies to make sure that we are taking all those correct steps and look at, Cathy, outcome data like yours to see longitudinally what it takes to help individuals head toward that successful future.

And I have to tell you that will continue to be the measure in my mind about how well we are doing as a community, not about how many articles we publish or how much funding we even bring in but to see where are adults on the autism spectrum and what are their lives like.

DR. HANN: Okay, David, did you want to say something?

DR. MANDELL: So services is tough because in this room, we can outline a research agenda and we are talking to the right people, if what we are trying to do is outline a research agenda. But we are also

trying to make systemic, organizational, functional change, and cultural change.

And so to some extent, for those things, the wrong people are in the room. And it may be why, it is sort of Mom and Pop and apple pie and, you know, for us, we can kumbaya around this. But the issue is for people for whom this is a third rail. For whom this is issue of funding and authority and policy, thank you, Pauline.

And so to make the transition for making this just about research to about actual implementation in the community or cultural change, I think we probably need some subset of this group that also encompasses many other folks for whom this is their daily life is about administering the systems that we are sort of glibly mentioning as potential partners.

DR. FILIPEK: I think that since you brought it up, David, I have been quietly sitting here waiting for an entryway into

this.

We have been talking about the sense on the mandate of urgency. And maybe this is not the forum for discussion but I think that it is important for us in the strategic plan to consider where do we go. We talk about communication from research to practice but all of this is going to be for not unless we go to policy. And if there is such a long time to get from research to practice to policy, how do we try to expedite that, given the sense of urgency that the government as acknowledged? And what can be done within the strategic plan to try to implement at least the beginnings and the initiation of policy change? Which is probably a rhetorical question with this group but I think it is something that we need to think about because ten years of research to practice isn't going to cut it.

DR. INSEL: So let me jump in a little bit. It is true, David, that it is a

different group of people that might be around the table for some of these issues. But I think if they were here and some of them do sit on the IACC and we are, after all, advisory to the Secretary who has to oversee a lot of the issues around what the policies ought to be, the kind of questions that they would ask would be can you give us the following information.

So show us what the saving would be if we invested X dollars in this and what the cost would be if we don't. And those are, actually research questions. So there is a scientific agenda that can inform those kinds of policy decisions. And that is what we are trying to tease out from this discussion. And I think where the panel will be most helpful is in telling the IACC really what you have done already. These are the targets that you should be thinking about. These are the questions that are going to be most relevant for policy makers, for changing the services.

And with my other hat, because we had this exact same conversation about serious mental illness, we talk about a dashboard. And the dashboard has you know, what is the suicide rate. What is the employment rate? What is the number of people on SSI? And we kind of follow all those metrics. And the question to us is how are they moving. And how do we track them. And what kind of information can we provide to people who are responsible for that side of it, to make sure that the dial moves.

So, you could think about that whole list or what the dashboard would look like here that would be most important for quality of life.

DR. PRATT: I think, Pauline thank you so much for that comment and David. I think state legislators are looking for good ideas about policy. And I know that we have, the Autism Society has worked closely with AUCD and with Easter Seals on looking at

legislation in different areas. And that is continually what we hear from is is that they know. They see the urgency. They hear from their constituents the urgency of autism issues. And unfortunately, sometimes what they respond to is the loudest voice. That may not always be the most accurate voice.

And for example, we had someone in our state tell our legislators if you put all of your money into zero to three programming, you will not need any money for adult services. And after I quit pulling my hair out and screaming, I had to do a lot of educating of the legislators to help them understand.

And I think, you know, making that link, we talk about it from research to practice, but also making that link to policy is very important. So thank you for that comment.

DR. FILIPEK: And I would like to make a little addendum to that comment is

that, and this is a rhetorical question again, do we really need to do this at a state level, since there is such incredible disparity across states as far as services or is it not in the best interests of the people with autistic spectrum disorder for whom we are all here, to try to do that at a federal level?

MR. CHAPMAN: I was just going to add, you know, George earlier talked about the summits that they did specifically around children. And something that we have done in Missouri they actually did back, in 2000-2001 was similar to what we are talking about right now, which was called the Missouri Autism Response and Research Agenda. And it was specifically led by our general assembly. Specifically, a couple of key state legislators. And then all of the state agencies from K-12 education to higher education to vocational rehabilitation, ED services delivery, etcetera, juvenile justice, all had to kind of come to the table and sit

there and come up with not only what are the key priority issues and policy issues around research but then what are we going to do about policy to get greater integration across the state agencies?

