

INTERAGENCY AUTISM COORDINATING COMMITTEE

FULL COMMITTEE MEETING

TUESDAY, OCTOBER 24, 2017

The full Interagency Autism Coordinating Committee (IACC) convened in Rockville, Maryland, at the National Institute of Mental Health (NIMH), 6001 Executive Boulevard, Conference Rooms C&D, at 9:00 a.m., Joshua Gordon, M.D., Ph.D., Chair, presiding.

PRESENT:

JOSHUA GORDON, M.D., Ph.D., *Chair*, IACC, Director, National Institute of Mental Health (NIMH)

SUSAN DANIELS, Ph.D., *Executive Secretary*, IACC, Office of Autism Research Coordination (OARC), NIMH

DAVID AMARAL, Ph.D., University of California, Davis (UC Davis) MIND Institute

JAMES BALL, Ed.D., B.C.B.A.-D, JB Autism Consulting, Chair, Autism Society Board of Directors (attended by phone)

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

DIANA BIANCHI, M.D., Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD)

PRESENT: (continued)

SAMANTHA CRANE, J.D., Autistic Self Advocacy Network (ASAN)

GWEN COLLMAN, Ph.D. (representing Linda Birnbaum, Ph.D.), National Institute of Environmental Health Sciences (NIEHS)

GERALDINE DAWSON, Ph.D., Duke University

RUTH ETZEL, M.D., Ph.D., Environmental Protection (EPA)

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

MELISSA HARRIS, Centers for Medicare and Medicaid Services (CMS) (attended by phone)

JENNIFER JOHNSON, Ed.D., Administration for Community Living (ACL)

LAURA MAMOUNAS, Ph.D. (representing Walter J. Koroshetz, M.D.), National Institute of Neurological Disorders and Stroke (NINDS)

DAVID MANDELL, Sc.D., University of Pennsylvania

KEVIN PELPHREY, Ph.D., George Washington University and Children's National Medical Center

EDLYN PEÑA, Ph.D., California Lutheran University

LAURA PINCOCK, Pharm.D., M.P.H., Agency for Healthcare Research and Quality (AHRQ)

PRESENT: (continued)

ROBERT RING, Ph.D., Vencorx Therapeutics
(attended by phone)

JOHN ELDER ROBISON, College of William and
Mary

MARCELLA RONYAK, Ph.D., L.C.S.W., C.D.P.,
Indian Health Service (IHS)

ROBYN SCHULHOF, M.A. (representing Laura
Kavanagh, M.P.P.), Health Resources and
Services Administration (HRSA)

STUART SHAPIRA, M.D., Ph.D., Centers for
Disease Control and Prevention (CDC)

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

MELISSA SPENCER, Social Security
Administration (SSA)

JULIE LOUNDS TAYLOR, Ph.D., Vanderbilt
University

LARRY WEXLER, Ed.D., U.S. Department of
Education (ED)

NICOLE WILLIAMS, Ph.D., U.S. Department of
Defense (DoD)

CARRIE WOLINETZ, Ph.D. (representing Francis
S. Collins, M.D., Ph.D.), NIH

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PROCEEDINGS

DR. JOSHUA GORDON: I want to welcome the members of the Interagency Autism Coordinating Committee and the public audience to this meeting of the Interagency Autism Coordinating Committee.

I want to first thank two public members who have departed from the committee. Amy Goodman, who left because she found a new job, and therefore was no longer eligible to serve in that slot, and Brian Parnell.

I want to welcome Carrie Wolinetz, Acting Chief of Staff, and Associate Director for Science Policy, in the Office of the Director of the NIH, who will be representing NIH director, Dr. Francis Collins on the committee.

Next, the first order of business, Susan is going to take roll call and present the minutes from the last meeting.

DR. SUSAN DANIELS: Thank you. Alright,
so let us go through the roll call. Joshua
Gordon.

DR. GORDON: Here.

DR. DANIELS: Jim Battey.

DR. JAMES BATTEY: Here.

DR. DANIELS: Diana Bianchi.

DR. DIANA BIANCHI: Here.

DR. DANIELS: Linda Birnbaum or Cindy
Lawler.

DR. GWEN COLLMAN: Gwen Collman is here
representing Linda Birnbaum.

DR. DANIELS: Oh, Gwen Collman. Carrie
Wolinetz.

DR. CARRIE WOLINETZ: Here.

DR. DANIELS: Ruth Etzel.

(No response)

DR. DANIELS: Tiffany Farchione.

(No response)

Melissa Harris.

(No response)

Jennifer Johnson.

(No response)

Robyn Schulhof.

MS. ROBYN SCHULHOF: Here.

DR. DANIELS: Laura Mamounas for Walter
Koroshetz.

DR. LAURA MOMOUNAS: Here.

DR. DANIELS: Laura Pincock.

DR. LAURA PINCOCK: Here.

DR. DANIELS: Marcella Ronyak.

DR. MARCELLA RONYAK: Here.

DR. DANIELS: Stuart Shapira.

DR. STUART SHAPIRA: Here.

DR. DANIELS: Melissa Spencer.

MS. MELISSA SPENCER: Here.

DR. DANIELS: Larry Wexler.

DR. LARRY WEXLER: Here.

DR. DANIELS: Nicole Williams.

DR. NICOLE WILLIAMS: Here.

DR. DANIELS: David Amaral.

DR. DAVID AMARAL: Here.

DR. DANIELS: Jim Ball.

DR. JAMES BALL: Here.

DR. DANIELS: Samantha Crane.

(No response)

DR. DANIELS: Geri Dawson.

DR. GERALDINE DAWSON: Here.

DR. DANIELS: David Mandell.

(No response)

DR. DANIELS: Kevin Pelphrey.

(No response)

DR. DANIELS: Edlyn Peña.

DR. EDLYN PEÑA: Here.

DR. DANIELS: Louis Reichardt.

(No response)

DR. DANIELS: Rob Ring.

DR. ROBERT RING: Here, on the phone.

DR. GORDON: David Mandell just walked

in.

DR. DANIELS: John Robison.

MR. JOHN ROBISON: Here.

DR. DANIELS: Alison Singer.

(No response)

PARTICIPANT: I just saw her outside.

DR. DANIELS: Okay, great, thanks.

Julie Taylor.

(No response)

DR. DANIELS: So is there anybody that I missed that I didn't call? Yes, we heard about you, David. Thanks. We've heard about you. I think we are through the roll call. So next is approval of the minutes.

So you have in your folder the draft minutes from the last meeting. Did anyone have any corrections or comments on the minutes?

So, can we have a motion on the floor to accept the minutes?

DR. BIANCHI: So moved.

DR. BALL: So moved.

DR. DANIELS: All in favor.

(Chorus of "ayes".)

DR. DANIELS: Anyone opposed?

(No response)

Anyone abstaining?

(No response)

The motion carries to accept the minutes as written and they will be posted to the IACC website after the meeting. Thank you.

DR. GORDON: Actually, you are going to continue. You are going to provide us some update from HHS Office of the National Autism Coordinator.

DR. DANIELS: I wanted to give you an update from the HHS Office of the National Autism Coordinator. Dr. Thomas Novotny, from the Office of the National Autism Coordinator, did previously provide updates at each IACC meeting to keep you posted on

the activities of that office. He stepped down in August 2017. He served as National Autism Coordinator from April 2016 to August 2017. During that time his major project was to help lead the development of a report to congress that was required in the Autism CARES Act on Young Adults and Transitioning Youth on the Autism Spectrum. My office, the Office of Autism Research Coordination, also assisted with leading that report.

Since Dr. Novotny's departure, I have stepped into help with the continued implementation and dissemination of this report. So I will be giving you an update on the report, which has been completed and you have a copy at your place here. For anybody who is in the public audience that would like a copy, they are outside. We have it up online, the PDF, and if somebody needs a hard

copy you can always write to the office and ask for one.

So I am going to take you through this report so you can hear about what the report has in it. We can discuss it a little bit.

Just as a reminder, the Autism CARES Act supports a number of federal autism activities. It came into existence on August 8, 2014. It is a reauthorization of the Combating Autism Act and the Combating Reauthorization Act.

It reauthorized this committee and it requires a couple of reports to congress. One is a report to congress on young adults in youth transitioning to adulthood. That is the report that we are going to be talking about today. It also requires a report to congress on all federal activities related to ASD, which is a project that hasn't started but will be led by the ORAC in the coming year.

The act, of course, reauthorize support for several autism related efforts across the government from FY15-19.

With this report, the purpose of this report in the law is to summarize existing Federal investments in transition research and services activities.

And also to identify gaps in Federal research programming, and services that support youth with ASD during the transition to adulthood.

So to give you a little background on the development of this report, the Office of the HHS National Autism Coordinator convened a federal working group, an internal working group, to develop this report.

So the Steering Group for the report included Thomas Novotny, myself, Alicia Richmond Scott, from the Office of the Assistant Secretary for Health, Robin

Harwood, who was detailed from the Health Resources and Services Administration. She helped actually, do some of the writing and editing of this report. And Julianna Rava, from my office, as a science policy analyst, to help out with the production of this report.

We had a Stakeholder Expert Panel that contributed as well. Our office provided IACC Stakeholder input to the report. There are number of people here at the table, who participated in this. I wasn't able to list all the members of the interdepartmental transition working group because it is a very large list, but in terms of the agencies represented, there were NIH, HRSA, CDC, CMS, FDA, AHRQ, ACL, ACF, HIS, SAMHSA, and a number of HHS offices, including the OASP, ASPE, ASL, OGA, OASA.

Among other departments, U.S. Department of Labor, Department of Education, Department of Transportation, Department of Housing and Urban Development, Department of Justice, Department of Defense, and the Social Security Administration.

It was significant coordination, that had a lot of membership across the entire federal government.

The Stakeholder Expert Panel that was invited to provide additional expertise on issues related to transition, and especially pointing out many gap areas, is included on this list. It includes some people that are sitting here at the table or are in the room. I wanted to express appreciation to everyone, all the federal members, and all the public stakeholders who helped with the development of this report.

So the structure of the report, it comes in four parts. It has background information on ASD and the transition to adulthood. All of these parts are required in the law. An overview of relevant federal programs. Three, is input from key stakeholders. Which wasn't specified exactly in the report, but it was something that the National Autism Coordinator felt would be very important for helping us identify gaps. It also includes conclusions and recommendations.

In overview, some of the challenges associated with transition for youth on the autism spectrum transitioning to adulthood include; include complexities caused by the heterogeneity of ASD and any co-occurring health and mental health conditions. Which results in a wide variety of needs that need to be met by a system of diverse services.

This is magnified by complexities in transitioning from a set of supports that's coordinated around and through the educational system to a set of health and social service systems geared to adults that may be provided by many different agencies and services that are not necessarily coordinated.

The report requirements included a review of the literature to be able to characterize the population. There were a number of facts that were stated in the report and all the citations are in the report. But it is estimated that 50,000 youth with ASD will turn 18 each year. Currently, about 450,000 youth with ASD aged 16-24 years old are living in the U.S.

Health and wellbeing in secondary school, that when compared to all youth with IEPs, youth with ASD who have IEPs are more

likely to have co-occurring chronic health or mental health conditions. Less likely to be able to manage independently and develop friendships. Less likely to take steps to prepare for college and employment.

In terms of the health and wellbeing of young adults that are in the age range of 20 to 25 years old, less than 1 in 5 had ever lived independently following high school. Nearly two-thirds receives SSI benefits. Only 58 percent had ever worked in their early twenties. And only 36 percent of youth with ASD had ever participated in postsecondary education or training of any kind between high school and their early twenties.

In terms of adulthood, adults with ASD compared to the general population, die an average of 16 years earlier than people not on the spectrum. Are 40 times more likely to die prematurely of a neurological condition

(such as epilepsy) if they also have a learning disability. Are 9 times more likely to die from suicide. Are at heightened risk for co-occurring conditions such as depression and anxiety. And are at higher risk for other non-communicable diseases including diabetes and heart disease.

This is pretty small type. I should of expanded this a little bit. These are some of the topics that emerged through IACC public comment that we collected as we were preparing the strategic plan. So our office went through and teased out all of the information that we could gather on what members of the public were telling us about the needs for transition age youth and young adults.

The areas of concern included services and supports that were more personalized toward individual needs. Postsecondary

education and training opportunities;
employment, treatment for concurrent
conditions, and access to occupational,
speech, and language therapies in adulthood.

Housing, transportation supports,
community integration services and supports,
coordinated or wraparound services. Relief
from barriers to access, coordination and
finance, and the fact that services are often
piecemeal for adults. They are not
coordinated in a way that makes it easy to
access. Then transition supports and
information that being at an earlier age.

The people who wrote in for this were
mostly family members, people on the
spectrum, other advocates.

So from our Stakeholder Input Panel, we
identified a number of gaps in research,
including gaps in descriptive data about this
population. The lack of existing programs

that are available to study to identify what works and doesn't work. Outcomes research to identify what kinds of outcomes are needed and what kinds of outcomes we actually have at the moment. And research on access and barriers to service.

In terms of services and programming, they identified the need for individualized planning to address heterogeneity issues. Coordination and comprehensive care that is responsive to individual needs. Earlier planning for transition.

High-quality services and programming that challenge individuals to achieve their highest potential and not as identified by a particular member of our stakeholder panel, leaving people with low expectations and thus not achieving their potential.

Better coordination of services. A strengthened workforce and increased access.

I guess I can keep going through these. I know this is kind of dense. This is a pretty big report and I am trying to consolidate it into a few points so you can get a flavor for what the report contains.

In terms of challenges and barriers to services; a number of points were identified including the coordination of services, access to a number of different types of resources. Facilitating managing a complex condition and co-occurring conditions. Independent living. Developing meaningful relationship and broader social networks to support people. The lack of availability and consistency in ASD-specific kinds of training and supports for adults. Communication challenges that have not been addressed or don't have a way of being addressed on an ongoing basis for adults. And the need to build a greater community understanding ad

acceptance of neurodiversity so that people have an easier time integrating into society as adults.

So in terms of research, part of the report addressed what research is ongoing right now in the space related to transition. The finding of the report was that there are four agencies; NIH, HRSA, Department of Education, and Department of Defense, that funded a total of 18 project devoted to transitioning youth with ASD that were funded between FY13 and FY 16. Which is a very small number of projects.

The portfolio analysis from the Office of the Autism Research Coordination, my office, identified with the 2015 project data across the entire U.S., that lifespan issues received about two percent of the funding. If you narrow that down to just transition research, it was more like one percent of the

funding - combined federal and private funding for autism research.

In terms of programs that provide services and supports. This was divided in the report to cover mainstream programs that are available to all U.S. citizens that meet certain eligibility requirements. But one of the drawbacks is that they do not usually track the diagnosis of ASD. So if someone were to be doing research on data related to those mainstream programs they might not be able to get ASD specific information.

There are cross-disability services and supports, but many do not track utilized services and goals according to specific diagnoses such as ASD. There can be differences in the eligibility requirements which can make it hard to compare.

Then there are some Autism CARES Act Programs, including population surveillance

and risk factor research at CDC. Then capacity building through training and intervention research that takes place at HRSA.

In terms of federal programs, ASD research and programming conducted under and it is administered through multiple agencies about all kinds of research and programs for ASD across a lot of different agencies.

Most provide broadly targeted programs that individuals with ASD may be eligible for if they meet program criteria. But oftentimes, programs are not necessarily tailored to people with ASD. In those cases, those kinds of broad programs don't track specific diagnoses and make it difficult to collect data.

So the report concluded that there is a need for a coordinated comprehensive approach to services and supports. Support

coordination across services systems. Increased family and caregiver support through adulthood. And data and research on transition-age youth and young adults with ASD. So we can really understand the needs and be able to improve the services that we are providing.

So the recommendations of the report included a few different areas. In terms of epidemiological data collection and monitoring the working group identified the need to assess and monitor experiences, needs, and life goals of transitioning youth with ASD and young adults.

The need for the National surveys to assess the full range of services and supports needs, barriers, and facilitators because some of them are not maybe collecting a full a set of data as would be desirable.

A more complete surveillance system to provide data on the full spectrum of autism in transition-age youth and young adults with ASD.

Longitudinal data to follow up on transition outcomes for individuals with ASD. Today in our SEED presentation we will hear a little bit about that.

In terms of research, some of the needs identified are targeted outcome research to assess efficacy of transition-oriented programs.

Program models to develop and test. Meaningful outcome measures or identifying what would be meaningful outcome measures to improve research. More research towards implementation and service delivery. And encouragement of more research that specifically on transition age youth and young adults with ASD and their caregivers.

In the area of program services and delivery, the report identifies a number of important recommendations. They wanted to identify coordination as a very important target that is necessary across federal agencies and across service systems at a state and community level, as well.

More integration of those programs that need to be designed for broad access, but with individual flexibility.

The need for more trained personnel to help families navigate multiple, complex service systems.

Better preparation of all relevant adult service and support providers, being essential.

Increased coordination between youth and adult services and supports.

Federal policies that encourage blending and braiding of funds across agencies which

that was identified as a key barrier because it is hard to do now.

Concerted communications efforts are important in order to dispel the stigma and encourage acceptance that will help people as they transition.

To tell you a little bit about the follow up. The HHS Office of the National Autism Coordinator was leading efforts on developing this report and was planning to follow-up on this report, but at the moment the office is vacant. So in the meantime, my office is helping out with some continuation of this but it will be up to HHS to decide how they want to continue with this process.

One of the things that we do have ongoing right now is that we have been seeking opportunities to collaborate with the Federal Partners for Transition working group. We actually just had a meeting of the

FPT the other day. I was able to co-present with Scott Michael Roberts in this report to the FPT. The FPT is a working group with several representatives from several federal agencies, including the Departments of Education and HHS, Labor, and the Social Security Administration.