And it has reaped incredible benefits. Many of you probably are familiar with John Constantino, Judith Miles, and Janet Farmer and some of their work. It has led to incredible increases in funding for autism research within our own state but then also within the provision of services.

We currently, as a division do our home and community-based waivers, expend over 65 million dollars a year. And predominantly, that money is going towards adult services but it has also led to greater linkages with the infant toddler program where we have better coordination and collaboration between that program and our state DD system.

And I think, Pauline your issue, I think there is some excellent work going on at

state level but what are the implications then? So if somebody moves from Missouri to Kansas or to Illinois and they similarly have that cliff at that age. And yes, it is the same process. Where can we have -- pardon me? Yes, yes. The cliff of the move. Exactly.

And I think there are some neat examples out there but it has also led then to opportunities where we have this initiative called rapid response which when families first get a diagnosis that then they get timely accurate information about autism spectrum disorder but then also about available supports and services in their local community and in the states. But then also how do you get connected with parent support groups, so people can sit there and get connected with other families.

And that was all developed out of that initiatives and partnerships with higher education and the research community. Just as an example, I think of what is possible, I

think when we all finally come to the table.

DR. HANN: Jeff, I think you had a --

MR. SELL: I just wanted to add on a little bit and I think Tec set up and added a little bit to what I wanted to contribute.

In terms of viewing individuals on the spectrum and adult services or the lack thereof, I think the focus has been or is heading towards employment first policies. And the way I have always viewed it is, you know, you have got to have the employment first policy of that mind set in place because if you go to transition and there is no employment or there is no meaningful employment, I should say, then there is essentially nothing to transition to.

You take that into consideration with the prevalence numbers that we are seeing, I mean, this is a huge problem. I think from a policy standpoint, we are starting to get a little bit of attention.

There are some really good meaningful practices in place and I have seen some really interesting, just over the last couple of months, economic data.

Robert Cimera from Kent State University has taken the numbers and crunched them. He got his hands on almost all of the vocational rehab numbers and just did a study. And it clearly shows that home and community based services are much more cost effective, meaningful in the appropriate way to go, versus the cost of institutionalization or other types of residential programs or workshops, sheltered workshops.

So I think we are at a point now from a policy standpoint to where it is very important that some of the data and some of the best practices in research is made known, so to speak, and it is made known to the right people who, Tec as you said, once you get all the right people around the table, good things happen from a policy standpoint. You take

that in combination with the data and you can show very effective cost savings, which is going to save Medicaid and Medicare a ton of money over the long run.

I think we are at that point. It is just as I look around just this table, the Interagency Autism Coordinating Committee, the Department of Labor and some other folks that I think would have a more meaningful impact in the daily lives in terms of employment, other folks need to be brought to the table perhaps and that should be considered. They can actually take some of the policies, take the research from a policy standpoint. When we really get down to it, it is all about money. These programs are going to cost a ton of money. When we look at adult services, that is the biggest cost that we are facing in autism community and we have just got to make it happen and really need to find a way to actually allocate appropriate resources to address long-term services and supports

employment and transition.

DR. GERHARDT: Well, I also just go with it. I mean, we have to get, and I hate this phrase, we have to think outside the box. I mean, and the reason I hate to phrase this because I think you really have to know the box really, really well before you can think outside the box. People use it to say that they don't know what is going on.

For example, we had a grant in Pennsylvania that actually got turned down because they didn't think we could do it, where we want to follow 12 kids from 18 to 25 in Pennsylvania and to transition them from the school system to no paid supports. We are going to work within the community. We are going to access Lions Clubs. We are going to access communities of faith. We are going to get retired senior volunteer people to transport because the assumption is the money is not going to be there. And us betting on the money being there, guiding our practice

isn't going to help us. So we need to start looking at research that actually circumvents that need and how do we best do that because that is the reality we are going to be facing for at least the next decade or so, that the money is not going to be there.

So we need to start looking at okay, let's accept that reality and move on, instead of what we tend to do is we need to legislate, we need to get more money, we need to do this. I don't really see it happening so we need to sort of push it in another direction in a way that really does bring people into the communities and supports real significant change and gives people the lives that they are supposed to have.

And they should have funded me.

MR. GROSSMAN: Pauline, thank you for bringing this up. I'm glad you put this on the table because I think that it is important for us to really understand that when it comes to public policy, that there is

a lot more to this than just the research.

The federal agencies, I don't know what the exact numbers are but I would imagine CMS is spending billions of dollars per year servicing parts of the autism community, the Department of Education spending, quite a bit of money, in the billions.

So the money is being spent already. And when it comes to public policy, we would be looking at reevaluating how it could be more appropriately and more effectively used. And that is the public policy. That is among some of the public policy issues that we should be pushing.

Yes there will be research that can support that but I think that we would be most productive now in looking at public policy not from the research angle from truly what is being delivered in terms of the services and supports and changing those systems that are now providing those services.

So it is not only more effective

use of the money, it is more effective to the lives that it is impacting.

Now one of the things that is most troubling right now is that when you think about all these billions of dollars that are being spent to service this community, and there is nobody around this table that would think that either the money is adequate or that the services are adequate, the shame here is that the majority of the money, the greatest amount of money that is being spent to service this community is coming out of families' pockets. And that is a shame. And it needs to stop, particularly in this country so that we can start putting these services to the public sector into place so that it works to the best, not only for the individuals but for the families as well.

DR. FILIPEK: And that begs the question of what happens to those individuals and the families who do not have the money in their pocket to pay out. And there is a huge

disparity there.

DR. COOK: I agree with so much of what has been said I just want to point out that we can't ignore the need for residential care. I think it was acknowledged because unless there are extended family to take care of people who can't make enough money to support themselves in housing, there is a need for housing. And it is so difficult in Illinois that that is only possible if the second parent is terminal. Meaning that we are talking about transition. We can't even transition the last few years of someone's relatively older life when we know that transition will be necessary.

So as much as want -- we just need to -- My point is the spectrum is so broad we have to think of all the needs.

DR. HANN: Okay. So it is just a few more minutes actually until this session was to be over at 2:45 and then we are scheduled to have a short break and then have

the IACC members comment on what they have heard, observed, interpreted, etcetera, from the sessions that have occurred. Don't look at me so puzzled. That is what is next.

And so I suggest that we do that. How about if we take a relatively short break, let's say ten minutes and we can kind of speed this up potentially a little bit. Because I can tell people are like no.

Thank you.

(Whereupon, the foregoing proceeding went off the record at 2:48 p.m. and resumed at 3:10 p.m.)

DR. HANN: Okay. why don't we go ahead and get started. This section of the discussion was originally set up to hear from the members of the IACC who have been serving as liaisons and/or have been here as active participants in other capacities with the group in terms of what their thoughts were with regard to the workshops proceedings, as well as their ideas, potentially, that they

wish to be carrying forward to the full committee, etcetera.

So there was no script. There is no definitive right or wrongs for this particular section.

So one thing I do want to remind the members particularly of the Planning Subcommittee is we will be convening a call for everyone to discuss the proceeds of the workshop and for you all to concretize essentially what you are going to be taking to the full committee which meets on October 23rd herein Bethesda. Because the primary reason that we have had the workshop was, as everyone remembers is to provide input for the IACC to consider how it will make any updates or changes to the strategic plan.

So that process needs to be worked out by the Subcommittee, who will make those recommendations then to the full committee. Okay? I know it sounds a little cumbersome, but that is the way it works.

And so I open it up now for the members of the IACC, those who would like to make comments

DR. SHORE: I will make a comment. Maybe even more than one. I was nonverbal until about four, so I have to make up for it.

(Laughter.)

DR. SHORE: I just want to say that I am grateful for this opportunity to hear some really intelligent, reasoned discussion that we so rarely see. We need more of that. People who can talk to each other, speak their minds, and come up with solutions, I think that is great.

I sense there is a sense of urgency and I think a number of us have talked about the need to collapse the time lag of about anywhere from 10 or 11, or 20 years between research and implementation. A related note to that is how can we get the stuff that we know now out and available? Because we know an awful lot now. We can do

an awful lot of good with what we have. So, how can we get that out? And that is a challenge that faces us and we need to do that now, not five years from now. Not ten years from now.

And it was great to hear discussions about that. And even though I am a little bit frustrated at how fast or slow this is going getting to implementation is, at least we are talking about it and I hope things can speed up. So, I thank everybody for that.