It was formed in 2005 to support all youth, including youth with disabilities, successfully. One of their major products was the 2020 Federal Youth Transition Plan that addresses the entire general population.

We met with the FPT to talk about this report and what we have identified as key needs for ASD to compare with what they are identifying for the general population. The FPT was very engaged and very excited about working with any ongoing efforts that would come out of this report from HHS. They are

very interested in engaging with the IACC, as well.

I am letting you know that in the future maybe we can invite representatives of the FPT to talk here with you all. They would like to see us work together, not to duplicate effort but to identify what are the key areas that we need to work on separately for ASD and which things that we have identified that are needed for ASD might be able to be incorporated into larger transition programming.

The report is available on online. You have copies. Those are my comments. If anyone has any questions I will be happy to answer them.

David.

DR. MANDELL: Congratulations on a very comprehensive report.

DR. DANIELS: Thank you, and to the entire working group that put this together.

DR. MANDELL: So I am reading through the recommendations, which I think attempt to synthesize a lot of stuff. The recommendations are still pretty broad. I wonder if the group had any ideas or if there was any consensus about more specific next steps that this group should be advocating for?

DR. DANIELS: I think that was the follow-up to the report that now with a gap at HHS in this area, it is not certain what is actually going to happen but I think that the IACC, if they are interested, if you all are interested in this area, could certainly also be a part of that follow-up, as you also have a mandate to be looking at all issues related to ASD.

The agencies that participated are all very much engaged as well, but I think that we need some kind of impetus to keep efforts moving.

Any other questions around the table?

Alison.

MS. ALLISON TEPPER SINGER: Are their plans to appoint a new National Autism Coordinator?

DR. DANIELS: I think that they are working on that at HHS. I don't know what the details are at this moment. Right now in the Office of the Assistance Secretary of Health there is some reorganization based on the changed administration that is still ongoing. I assume that we will hear something in the future but I don't know exactly when.

Anything else? Thank you very much. Feel free to talk to me afterwards if something comes up and you are interested in finding

out more about the report or what we can be doing to keep this area moving because we all know it is really important.

Thank you.

MS. MELISSA HARRIS: This is Melissa Harris at CMS. I wanted you to know that I was on the line.

DR. DANIELS: Hello, Melissa.

DR. GORDON: I see that Alison Singer has arrived. Anyone else who missed the roll call? Julie Taylor

Thank you, Susan. It is something for this group to consider is how much to remain involved in efforts to define the Interagency efforts around transition. Just looking over the document myself, I noticed two things. There are hundreds of programs and I agree with the overall recommendations. How does one person even navigate to figure out which

ones they are eligible for? In reading this document, it is rather challenging.

The second one is that there is not really - none of these programs are actually truly autism specific - or I should say, very, very few. That is probably well and good because lots of people share common issues around the age of transition. But at the same time, going back to the first point, how is someone with autism to approach this to figure out which programs they are eligible for, is very challenging and without some central coordination I can imagine that it will remain challenging.

Moving on, our next topic of the day - actually just let me sketch out the day. This morning we are going to hear in a few moments, from the CDC on their Study to Explore Early Development. We will have some discussion around that. Then we will take a

break and we will turn to committee business, where Susan will announce the final publication of the update of the strategic plan. Where we will turn our attention to what the committee will be tackling next.

Then we will have lunch. After lunch we will have a public comment session. We have several members of the public who have come to testify before us today, as well as the usual written summary of comments from people who have submitted them online.

In the afternoon, we are going to have a science session on autism and suicide. You heard earlier from Susan's report on the Transition Report that individuals with autism are nine times more likely to die from suicide. It is not something that we think about all that often. But we are going to hear from several presentations from scientists from both here at NIMH and

elsewhere, as well as from the Deputy Director of the National Action Alliance for Suicide Prevention.

Following that we will have our discussion of the summary of advances and then round robin discussion at the end. So that sketches out the day.

But as said, first we are going to hear from Dr. Stuart Shapira, who is of course, a member of our committee, from the CDC. He and his colleagues, are going to be sharing an update on the Study to Explore Early Development.

Stuart, would you mind taking the podium and introducing your colleagues and commencing with the program.

DR. SHAPIRA: Good morning. It is a pleasure for our group to provide an overview of SEED, the Study to Explore Early Development, to the committee this morning.

We have a number of speakers. Their biographies are in the packets that have been distributed. I would like to just go ahead and get started and call our first presenter, Nicole Dowling, who is Chief of the Developmental Disabilities Branch at the CDC, to the podium.

DR. NICOLE DOWLING: Good morning everyone. Thank you, Stuart, and thank you to Susan Daniels and Joshua Gordon for the invitation to be here today. This is a really nice opportunity and we are pleased to be able to share some of our ongoing work about the Study to Explore Early Development.

Really the timing for this presentation I think it really could not be better today. We have been thinking about - SEED has been in the works for a long time. We have been building the study, collecting data for many years now, and we are now really at the point

where we will be publishing findings from multiple studies, with about 40 manuscripts or more, that have gone through CDC clearance and are in some stages of publication. Some already out, and as many in the pipeline, if not more.

This really is a nice opportunity and I hope that we will be able to come back and share along the way, as we continue to have more findings.

SEED, just to give you - you will hear a lot more about SEED from my colleague, Dr. Laura Schieve, but just to give you the high points. It is one of the largest studies of ASD risk factors in the U.S. and we have enrolled over 6,000 children and their families to date, in the study. These are from families from very diverse communities throughout the United States. The methodology

for the study is also quite rigorous, and you will hear a good deal about that as well.

SEED will contribute to the growing and complex body of knowledge around what puts children at greater risk for autism, with a key strength being the ability to look simultaneously at detailed information on characteristics, environmental factors, genetic factors, as the study includes collection of bio-specimens from all the participants.

I wanted to start by just giving you a big of context about how SEED fits into CDC's broader efforts around ASD. We work within CDC's National Center on Birth Defects and Developmental Disabilities within the Division of Congenital and Developmental Disorders.

The vision of our division is healthy birth and optimal development for all

children. With a mission to be the public health leader in preventing the occurrence or adverse consequences of birth defects, developmental disabilities, and pediatric genetic conditions through surveillance, research, and intervention programs.

I included this just to give you a snapshot of our current organizational structure. Sometimes that is helpful. I know it is always complicated to think of how all these government agencies are organized. Just to give you a snapshot, this is of our division, the Division of Congenital and Developmental Disorders. We are within the Developmental Disabilities Branch. We have three branches within our division and we have two teams within our branch. One conducting epidemiologic research, where SEED resides, and then the other, the surveillance team, which you all are familiar with our

Autism and Developmental Disabilities
Monitoring Network.

I also should mention, you have heard in previous meetings of this committee, about the Learn the Signs. Act Early. Program. While not located within our branch, the Learn the Signs. Act Early. Program is with our sister branch, the Prevention Research Translation Branch.

Just briefly, the focus of CDCs autism programs are to one, track the number of characteristics of children with Autism Spectrum Disorder and other developmental disabilities. Two, to conduct research about what puts children at greater risk for ASD. Three, to improve early identification of developmental delays and disabilities so children and families can get the help they need.

The Study to Explore Early Development or SEED, is a case-control study conducted at five extramural sites and one additional site in Georgia, which is led by the CDC. The study had three phases, we are currently collecting data for phase 3. We also include a bio-repository and a Data Coordinating Center.

You will hear today also about SEED Teen, which is our newest study that is part of the SEED network. It has been newly launched and is being implemented by one extramural site, and also within Georgia, by the CDC. We anticipate data collection for SEED Teen, are hopeful it will begin early in 2018.

This map shows you the location of our currently and previously funded SEED sites, as well as a bio-repository and the Data Coordinating Center.

Just to give you an idea of where we are going today with this presentation, we look forward to sharing a good bit of information with you about SEED, and then having time at the end for a panel discussion and questions from you all.

Just briefly, you will hear first from Dr. Laura Schieve, my colleague at CDC, who is the PI of SEED, to talk about the study methods and also about some risk factor studies, you will hear also from Dr. Laura Schieve and Dr. Danielle Fallin, who will present on behalf of Dr. Lisa Croen, who has joined us by phone today.

We will hear then also from Dr. Fallin about ongoing work to evaluate genetic associations, and from Dr. Ann Reynolds, who will share findings from her work, to assess health effects for children with ASD.

Last, but not least, Dr. Stuart Shapira from CDC, will present his work to characterize dysmorphology for children with ASD. Again, following the presentations, we will have time for Dr. Shapira will lead us in a discussion and question session. I do ask if you could please hold your questions to that point, and then we will have enough time for a rich discussion.

So, thank you. I am now pleased to introduce Dr. Laura Schieve.