MS. SINGER: I think one thing that we heard from almost all of the panels was really a good amount of support for a lot of the priorities that are currently in the strategic plan. And I think that one thing that we should think about as the plan review committee was that our charge to the workshop members was really to focus on gaps, when maybe we should have asked them to focus more on research opportunities.

I think that there was less emphasis on some of the items in the summary of research advances and a little less time spent working on how we can build on some of the research that has taken place since we last put together the strategic plan and what we have learned since then and how we can continue to keep the strategic plan as a living document that is really ahead of the curve, not playing catch up to the research but really driving the research.

So I would suggest to the members of the Subcommittee that in the next couple of days before our meeting we really take some time to review the summary of research advances and look to see if there are additional research opportunities that we want to incorporate.

DR. JOHNSON: I think related to that you probably want to look at what has been funded recently to see what is being conducted currently.

DR. HANN: Any other IACC comments?

Well I would venture to guess that we are somewhat quite because it has been an overwhelming couple of days. A lot of information was given. And I think there has been a tremendous wealth of knowledge that has been shared here so it is a little hard to digest all of that at this moment and be able to articulate in some meaningful ways some of the feedback to the Planning Committee.

One of the things I think though will be important is taking a big picture look. Once, I guess the plan is reviewed to make sure that there is connectivity across the different panels. Because I think one of the things that happened was there was discussion within the panels and there was a little discussion about cross over. Is one occurring here or does it belong here? Does it belong there? And I think somebody does need to look at it from a comprehensive view

to say is everything being covered and are there gaps within the plan overall, not just within the panels but overall are there some gaps?

So that was one thing that I was thinking of in terms of what has come out of these discussions.

MS. McKEE: One other thing that I would recommend is are the minutes from each of the telephone conferences available for the members? I mean, each of the panels got their own minutes but it would be helpful for me to read through the minutes of the other committees because it is really hard to summarize six hours or I guess the other panels had four hours of telephone conversation in a much more condensed way here.

DR. HANN: Sure. To that end, too, I think, for those of you who have worked so very hard and we really appreciate it, if there are additional, for the panelists, the

individual panelists, if there are additional ideas that you feel after today's discussions and yesterday's discussion, etcetera, that you would like to see added to the slide sets that you have all worked so very hard for, I would strongly endorse you sending those the group and saying I think these really need to be added. These are important points, etcetera, so that those can be captured.

I would appreciate that that be done hopefully over the next week because the Subcommittee is probably going to be meeting on the 15th of October. So we need to be able to get all of that information and get it to the Subcommittee for them to use.

But I think that would be good. I know I do the same thing when I am at groups. You think of things later and so forth like that. So I am opening the opportunity for that. Just as you have been doing when you do that, please include everybody on the group and include Susan and I, etcetera, just like

you have been doing.

We can send around little reminders to everybody, too about that because I know we have had a number of people who had to leave early to catch flights, etcetera.

The other thing too, if the IACC has some questions, some additional questions that they wish to ask the panelists, since you all are still here, in terms of any points that you can still think of that you would like to take advantage of this group situation.

DR. DiCICCO-BLOOM: I don't want to ask a question. I just want to reemphasize something which I think I have heard over the last couple of days is the need to encourage development of the workforce. So each of the questions are people at different stages of their career and it is very, very multi and interdisciplinary. And of course we all know that the very disciplinary universes from which we originally merge tend to work against

this.

And so continuing to create mechanisms and communicate to those who should be applying to find ways to cross these boundaries. I know some of the, in fact, the advocacy groups are a little bit more flexible and have been able to come up with RFAs which do that and I think the NIH has been responsive but I think particularly within addressing the issues of IACC, looking for creative new solutions.

I know something that INSAR has been thinking about and Dave Amaral and you can tell he is on the Board, talking about having a summer autism camp, essentially, as a way of bringing investigators in to get a smattering over maybe two or three weeks of a number of individuals in different areas.

And so we heard today of course from occupational therapists and just to many different types of providers and universes that need to continue to interact. And we

need to find ways of promoting it. The INFAR meeting is a great way but it is a once a year event. So I just encourage that.