DR. LAURA SCHIEVE: Thank you. I would like to start by thanking Susan Daniels and the entire Committee for your invitation to present some of our work. I would also like to thank on SEED who very generously agreed to come here today and take part in this presentation. I know it will be a much richer presentation getting to hear from them directly.

So as Nicole mentioned, SEED has completed two phases of data collection and we have just embarked on our third. In all phases we have maintained three overarching objectives. We look at risk factors for ASD, with a focus on genetics, and also non-genetic exposures that occur in the pre-natal period. We are looking to characterize the ASD phenotype and to assess the health of children with ASD and other DD.

So it is a case-control study. The intention and design of this study to enroll a demographically diverse population of children from various areas in the United States.

All phases of SEED follow a common protocol in which we enroll three groups of children and their mothers. Our ASD case group, and then two comparison groups;

children of other developmental disabilities and children from the general population.

We identify our ASD and our other DD group from various schools, special education programs and clinics in each study area that service pre-school age children with developmental needs. We identify our population controls from random sampling of birth certificates of each site.

We target defined birth cohorts in each phase. Those are listed here. And we enroll children and collect their data when they are 30-68 months of age.

An important feature of SEED is our standardized case classification strategy. At enrollment, children come into the study as being a presumptive ASD, DD, or POP group child. Depending on how we identify them and whether they have a previous diagnosis.

But at enrollment, we screen everyone for autism symptoms. We use the Social Communication Questionnaire, so any child who has a high SCQ score, also any child with a previous ASD diagnosis, regardless of their SCQ score, is considered a possible case at that point. Those children and their mothers will undergo our confirmatory assessment, which are the ADOS and ADIR. I think most of the people on the committee are familiar with those.

And then those who meet our final criteria on the ADOS and ADIR, will be the ones that are classified as our final cases.

Okay, so we collect a lot of data in SEED. This table summarizes our data collection for SEED 1. As I mentioned, we started with the SCQ. Then we conducted an in-depth telephone interview with the mother. We asked her about the family socio-

demographics, her reproductive health history, and her pregnancy exposures. Next we asked the mother or other caregiver, to complete a variety of forms on the child's and family's health history, and also the child's current behaviors and development.

At that point we ask that they come in for an in-person visit, either the study sites clinic or in Georgia, we also do some home visits. We do a number of things there. We give an in-depth developmental assessment, whereby all children are given a general developmental assessment consisting of the Mullen Scales of Early Learning. And those who were classified as possible ASD cases, giving them additional assessments.

We collect bio-samples from the child and from both biological parents, if they are available and willing. Then we have trained staff conduct a general physical assessment

whereby they take measurements and photographs. Those will be shared with a team of medical geneticists, who will assess whether the children have dysmorphic features.

Dr. Stuart Shapira is going to tell you more about that in a minute, but basically they are looking for physical features that don't follow a typical pattern of growth or development. Then we asked mothers to complete and return a three-day diet diary and a seven-day stool diary for their child.

Finally, we asked for their consent to abstract both their records and the child's medical records. So a comprehensive data collection protocol.

We kept the same basic protocol when we went to SEED 2, but we streamlined it a bit. We took out our dysmorphology and diet and stool diaries, because these have been really

pretty labor intensive for our participants and we felt that we had collected sufficient data in SEED 1. But we did retain a few of the basic child measurements; weight, height, and head circumference. So these are pretty easy to collect.

We reduced the number of forms for the mother to complete. We cut them in half by consolidating a lot of the health history information and cutting out a few of the developmental forms that we were asking them to complete.

We did add one brief form, a maternal and child residential health history form - history form, not health history, because that will help us better understand residential environmental exposures. We started collecting saliva in place of buccal samples, to increase our DNA yield for those

cases where we are not able to obtain a blood sample.

And then the SEED 3 protocol, very similar. Streamlined a bit further that eliminating the medical record abstractions. Those have been very valuable, especially in helping us understand the validity of our self-reported health history data, but we were not getting medical records on a 100 percent of our sample and they were a resource intensive part of the study.

As Nicole mentioned, we have already enrolled over 6,000 children, and that includes over 700 cases in each of our first two phases of SEED. We expect this to be very similar when we get to SEED 3, as well. We have more individuals in each of our comparison groups. But I will say that when we look at any individual analyses, these are the numbers enrolled, our actual numbers that

contribute to a given analyses will be less, because we have various amounts of missing data because not everybody completed all study steps.

So SEED 1 is ongoing. We have completed over 40 papers, and 17 of these have been published or are currently in press.

We have just finalized our data files for SEED 2. and We have already begun planning many additional analyses and many of our investigators have already implemented some analyses with our expanded sample size.

Seed 3 data collection, we just started collecting in August.

So I am going to switch gears for a minute and tell you a few things about SEED Teen. So the objectives are to compare adolescents with ASD, with developmental disabilities, and in the general population. So our same three groups. We are going to be

looking at their developmental trajectory, health and functioning, healthcare utilization and needs, education attainment and needs, and several family impacts.

The first phase will be a follow-up of children enrolled in our SEED 1 case control study. We will include children from four of our six sites. Data collection will occur when these children are about 14 to 15 years old. And as Nicole said, we expect that to start soon. Sample size estimates for eligible children are about 1,400. That is the number we initially hope to trace and invite.

So in terms of data collection, we are going to ask the mother or other primary caregiver to complete two questionnaires. The first one is the Social Responsiveness Scale, that is a standardized form that we also included as one of the forms in our case-

control study. Those data are going to allow us to assess the child's developmental trajectory on a few key aspects of child development.

The second questionnaire we developed, the study investigators. We will be collecting a wide-range of data on various aspects of child's health and development and also the mothers or other caregivers health.

Total data collection time is about an hour. So it is a much shorter protocol. Then we are also going to take this opportunity to ask those responding who previously provided us bio-specimens in SEED 1, if they will provide consent to share some of their genetic data with NDAR and dbGaP because when we originally started SEED1, those NIH repositories were not yet on our radar so we did not get that specific consent.

As Nicole mentioned, now we are going to try and show you some highlights of how we are actually using our SEED data. We looked through the many great papers, we chose five that really, I think, highlight the breadth of subject matter that we are able to address. I think these studies also showcase how this very rich database is allowing us to make some novel contributions to the field.

I am going to kick this off by telling you about a study we just completed on ASD and Birth Spacing. I would like to start by thanking my co-authors, the SEED network staff, for all of their hard work collecting these data, and the many families who contributed their time and were so dedicated to making this project a success.

There have been in previous studies, that have reported associations between ASD and birth spacing. But they have had some

limitations. Case definitions were often based on non-standardized diagnostic coding. There has been limited assessment of case subtypes. No assessment of other non-ASD developmental disabilities. And little examination of the why or the underlying mechanisms for the associations.

As I just told you, with SEED, we had a lot of very nice data to address some of these limitations. So this analysis is of SEED 1 data. And we necessarily limited it to children who were second or later births. We defined inter-pregnancy interval as the time between the mother's previous birth and the estimated data she conceived the study child. And then short and long birth spacing were defined as IPI's of less than 18 months or greater than or equal to 60 months. Neither of these are rare occurrences.

So about 16 percent of our POP controls had a short IPI and 33 percent had a long IPI. That is comparable to what we see in the U.S. overall.

We compared several case groups to our POP controls. So we looked at the total ASD group. Then also sub-divided the ASD kids into those with and without intellectual disability. Also, those with a high symptom severity score for core autism symptoms versus a lower symptom severity score.

We looked at the total DD group. Then we also sub-divided those into those with or without intellectual disability as part of their disability. We also looked at those with or without ASD features. So none of the kids in our DD group have a classification of ASD, but some of them did have autism traits reported.

We derived odds ratios from logistic regression and we adjusted for several demographic factors. We ran our analysis both for the total sample, and for a sample that we limited to children born at term. That eliminates some competing risks that might be there because preterm delivery is also a risk factor for ASD.

Then we assessed several factors possibly related to the underlying mechanisms.

Turning to results. This slide shows odds ratios for associations between IPI and ASD and it shows both the total sample and the term birth. What we observed was a modest association overall. An adjusted odds ratios of 1.3 or 33 percent higher odds of short births spacing in the ASD group versus the POP group. That association is a little bit

more pronounced when we look at the term birth group.

Now when we looked at our various sub-groups there wasn't much difference depending on whether or not the child had intellectual disability, but there was a pretty big difference depending on their autism symptoms severity. So the most pronounced association was with those children who had ASD and had the highest scores of symptom severity.

Then this is the findings for our associations between long birth spacing and ASD. It looks really similar to the graphic I just showed you. Modest associations overall, slightly more pronounced when you get to the term births, and much more pronounced when we look at those ASD cases with the highest symptom severity.

We also looked at the total IPI distribution in our sample. We ran a cubic

spline analysis. That allows us to assess associations that don't necessarily follow a linear pattern. That is what we have here. We again, see a U-shaped association such that both short and long inter-pregnancy interval is associated with increased risk for ASD. Then the lowest ASD risk occurred at about 18 to 60 months.