DR. SPENCE: I remember at Cure Autism Now there had been a thought about sponsoring post-doctoral fellows, not necessarily for research but actually for clinical training that one of the issues was that it is very difficult to have a post-doc you need to come with your own money and to do just clinical training, just really work in an autism clinic, learn how to do the diagnosis, learn psychopharmacology, etcetera, etcetera. It is kind of a hard thing to tell a psychiatry department that they need to take that person or tell a psychology department that they need to take that person. So that was something that came up. It was before the merger and I am not really sure kind of where it went. But I thought that was a reasonable way to go.

I will say people were talking

about training. And in pediatrics they are working very hard with papers and toolkits and that kind of thing but it is not part of the curriculum. Child development wasn't even part of the pediatric curriculum when I was a resident and it wasn't all that long ago because I went to med school late. I am not saying I am young, I am just saying I went to med school late.

And I know it is not a neurology. And we had to fight to make the UCLA psychiatry fellows come to the autism clinic. So it isn't something as prevalent as the disorder is and as much awareness there is, there really is a dearth of training.

MS. BLACKWELL: I think one of the things that came out of this exercise for me is that now that we have expanded our "what do we need" column, in this era of diminishing resources, it is going to be very important for the Subcommittee and for the IACC itself to try to decide what is the most important

when we write the plan.

So I mean one of the things our group talked about was that we found it a little unwieldy that some of the objectives had make four studies or make two studies. And we couldn't figure out why four, why two, or why three, or how the numbers got into the plan. So I think that is something the Subcommittee might want to take up. We actually eliminated numbers of studies because we just weren't comfortable dealing with it.

But I do think in terms of the research landscape and the amount of funding that is available, it is going to be really important to prioritize if we can.

MS. REDWOOD: Della, I just wanted to take advantage of what you offered a minute ago, especially with the last panel that met. I wanted to make sure I was understanding you right on this that you are wanting to re-label question number six, "What does the future hold" and to add to that "for the spectrum of

adults with ASD."

And when I look at the disorder, maybe I am wrong, but the majority are still under the age of 21. And I would think parents of some of the other younger children might have questions like was the transition going to be from babies can't wait into the school system. What is the transition going to be from elementary school to high school?

So I wanted to know if that was a unanimous decision from the committee or what was some of the dialogue that made you come to that decision on that question.

DR. HANN: Panel?

DR. MANDELL: A big part of it was trying to interpret what we thought the IACC meant in the first place. So that was it.

So the guiding principle was exegetical. That is, you know, trying to just discern where this was supposed to go, based on the information that was already there.

The other thing I think that

guided that was that we felt that because the needs of adults with autism have been so overlooked that it was worth making sure that there was a place in the report.

And by the way, you know, please feel free to disagree or correct at any point but that we felt that it was really important that that be addressed somewhere very definitively, loudly. Having said that, I think that your point about what the future holds really being about transitions that occur throughout the lifespan is really well taken and that I guess we thought that those, and maybe this is an artificial and potentially iatrogenic distinction, but to think about those transitions as being part for under 21 as being part of question five. And two, becoming an adult and what happens in adulthood as part of question six is I think is how we were trying to address it.

But that may be an inappropriate and, like I said, ultimately harmful way to

address it.

DR. GERHARDT: I would also think though I don't have the numbers, I think it is an empirical question whether or not there are more adults than children is still questionable.

And I would think that if we stick to current diagnostic criteria, that we are going to find comparable just based on population demographics and the fact that they have 60 years of being an adult versus 20 years of being a child. We actually have more adults out there than children just waiting to be diagnosed.

So it is, I think, a very pressing problem as we move forward.

MS. GIBBONS: Also I think that it was almost like biblical exegesis. What did Jesus mean here. You know, and we got the terminology because we weren't privy to the discussions of the authors of the questions, although we did cheat later ask. And we were

confirmed that it was pointed towards adulthood.

But we looked at it actually grammatically. The questions are spoken in the voice of a person dealing with an individual situation for the most part. So for us, felt comfortable interpreting that to mean what does the future hold for the individual not for the future of science, or the future of the diagnosis, or the future.

And we were somewhat pleased to see that the UK rushed that research when we were in the middle of discussions with a headcount of one out of every hundred, just for us, that there had been some head counting for adults.

So we did struggle with that and I was particularly upset that people spent so much time in the public comment period writing those long answers about what they thought the future would hold when we chose to not study that. And we felt confident that the other

panels would address those concerns. So we kind of picked our battle.

Oh, and also I am confident that most of my son's life, he will be an adult mathematically speaking, at least I hope so.