We conducted several further analysis to see if these associations with having a short or long birth spacing were really because those pregnancies might be more likely to be unplanned and thus possibly less health conscious, whether they were linked to more maternal infertility disorders or whether they were linked to maternal complications during pregnancy.

We find that none of these factors explains the associations that I just showed you.

In contrast to our findings for ASD, when we looked at other non-ASD developmental disabilities, we found that there was no association with either short or longer spacing. This flat line indicates no association.

This is looking at the total sample but the line is also flat. Very similar results when we look at term births only or when we look at any of those sub-groups that I had mentioned.

What these results tell us is that in our sample, the association we saw for ASD appears to be very unique to ASD, rather than being reflective of a more general neurodevelopmental effect.

In conclusion, we found that ASD is associated with both short and long birth spacing, particularly in those children with a high ASD symptom severity.

The association was not explained by several pregnancy factors, which we had data to examine, nor was it explained by demographic difference between groups.

Two areas to investigate further are maternal nutrition and inflammation. Both depleted maternal nutrition stores and lingering information from a previous pregnancy have been hypothesized to be potential reasons for the association with ASD. We could not investigate those factors here.

Thank you for your attention. With that, I would like to turn it over to Dr. Daniele Fallin to present two talks.

DR. DANIELE FALLIN: Hi everybody. I am Dani Fallin. I am the PI of the Maryland SEED site. Where I am the Chair of the Department of Mental Health and the Wendy Klag Center for Autism and Developmental Disabilities at

the Hopkins Bloomberg School of Public Health. Right now I am going to do my best to impersonate Dr. Lisa Croen, who is at Kaiser, Division of Research, in Northern California, because she could not be here today and because I collaborated with her on this particular paper, I offered to give this on her behalf. Although she is on the phone, so I think during any questioning/answering time, she may be able to participate in that.

So this first part is on behalf of Lisa, where we have been looking at maternal infection and ever during pregnancy as a risk factor for autism in SEED. Many of you may know this, that that is not a sort of new hypothesis, infection during pregnancy has been one of the sort of oldest and longstanding questions about a non-genetic risk factor for autism from the case stories of rubella exposure, CMV, things like that.

To several modern day questions about influenza and other kinds of infections during pregnancy and risk.

A recent paper that is not this one but a little bit prior to this one, that I put on the right, just to give us a little bit of context, is a paper by Martha Brucato on the Boston birth cohort. I thought she did a nice job of summarizing what we have seen in the last, say, five or six years. In fact, there have been a couple of papers since this was made, to add to this, so we will make a new tree sometime soon.

What this does is sort of summarize across the studies that have come out recently, that there has been some hint - this dashed line is if there were no association. So these show you that there is a little bit of positive association. Although their precision would cross that no

association in these cases. So there is a little suggestion for genital urinary infections, but more consistent suggestion of flu, although often crossing the knoll.

Then probably the most consistent is previous evidence for fever. But you also see these very wide bars, which says that that is probably the least precise information we have. Although it seems to be the most consistent.

The question really has become if this is true, what is the right timing? Is it prior around conception or is it first, second or third trimester? Or is it the fever itself, which would be the response, or is it the underlying infection that might be part of the biologic story?

In SEED, you have heard a lot about the design now, so I won't go into too many details, but this is only in SEED 1 data. So

this is that group that was born between 2003 and 2006. We were able to characterize infection and fever during pregnancy primarily from a caregiver, which is typically a maternal interview. So this is asking her, when the child is now around two to five, about things that happened during pregnancy. Turns out that is pretty good reporting.

We asked specifically about 36 infections and the timing of those from three months prior all the way through birth. We also asked about specific medications and fever that might be co-occurring with it.

In addition, we did Med record abstraction for labor and delivery records. So we were also able to query infections, medications and fever, as they are found in the chart review.

We then made definitions that were; any infection or by organism type, or by organ affected in the mom, and then by timing in trimester.

So I am going to show you a couple of tables of results. For this work, just to orient you. This is the information from the ASD cases, from the population based controls, and then from the DD group that Laura has already described to you.

You can see right away if you just characterize any infection during pregnancy, pretty frequent occurrence of that kind of exposure - about 60 percent of moms in each of those groups were exposed to infection sometime during pregnancy.

What is over here is just a crude comparison of these percentages via p-value for ASD versus POP, and then separately for DD versus POP.

So I will orient you a little bit to organ systems that were looked at. You can see that generally speaking, there were no statistically significant differences in these crude comparisons of frequencies. Except here, for the genital urinary. If you recall, that was one of the ones on the previous review of the literature slide that had already started to come up. And these of unknown tissue infection.

Then if you look at the type of organism involved in the infection, bacteria for the case comparison, showed some differences, 36 percent versus 31 percent.

That is just to show you the raw data frequencies as they look. Importantly, we then perform logistic regression, where we could adjust for a large set of potential confounders. I won't say them all out loud, but there are many here. We did that and we

also adjusted for medication use. So that is the adjustment one versus adjustment two.

If I show you any infection by timing, in this kind of any infection analysis, what we see is that the crude odds ratio and the adjusted odds ratios, are statistically significantly higher than one. So, an increase risk of about somewhere between 60 and 70 percent, depending on which one of those you look at, that did not show up when you are comparing DD to POP. So seems specific to the ASD case risk.

So if we ask the question of whether that is with or without fever, that is when things get a little more refined. In this case, it is any infection that did co-occur with a fever. Here we get the trimester two association, that is much stronger than that any infection association from the previous slide that is specific to that trimester.

Although, one could argue that there is still some increased risk in that T0, which is what you saw in the previous slide.

This is what is consistent with some of those figures I showed you in the prior literature, and also with a recent paper from the MoBa Study, which is a Norwegian Birth Cohort, that sees the same fever effect in second trimester.

When we look at any infection without fever, it really is just this periconceptual timing.

So the summary of this infection analysis is first, these are quite common exposures. When we look for risk of ASD, we see women who had infection accompanied by a fever may be at increased risk in the second trimester - if that occurs in the second trimester. But the infection that was not

accompanied by fever, is still in this three months prior to conception.

And that we see this even after controlling for important covariates and also for treatment with medication. Importantly, we did not see this association with DD. It seems to be specific to ASD. While no one study can be definitive, this is, as you have heard, a nicely designed national case control study that is consistent with the growing evidence of a fever based association to ASD. It still begs the question of how do we further explain and what would we do about it.

It is sort of, in my mind, interesting that this is a potentially modifiable idea. But it is really important for us to understand the biology of whether it is the immune response part or the underlying

infection part that needs to be considered further.

So I think we have contributed to this literature in important ways. What I think is exciting is we can then use these same SEED 1 data, or when we put them together with SEED 1, 2 and 3, be able to answer these more fundamental questions.

That is my summary for that piece.

Then Laura asked me to tell a little bit about what we have been doing with the omics data that have been generated in SEED 1. At the end of this I will give you a table that shows you what kinds of omics data are available generally, for SEED 1 right now.

Verbally there are genome-wide associations, SNP based kinds of data available for the majority of SEED 1 children. And there are DNA methylation array

data available for a subset of SEED 1 cases and controlled children.

Coming out today is a paper I was going to tell you just a little bit about. I put Shan's picture here because this is really the work of a doctoral student of mine, Shan Andrews, working at Hopkins, who wanted to think about what can we learn from the methylation data that comes from blood of two to five-year old's in SEED, in the landscape of trying to understand biology for autism that is at least somewhat brain-based disorder. This is an ongoing question.

I did not put in here a couple of slides of introductory of what epigenetics are. I apologize for those of you who don't know this terminology really well. In the interest of time, I did not spend a lot of time on that. But I will say verbally, if we think of genes as those sequence, the A, T's, C's and

G's that you hear a lot about, on top of those are chemical modifications that you could think of them kind of like a tab in a recipe book. We have the entire recipe of the human genome in every part of our body. But our eyeballs look up at particular places and express some genes and our kidneys look up different parts of whole recipe and express other genes.

So these epigenetic sort of modifications, if you will, help to regulate what is turned on and off where and when in our bodies. So you can think of them as kind of a choke holder part of the control mechanism for the sequence that exists everywhere but is not used everywhere in the body.

What we wanted to ask was what can we learn by integrating that kind of epigenetic measurement - in our case, DNA methylation,

with genetic questions already being asked in the autism field.

As background, I mentioned to you that epigenetic variation contributes to gene regulation or expression. By nature of that it is tissue and timing dependent, so you could not necessarily expect the same patterns of something like DNA methylation in your kidney as you would in your brain or in your blood. Some of those would be similar and some won't be, and that tis by design.

Our question is, realizing that, can we still use information about epigenetic marks to answer questions about ASD biology. The place that we focused is we and others, have sort of contributed to this recent knowledge - recent meaning this last decade - that epigenetic variation, this idea of DNA methylation or other kinds of epigenetic

patterns, are at least in part themselves controlled by genetic variation.

It may be in those places where there is some genetic control where you might get cross tissue information that is useful.

Here is what I mean by this, if this is the genotype - many of you in here are used to seeing genotype data where you have three categories because there are two alleles possible at one site, so you can have two of the same kind, two of the same kind in some other version, or two different kinds. Then if you look at methylation, which really has a zero to 100 scale in the way that we measure it because it is the proportion of cells that have methylation at a particular spot in the methylome, in any one sample.

You can see that you can group methylation here at somewhere between 60 percent and 90 percent on this figure. You

can group them by genotype and you see a very specific pattern. So for a particular location in the genome on the genetic scale, in a particular location in the epigenome on the methylation scale, you see a pretty obvious pattern that some genotypes correspond to this kind of range of methylation, other genotypes correspond to this kind of range.

So that idea that there is some association between genes and epigenetics has been shown over and over now. In fact, we can start to make maps.

We can plot, here are the genes that might be in a particular area of a chromosome. Here are the SNPs that exist near those genes so that is where there is genetic variation. Then up here, is where there is epigenetic variation. These line - each line represents a figure like this. So when there

is statistically significant association between the gene and the epigene or the genetic and the epigenetic marks, you will see a line.

So what you see in something like this map is this is not an uncommon thing. That many, many places in the genome are associated with variability in the epigenome. So you can make these kind of cross maps that connect epigenetic level information to genetic level information.

I should say one more thing. We often call these meQTL, for methylation quantitative trait loci or meQTL targets for the CPGs or the methylation that is the target of that meQTL.

I know that is a lot of lingo but I think it is important for what I am going to show you next because this is critical to understanding to what we did.

So what we had were these kinds of maps. Now remember, if you have SNPs or genetic polymorphism here - remember the methylation quantitative trait loci (meQTLs) is the same thing as SNPs. So if you remember SNPs better just keep remembering that.

For each kind of tissue type we can make these maps. Remember, the methylation information can be different for child blood. It could be different for infant cord blood and it could be different for fetal brain tissue.

We actually have this kind of cross information between the genetic signal and the epigenetic marks for peripheral blood from SEED. We have some cord mapping data from a different cohort that I work with called EARLI. We had fetal mapping information from our colleague, John Mill, in the United Kingdom.

So we could make these kinds of maps where we can say, okay, in blood, if we wanted to look at which SNPs control methylation, we could highlight those. In cord blood, which SNPs control methylation and highlight those. In fetal brain, which SNPs control methylation and highlight those.

So what we asked really is what can we learn by integrating genetic and epigenetic information? We really asked, what can we learn by using this meQTL information? That is what we have and that is what we think cross tissue relevance may be most tangible.

Specifically, the questions we asked are; are ASD-associated SNPs - that means ones that have already been seen. So for example, the psychiatric genetics consortium autism group has the largest collection to date of genetics or GWAS data, where they can start to discover common variance that might

be associated with autism. So if we were to take that list of discovered common variance and ask, what do we know about those? Are they, for example, enriched for these meQTLs? Do they have this kind of regulatory relevance? That is one thing we could ask.

We can ask, would that be true even if we were looking at meQTLs from blood versus brain?

Then we could ask, okay, well that is the genetics. What about the epigenetics? If we look to see those targets do we learn something new about the biology if we look at their targets, their regulatory targets, rather than where the SNPs themselves are located?

Finally, does that point to new genes or new biology? So I am going to walk you through with just one result in each of those.

This first one, are already known ASD-associated SNPs from something like the psychiatric genetic consortium, enrich for these meQTLs? So remember, we can make these maps and we can also lay on these maps SNPs that PGC has associated with autism. So that is what is here in purple. The simple question is, if we looked at SNPs annotated by purple as being associated with autism and we look at which ones of those are now mapped to be considered meQTLs, are these enriched? Are there more autism associated SNPs that are meQTLs than generally expected?

We can do that for something like brain, but we could also do it for blood.

The answer that we get is, indeed there are. Just to orient you, these are just considering different kinds of thresholds for what you call an associated SNP and what you call a mapped meQTL. But generally, in fetal

brain, we do see statistically significant enrichment. Importantly, if we look in the other kinds of tissues, we also statistically significant enrichment. This is because we wanted to be as careful as we could about our own calling of meQTL maps. So you can look at any one of these, but it is consistent across them that we see that kind of enrichment. Not as strong as with the brain meQTLs, but still there in peripheral blood.

One might argue still there in cord blood, although you can see those p-values in parentheses that did not meet statistical significance. One important thing we did was ask, what happens if you take any tissue meQTL list. We looked at lung, and indeed, you do not see it if you ask this question in lung.

I would say, at least preliminarily, that is a yes to the first question. The next

one is if that is true, is there is enrichment for these meQTLs, what is happening to their targets? Those methylation sites that they controlling.

Instead of looking down at the SNPs for enrichment, let us see what those SNPs are controlling and let us ask about the biology implicated by these methylation targets of those ASD associated SNPs.

When we do some enrichment kinds of analyses like that, we get a list, and I know this is quite long, I am just going to highlight for you that one way that you could interpret on a list like this, which is where these three have come up as highly ranked on all three lists of enrichment questions. So from peripheral blood cord blood and brain. These are response to interferon-gamma, positive regulation of relaxation of cardiac

muscle, but then production of molecular mediator of immune response.

So two of those may have sort of immune ideas. If we look where there is at least overlap of brain in one of these other blood based tissues, we see a lot more immune response kind of stories. And that doesn't have to be the case. We did this in other controlled situations and you don't get this immune list.

I guess the answer for this second one is, we think, is potentially you learn more about particular biology by looking at these meQTL targets. We think may be importantly, you learn about the immune system. That is consistent with ASD findings today.

While the rare genetic variation has not generally pointed to the immune system, has rather pointed to epigenetic regulation or synaptogenesis and things like that, the

expression, and now some methylation data, have been pointing to immune response or immune system, as well as the epidemiologic findings, including something that I just mentioned in Lisa's paper.

So this is a nice summary of that. Previous brain studies looking at gene expression or methylation have implicated the immune system. In fact, some previous blood studies that have looked at expression have done this. So our study would sort of fit here and here, looking at new information that might imply immune system. Connected to actually, genetic results.

Then lastly, let us go to that very sort of one spot genetic result to give you a zoomed in view of why we think this is important.

Here is one of those genetic maps again. The SNPs down here. The CpG or methylation up

here and the association between them. But this is one of those PGC associated SNPs. It would map onto a particular gene right here, PPF. So that would be the gene that maybe you looked up for biology or you did enrichment analysis of and things like that, if you were looking just at the GWAS signal level.

But if you follow these maps, in fact many other places might have regulatory relevance based on the association between that SNP and that methylation signal. So that opens up a whole bunch of different questions in terms of the biology or the biological relevance of that common variant association that may not have been what we were looking at previously.

That is what we were doing at the large scale when we asked and got that immune response, but it also means as we become more and more confident, PGC will now have a new

round of results with much larger samples, we may want to do this for each one of those hits to make sure that we understand at least the regional regulatory relevance.

One thing that I showed you - this is just that in a smaller scale now. That is with peripheral blood. You could do that map in just cord blood or you could do that in brain and you can start to see where you get sort of overlapping importance of these other regions beyond this SNP itself that is affecting a gene. We see this kind of pattern across many of the ASD SNPs that we have looked at.

In summary, I think we can somewhat start to answer all three of those kinds of simple questions. Interesting for us the blood based meQTL information did give us some more answers to brain based meQTL information. This is not primary discovery of

new methylation sites between cases of controls, but rather exploiting information about the connections between genes and epigenetics that can then help us to best interpret our genetics findings.

I will give you a caveat. There are some important limitations to this so far. First is that those meQTL lists are currently still building with larger and larger numbers. Meaning those maps that we are creating. Also, the ASD common variant hit list is ever changing and gaining in precision.

So this is what we do have in SEED. We have ASD, POP and few DDs genotyped on a various set of genome-wide platforms that have had to be imputed back together for joint or mega analysis. Importantly, we now are also genotyping SEED mom and controlled mothers. That is important for some GYE

questions that might be at the maternal susceptibility level.

The data I showed you were based on these GWAS data, as well as these epigenetics data on about 450 cases in 500 controls.

While we cannot be a discovery set on our own for common variant analysis, or probably even for rare variant analysis, these data are really valuable in contributing to collaborative efforts on the genetics and epigenetics scale. So I just wanted to highlight that that we are already participating in GWAS meta-analyses and replication with PGC. We are already contributing to EWAS, meaning epigenome-wide association studies in a meta-analytic way. As well as some other non-ASD specific epigenetic/epidemiology kinds of questions. Particularly through other collaborative meta-analysis efforts, as well as other

multi-omic, meaning trying to put epigenetic and genetic data back together. These have been quite useful for metho-logic advancements as well.