DR. INSEL: So in the same vein, I had a question that I just wanted some clarification on and I am not sure if it is panel one or two.

And maybe this was discussed when I was out of the room yesterday. But a question that we often hear which was not fully addressed in this version of the plan was is there a true increase in the number of kids affected or are we looking at changes in diagnosis or ascertainment or something else. And that seems like a question that science ought to provide a definitive answer on.

Was that something that you talked about either in panel one or two and whether that should be in the plan? Cathy?

DR. RICE: Well I think, Lyn, you

brought that up particularly not just about the increases but also about our studying subgroups and changes within subgroups in terms of prevalence and we were trying to figure out exactly where that was. And my read on the original plan that it was in the last objective in question three but that it really, that was kind of squeezing it in there, that it never really was specifically called out or put in any particular place.

The one area we did talk about it yesterday was in terms of question one in diagnostic issues having more clarity in terms of what is the line. I know we have had a lot of discussions about terminology. But in terms of practical purposes for looking at prevalence, understanding that line between disorder and diagnosis versus features and a consistent way of having tools to measure and assess that would be very essential to answering that question and are getting a handle on it over time. So that is really the

only ways it has been addressed and it seems like a big gap.

DR. INSEL: Right. So, we really what we have, reports of prevalence, there is not, as far as I know, there is only one study of incidence looking at a change in incidents over time in the literature.

And if that is the case, that sounds like a big gap that you would have thought would have been in the plan as a very important initial thing to address. So if it didn't come up in your panel discussions, except in the sense that mean, is this something you think we should take forward the IACC? Because it may be that it is not that important, it just seems important to me.

DR. RICE: Can I respond? So I remember in the first iteration of the plan, when the original I can't remember if they were called workshops or workgroups, whatever was assembled, there were quite a few objectives around that and trying to tease out

it is not just a simple issue in terms of, one we need to understand the numbers in terms of the impacted and who is effected today and what that means for services.

Another issue is that we have kind of polarized this question about is it all awareness? Is it all risk? And it is highly likely, as in everything in autism, it is clearly neither. That we are having a mix of multiple factors going on. And so we do need to understand subgroups and have more complexity of it.

And I don't remember exactly how within the process of what in prioritizing what ended up in version 1.0, a lot of those objectives were removed. So, I can't remember if the whole IACC decided it was because it is a very challenging and possibly never fully answerable question. Is it not worth pursuing? I still think, you know, clearly I have a bias but I definitely still think that is a question worth pursuing and CDC will

continue to work on that, certainly not as fast and not as fully as everybody would like that to be answered. So having that be a priority, I think is very important.

DR. NEWSCHAFFER: Just real quick, Tom on the point about incidence versus prevalence studies.

So in some cases for autism, emphasizing incidence is a bit of a red herring because the utility of incidence over prevalence is predicated on the idea that incidence time is meaningful, that the time of occurrence is meaningful etiologically. And because for autism much of time of incidence is probably related more to factors affecting recognition and diagnosis than the actual incidence of the underlying pathology in some ways compared to something like cancer or heart disease focus on incidence versus prevalence in autism is somewhat less important.

That said, as some recent

literature has shown, looking at cumulative incidence as opposed to prevalence can be somewhat enlightening for understanding things like the effect of changing age at recognition on prevalence numbers. But the epidemiologist often will say you have to study incidence if you are interested in learning about risk. But incidence in autism is a little bit, has somewhat less utility for etiologic research than we commonly think it does for other conditions.

MS. SINGER: I wanted to get back to the discussion of question six. My understanding of when we originally put together question six, it really was not designed specifically just to look at adult. It may be a good idea to change it to look at adults.

I think a lot of the points that were brought up today make sense but that was not the idea, as Lyn was saying, when we put it together originally. It was really to look

at across the life span how people deal with transitions, When a child is just diagnosed, what is the future? A lot of times the future is, are they going to go to mainstream kindergarten. Or the future for someone in elementary school is high school. The future for someone in high school could be college.

So it was really looking at those issues across the life span. And I think our intention, when we put the plan together, we included in the cross-cutting themes, an overall emphasis throughout the entire strategic plan that we needed to focus on life span issues, including issues related specifically to adults.

Now that said, I am not, I think a lot of the points you raised today are good and we should talk about whether we should change section six. But if we do change section six, it also brings up some other issues because some of the items that we included in section six don't relate to

adults.