While I think that it is important that we share as much of this data as we can, as soon as we can, it was helpful to me to know that we are still contributing in these ways because in the meta-analysis world you can contribute summary statistics rather than individual-level data, and still make a very important contribution. So it has been nice to see that.

This is just a thank you to my group, but also all the SEED investigators, particularly the SEED 1 investigators, that are part of the stuff that I showed. Homay Farzadegan, who runs the biosample repository that Laura mentioned. That is for all SEED sites. Jon Mill, I mentioned, because of the

brain data that he contributed. Then Dan Arking and Shannon Ellis at Hopkins, as well as Andy Feinberg's group at Hopkins. Finally, the group that was part of that cord mapping, that is a network led by Craig Newschaffer. Thank you.

Then I think, Ann, is who I am introducing next.

DR. ANN REYNOLDS: I am going to talk about GI symptoms and children in SEED I. It is good that this is not too close to breakfast or too close to lunch since I will be talking about gastrointestinal issues.

When we were designing the SEED study, we knew that we wanted a more community-based sample so that we could avoid selection bias for children that were seen in clinic-based samples. We also wanted to look at associated features, which might give us more information about etiology and then obviously

using gastrointestinal symptoms as a phenotypic subtype.

When you think about gastrointestinal symptoms, it is very complex and multifactorial. Just quickly, cognitive and behavioral issues could affect GI symptoms so limited diet. Withholding stool during toilet training can lead to problems. But we are learning more and more about motility and how arousal dysregulation and anxiety, which are common in kids with ASD, can also have an impact on the motility of the GI system.

We also know that there is data to suggest a mean microbiome and genetic differences in kids with ASD and all of these could be impacting GI symptoms as well.

You are already know about the sample. We looked at children who had a clinic visit and had a GI questionnaire. Of the children

who had clinic visits, about 94 percent of the parents filled out the GI questionnaire.

We also had stool diaries, which looks at stool frequency and consistency. The Bristol Stool Scale is a 7 point Likert scale. I can give you more information about that if you would like, but I think I will refrain at this point.

And then we looked at any kind of GI medications.

We also collected data on associated anxiety and aggression and a child behavior checklist. The Children's Sleep Habits Questionnaire gave us a measure of associated sleep issues. In the children just with ASD, we looked at the ADOS Calibrated Severity Scale to look at autism severity and then regression questions from the ADI-R.

Our parent questionnaire just was a yes/no questionnaire about regular issues

with certain GI-type symptoms. And then with the stool diary, we knew that there were things that would contribute to GI symptoms, but would not be in just the stool frequency and consistency data. If you are being treated for constipation that may normalize your stool consistency. We needed to know if the child was actually getting treatment and then things like vomiting and abdominal pain would not be captured by the stool diary. We came up with a complex algorithm to just look at differences in GI symptoms based on parent report and then parent report with the stool diary.

We used multivariable logistic regression and we adjusted for site and sociodemographic variables, child sex and cognitive skills.

In the SEED data, we found that children with ASD were two to three times more likely

to have GI symptoms than children in the POP group. We also found that the children with ASD were more likely than the DD group as well. Although that difference was not as great.

The stool diary data does not show as much of an association, but we also were really looking at different things because when we look at - about 51 percent of the families filled out a stool diary. That group was different from a sociographic standpoint.

We also were just measuring different things as far as treatment for constipation because in that group, children with ASD were less likely to have a stool diary if they were being treated for constipation and then they were more likely to use a treatment for constipation that was not a laxative or stool softener, which is what we had initially a

priori had defined as treatment for constipation.

Then in children with ASD and regression, they were 1.5 times more likely to have GIS. There was no difference in autism severity scores for children with ASD with and without GIS.

We replicated other studies that have shown an association between anxiety and behavioral issues in children who have gastrointestinal symptoms.

What we found though that this was - we found similar results in both the DD and the POP group. This association does not appear to be specific to children with ASD. We found the same for sleep issues. Many studies have shown an association between GI and sleep issues. We found the same, but again in all three groups.

We have some limitations. We do not have a clinical diagnosis of gastrointestinal symptoms. We just have the measures that we used. The questionnaire has not been validated. It was created for the study and then the differences in the group that completed the stool diary, as I spoke about before.

What we found was or the take home message is that gastrointestinal symptoms in this group were more frequent than children with DD and children from the POP groups. When we used a more objective measure such as a stool diary, we found similar findings. We were able to control for cognitive skills, which I think was very helpful. We also were able to look at associations between anxiety and GI symptoms.

And then next steps would be to look at perinatal risk factors for changes in the

microbiome such as C-section delivery, antibiotic use or breast feeding that might be associated with GI symptoms. Obviously genetic and gene by environment interactions would be a next step as well.

We do have some diet records to look at and information about food allergy.

There were also genes that are associated with things like eosinophilic esophagitis, which we may be able to look at.

The biggest thank you to the family. We know that a lot of this data collection was time consuming and then all the collaborators on SEED.

DR. SHAPIRA: Good morning. Last but not least, this morning I will focus on characterizing dysmorphology to enhance the phenotypic classification of ASD in SEED.

First, in terminology, dysmorphology is the description of physical features that are

dysmorphic. What I mean by that is a physical feature is defined as dysmorphic if it has not followed the normal pattern of growth or formation. It is often disproportionate when compared with the typical features so maybe too big or too small or too long or too short or too wide or too narrow. There are hundreds and hundreds of potential dysmorphic features. Each one exists in less than 5 percent of the general population.

Here are some examples of dysmorphic features. This child in the upper left has increased spacing between her eyes. This child has a fold of skin covering the inner corners of the eyes called epicanthal folds. This child has ears protruding from the side of the scalp. This child's ear position in the middle at the bottom - the ear is positioned rather low on the scalp compared to the normal position. This child has a

series of birth marks or café-au-lait spots. This individual has rather long fingers. All of these are dysmorphic features.

Why is it important to evaluate dysmorphology? Well, it can potentially provide clues as to a cause. For example, we have a couple of individuals here who have relatively flattened faces, have upslanting eye fissures from the inner corner to the outer corner, have the epicanthal folds that I mentioned, prominent tongue, small ears, extra redundant skin on the neck, have this wide spacing between the first and second toe, and have a single crease that goes across the palm. All of these are dysmorphic features. This cluster of features is pretty indicative of Down syndrome. Evaluating dysmorphic features could give us clues as to what is going on.

Why evaluate dysmorphology for children with ASD? In children with ASD, the presence of multiple dysmorphic features might identify distinctive ASD phenotypes that have not previously been described. It may serve as a potential marker for understanding cause and prognosis.

The dysmorphology and protocol in SEED consisted of three components. The first was data collection, which was done during an in-person clinic visit. This was performed by study staff who were familiarized with dysmorphology. They did a series of measurements on the child of the height, weight, and head circumference. They measured the length of the child's foot in the clinic.

Then there were hand scans performed for all children. An example is shown here on the lower right. And from the hand scans, various measures as listed here were obtained. And

then there was a physical exam for dysmorphic features on all the body regions listed here and is shown in the various pictures on this slide.

And the last component of data collection was taking a series of standardized photographs of each child so that measurements could be obtained from various photographs and dysmorphic features could be documented as shown in these series of ears with various dysmorphic features.

The second component of SEED dysmorphology was a review process. There were seven clinical geneticists involved in this review. Each one was assigned a particular body region to review and perform a standardized dysmorphology review further body region on all children in the study. The geneticists are shown here in the column to the left, the body regions in the middle, and

the number of features in each body region, potential dysmorphic features is shown on the right. The total number of features reviewed for every child was 397.

When is a physical feature considered dysmorphic or not? I mentioned previously that it occurs in 5 percent or less of the population. We used our POP controls to assess dysmorphology. Some features are easy to assess. They are either present or absent. An example is shown here for an ear tag where it is present in the ear shown on the right. It is not present in the ear shown on the left. It would be considered dysmorphic in the ear shown on the right.

Now, many features are not yes or no. There is a spectrum in the population. An example shown here is ptosis, which is a drooping of the upper eyelid. There is no ptosis in the eye shown on the left. And then

mild versus moderate versus severe ptosis in these pictures on the right. Which of these is dysmorphic? Which occurs in less than 5 percent of the population? Is it only severe ptosis? Is it moderate or severe? Is it mild or moderate or severe? We applied a statistical method to the POP group in order to categorize what part of these various spectrums correspond to dysmorphic.

The third part of the SEED dysmorphology protocol was classification where for each child in the POP group we summed the number of dysmorphic features that each child had. Then each child was assigned a dysmorphology score based on the number of dysmorphic features and the scores were fit to allow normal distribution and they fit quite well. An example is shown here of what this would look like. And those children who had dysmorphology scores that were less than or

equal to the 90th percentile were considered overall non-dysmorphic. Those between the 90th and 95th percentile were equivocal and those greater than the 95th percentile over out here in the tail were considered dysmorphic.

This was the group of children that we evaluated. Three racial and ethnically distinct groups and dysmorphology reviews and classifications were performed separately for each race and ethnicity. These are results.