So this is the area where we put in sort of the other with regard to administrative databases, with regard to questions of prevalence studies, with regard to questions of care giving studies. I mean, question six sort of because this catch all for items that didn't fit neatly into other areas of the plan.

So if we do decide that question six should focus on adults, we may have to look at adding another section so that we can take care of issues that really don't fit neatly into any of the other areas of the plan.

MS. GIBBONS: So does that mean that the smart person who put together this pie chart would have counted Dr. Fein's research under what does the future hold, since you talked about recovery in youngsters? I mean, I don't know who compared it.

MS. SINGER: I can't see all the

way over there. I don't know what you are holding up.

DR. HANN: The backup data for that is included in your book. So we would have to look it up to see exactly how it was coded.

MS. GIBBONS: Okay. I will spend my time doing that then.

DR. HANN: Sorry.

DR. MANDELL: So the challenge with that -- so if that were the case, then I even more strongly encourage a separate panel or a separate workgroup for question six than for question five. But in some ways, that means that question six encompasses questions one through five. Because it becomes all about the trajectory of adults or people with autism from birth onward and there are two separate issues. One is what is the trajectory of autism and the second is what is the interaction of autism in the context in which that individual lives. And that

stretches from birth to death and from biology to philosophy.

And so I guess I wouldn't even -- I would feel overwhelmed then with the task of -- now I can see it. You know, anytime you establish a framework, like here are the six questions that are sort of going to guide how we divvy up work, the framework leaves things out. And you definitely want to have a place to put them.

I would more strongly encourage them, looking at those things that were in six and say where does this really fit? If it is really a priority, then it must fit somewhere between questions one and five. And if it doesn't, maybe the framework of the questions is not as inclusive as it needs to be.

Because having six is that kind of catch-all category would make it very challenging, I think, for any group to meaningfully lay out what the agenda is.

MS. SINGER: Well I think one way

to capture it is some of the issues that came up over the last two days were with regard to replication and databases. And those really are across all five questions. So maybe we need a separate area for those infrastructure issues. We also talked about the need to improve speed with regard to clinical trials. We talked about the need to improve communication and dissemination. And none of those really fit neatly into any of the five questions.

So I think that we should, as a Subcommittee consider how we are going to handle those issues that don't fit in there.

I mean, I actually like the idea of one of the questions focusing on adults. But I think the ramification of moving in that direction is that there are things that are currently in here that are going to get lost. And I just want to make sure that if we move in the direction that panel five is suggesting, that we have a place for some of

these other really important issues, some of which are already in the plan and some of which came up over the last two days.

MS. McKEE: I know we had discussions even amongst the panel members, if we change the title are we going to lose our transitioning use as well? Because there is a lot in here you read the language about the transitioning youth. And so we even have that as a key issue listed, even though we have re-titled the section.

So I think that there is some ambiguity here. We don't want to leave anyone out but we also wanted to highlight the absence of research in the area of adults on the spectrum.

MR. CHAPMAN: And I would just add that I think -- oh. Maybe not that loud I won't add. And also just looking at the narrative that accompanied the strategic plan that oftentimes it was communicating the issue around adults and the lack of information or

knowledge about adult services and what is available and how do people access them. I think that was also part of where we drew from to put some of that focus but I would concur on the transition issue to how we address that.

DR. SAMSTAD: In looking at what Alison was just saying, it almost sounds like you need a category specifically to look at how to improve research in general, how to do things faster, how to get the results out, how to coordinate better. I mean, most of those seem to fall in one category.

DR. SPENCE: I wonder, I know there is the cross-cutting issues and I wonder if that could be just another category. Because I think that that really is where a lot of these things could go, that the databasing really was in almost everybody's sections. And so and the communication was in almost everybody's section.

So I think that even if you did

focus question six on just transition to adulthood or transition to adolescence, I mean the two questions right underneath what does the future hold or what happens when you get to older and what happens to adults. So I mean, really two of the three questions really were that.

And then I think the other one was the database, the support system. And I think that could be something you could deal with just through the cross-cutting issues.

DR. CHUNG: I want to say that having been involved with the writing of that first plan, there is not a lot -- I mean, I am sorry people are trying to read our thinking. It wasn't that we had some great completely coherent framework.

I think the thing to remember is the questions are things that we thought were the questions that individuals who are facing having an individual in their family with an ASD would be asking. And so they were meant

to be consumer-focused. They were meant to try and get as close as to where people's thinking are in the community and the public and then try to walk from their question over to the science, rather than the other way around which was always the case. We have science and we try to explain it to the public. So starting with questions that are pressing and then moving over is the way we went.

Now the way that they are worded may not be perfect and I think is certainly up to the IACC as to whether or not they want to revise it. I think that would be a great way to improve it, if that were the case. But I think that adults were in there but it was meant to be more generic. I can say that.

MS. GIBBONS: Okay. So, Peter takes us back to the book and it says: "What does the future hold? What will my family member be like when he/she gets older? What is known about adults with ASD and how can I

plan for the future? How does American society support people with ASD?"

So we thought we were in the same vein. Maybe we were wrong.

MS. BLACKWELL: Well and I think it is also important to add that we reviewed, as I said earlier, a lot of public comment. And a lot of the public comment went directly to what will happen when my child is an adult. Or my child is an adult and this is what is happening.

So we were trying to also be, as you said Joyce, at the time when we wrote this, I mean, maybe we weren't as clear as we could be, but certainly the public comment reflected that we needed to be addressing the issue of adulthood and transitioning youth.

So I think out group really tried hard to get at that and be responsive in that way.

MS. SINGER: I think however you got there, it is a good improvement. I just I

think to Sarah's point, the reason I would say it needs to be in a separate part of the plan as opposed to in the cross-cutting themes is because of the way we measure the success or failure of the items in the plan.

Just from a very practical standpoint, what gets measured are how well we are doing against a short-term and the long-term objectives.

So my concern is that if we don't take some of the recommendations that we had today with regard to replication, dissemination, focusing on the symptom domains or having a workshop to focus on, which symptom domains lead to the most disability and therefore, need to have the focus, if we don't include those in the short-term objectives or long-term objectives, we won't measure how well we are doing.

And I think one of the reasons why the issue with regard to adults may have come up and moved into its own section, even though

it was in the cross-cutting themes, is because there was no way to measure our success against the cross-cutting themes. So that is why my suggestion would be to take some of these items that have no home and create a place for them, so that we can make sure that next year when we have this review meeting, we can track our progress against some of those items.

DR. STATE: So I understand the rationale behind the way that the questions were put together. I think they are great.

It also seems to me that a question that sort of would lead to that section is from a consumer. How can scientists get their act together in order to be able to advance research? Because I mean, that is largely what we have all been talking about and there are very concrete short-term goals we need to address. And long-term goals in this would include things about communication, and dissemination, and speed,

and access. And I think it is a great seventh question.

Basically, what is wrong with you?

MS. SINGER: No, just, "What else do we need?" I would say would be question number seven. And then that would be an area where we could be in issues of we need more replication. We need certain conferences. We need to speed our dissemination. Something that catches other items. Or "What is wrong with scientists?" would also be fine.

(Laughter.)

DR. HANN: Any other comments?

(No audible response.)

DR. HANN: Apparently not.

Well, I have one. I have a closing comment. I want to thank everyone. Really, I think this has been a very good experience in a number of ways. I commend all of you for the amount of effort and time and thought that you have given prior to these last two days, in terms of the phone calls,

etcetera.

This is the first attempt to try to do this update. The Planning Committee developed sort of this overall strategy but none of us knew how it was going to work. We all just sort of said we will give it a shot and here it goes. And it has been really great.

The other thing that I found which is great when we have groups of people like this together is the opportunity for people who don't necessarily bump into one another to have a dialogue and to get inspired potentially with some other ideas. So the exchange just is one example today between Cathy and David in terms of opening up potentially new vistas to be thinking about. It was great.

And I am sure that has happened for everyone here. And that is really a true benefit of these workshops that in addition to helping the IACC hopefully gets propelled

forward in all of the important work that all of you are doing.

So I really, really want to thank everyone very much. You will probably hear from us again. But I think too, I mean, the IACC has a big task in front of it in terms of how to digest this information and you can follow it along. It will all be out there in public and well known and so forth like that, so you will have opportunities to sort of see that and see how it goes.

So does anyone else have any final comments?

(No audible response.)

DR. HANN: Adjourned.

(Whereupon, at 3:48 p.m., the foregoing proceeding was adjourned.)