Now, for the POP group, of course the POP groups were fit to the lab normal distribution. The expectation is that about 90 percent would be non-dysmorphic, about 5 percent equivocal, and about 5 percent dysmorphic. This met our expectations and there were no significant difference between non-Hispanic white and non-Hispanic black and Hispanic.

What about the group of children with ASD? It turns out that for each racial and ethnic group, about 17 percent were dysmorphic. About 70 percent were non-dysmorphic and then the equivocal is in the middle. It was surprising that although each of these analysis and reviews were run separately we got exactly the same. About 17 percent of children in each category were dysmorphic. No difference between these groups. If we combine everybody together and we look at just the POP versus the ASD, again about 5 percent of the POP group is dysmorphic, 17 percent of the ASD group.

If we exclude everyone who has a known genetic syndrome or a known chromosome abnormality, the association is attenuated a little bit, but we still see a very significant group of those in the ASD who

were dysmorphic compared to those in the POP group.

In summary, this is a novel protocol that defines a quantitative dysmorphology classification and identifies dysmorphic and non-dysmorphic children with ASD in SEED. This classification allows us now to stratify ASD phenotype for potentially more homogeneous assessments for studies of etiologic risk factors and genetic susceptibilities. We have already begun future studies that are identifying patterns of dysmorphic features that are predictive of various ASD phenotypes.

These are all the collaborators involved in this study. We also thank the families and the many staff at each site that collected the data.

I will return to our program again. This morning we have given you a taste of studies

that are going on in four areas in SEED looking at risk factors, at genetic associations, as ASD and child health effects, and characteristics of children with ASD. This is only a few of the many studies that are currently going on in SEED.

What I would like to do is to invite all of the speakers back up to seats here up front and we will open the floor for questions at this time. Thanks very much.

(Applause)

DR. GORDON: Thank you for some wonderful presentations. Are there questions from the committee?

DR. BIANCHI: Stuart, you knew I was going to ask a genetics question. Is somebody looking at all of the features because there is the possibility that if you look at just the feet, you might not recognize that the feet plus the skin plus other things would

all collectively go together and ring a bell for a dysmorphologist that it is such and such a syndrome?

DR. SHAPIRA: Yes. Great question. That is exactly what we are doing right now. This is the second step in the dysmorphology assessment. We have identified features that are more common in our ASD children compared to the population controls. We are now evaluating for clusters of features that would predict a particular phenotype and then comparing to what we know about children from their previous genetic evaluations. And also from the genetic studies that we have going on in SEED, we have copy number variation information on children and their parents. We will begin to sort this out.

But you are right. Each geneticist was focused on a particular body region. I became the expert when it came to evaluating ears.

Those in the room may want to cover their ears when I walk around because I am always looking for dysmorphic features in ears. I focused on ears, but I was able to see all the other - what the child looked like from photographs and was able to think about genetic conditions or syndromes, but that is what we are doing right now as the second step in this process.

DR. GORDON: Alison.

MS. SINGER: Thank you for this presentation. I think what you showed today and what you have been publishing - I know you have been publishing a lot in the last couple of months. These are really important findings. These are really important clues for us. But this study has been going on since 2002. Why has it taken so long for us to get this important data out of CDC? It is 14 to 15 years it has taken to literally - it

feels like wrench this data out of the CDC. It has put us behind. We could have been moving on some of these findings. Why does it take so long for CDC to report out?

DR. SCHIEVE: Hi. Thanks for the question. I often share your frustration. It does take a long time. I will say the study was initially funded in 2002 and planning began at that time. There was an interruption in planning due to funding. We did not really start planning the study again in earnest until about I would say 2006 is when we really got moving again and it got reinstated. The funding came back. I will let Stuart or Nicole maybe answer that. I was just coming on into the branch the year before that.

We got into the field in 2007, but you are right. We are about to celebrate our

tenth year of collecting data. In December 2007, our first child was enrolled.

Part of the issue is with the massive amount of data that we collected. The data coordinating center really had their hands full and we wanted to do proper QCM on the data. I know that sounds kind of like boring. We did not finish data collection for the first wave until about 2012 because we had all of the medical record stuff to abstract. Then it took about two years for data prep. We, ourselves, felt like we have to get better at that.

I will say with SEED 2, we just finalized data collection in 2016 and we have the data files ready. We have learned a lot from SEED 1 and are getting better at getting our data files together. But part of it was we thought we might do some preliminary studies once we are in the field, but it was

just amassing all of that data into quality control data files so we did not make any mistakes. It took a long time. I know that it is still frustrating.

MS. SINGER: Is there anything we can do to help you to expedite the reporting out of data?

DR. SCHIEVE: I actually am open to suggestions, but I really think it is just - putting the data together has taken that long. I do think we are going faster now in terms of - now that the publications are ongoing. People are moving a little bit faster. I agree with you.

We also need to get faster at completing our analyses. We all get bogged down with multiple things. I will say one thing. As we have been just - at CDC, I personally have been delighted by - all of our SEED PIs have been great about getting graduate students

interested in this. I think some of our best work - Dr. Fallin showed one example of that today, but at every site - they are a lovely group to work with. They are really smart, really dedicated. I have appreciated - that has been a huge help to us.

DR. AMARAL: Thanks. That was a great series of presentations. I guess this question is directed maybe at Dani but everybody.

One of the gap areas in the strategic plan was the fact that large epidemiological and large genetic studies rarely interdigitated. It was not clear to me in the SEED study the extent to which mature genetic data, whole exome or whole genome, is being collected. That is question one.

And question two is has there been any effort to try and collaborate with some of the large private genome sequencing studies

that are going on like MSSNG or Spark to foster that cross-study integration.

DR. FALLIN: I am a broken record about this, so then Laura will jump in. We do not yet have whole exome or whole genome on any SEED samples. We only have GWAS data on SEED 1 samples. Absolutely, that needs to happen. Figuring out how to do that in an appropriate way given the consensus of SEED 1 versus now the way that SEED 2 and SEED 3 are happening. Hopefully, that will go much faster for SEED 2 and SEED 3 samples that are sitting in the biorepository now.

With SEED 1, it was to be (inaudible comments) to get the funding to make sure that we could do the genotyping on that. And now that there are these collaborative possibilities to get genotyping like that done in the public done. Absolutely. I and other PIs have been beating that drum. Can we

do that? Because we are sitting on such great opportunities.

DR. SCHIEVE: I will follow up on that just to say that it is true. The funding we get -- we collect all these biosamples. We have not had dedicated funding to analyze them. We have been really grateful to Danny and her colleagues have gone out and gotten some -- applied for grants to NIH and Autism Speaks. We had some supplemental funding available. I think I was asked -- in the next 12 hours, what would you do? It is like we finished all the genotyping. We sort of cobbled together funding.

We are going to need to do that for SEED 2 and SEED 3 as well, but we are already thinking about that and had been planning on what the priorities would be if and when. And I should say when because I really hope it will become available.

We are consenting our SEED 1 participants. We are going to start that so that we can share with biorepositories. We do have consents for genetic data sharing for SEED 2 and SEED 3. That process will be smoother. I do not know if Nicole or Stuart if you wanted to comment further on that.

DR. AMARAL: I would just say that it is a pity that Louis Reichardt is not here because I know they are actively soliciting subjects. This seems to me like an ideal situation where you have this enormous array of epidemiological data. They are looking for subjects for carrying out whole exome sequencing. This is a perfect marriage. It just perhaps takes a phone call to get it going. I would encourage somebody to make the phone call.

DR. GORDON: John and then David.

MR. ROBISON: First of all, I want to thank you all for the presentation of quite a large packet of data and work. It was a long time coming, but you have a lot to share with us.

I wonder if I could offer first a simplistic and blunt assessment of what you and some of earlier studies have presented, which is that more and more studies show that these mutations that appear in the genome out of nowhere in a child, and significant illness in mothers and also injury to mothers who are pregnant can result in pretty severe autism in children.

I think that as you show that, we have to realize that there is only so much we can control in this life. You say that there is an association between high fevers and the development of severe autism in the infants who were born later. Then you ask is it the

fever or is it underlying infection. Those are valid questions, but the larger point is that there is almost so much we can control in our lives. Some of these children simply will be born despite our best efforts.

And that takes me then to the point that we raise in our new Strategic Plan Update that I hope you all will take to heart and that is when people hear that kind of news, they say what is the government going to do for me. That is exactly the sort of thing that is not subject to preemptive cure or remediation. It is only really addressed by comprehensive care through the lifespan, which is nowhere with CDC activities that I can see yet.

The second point that I hope that you will take in the same line with this, is what do you do as a follow on for what you have presented us. It is very tempting to say what

you do is dig deeper into the issues of children. I suggest to you with all due respect, that that would be the wrong next step.

I believe that you have shown us what your epidemiologists, geneticists and other scientists can do. You should deploy those people and that knowledge to explore the unknown and ill understood issues in adults because when you present studies like this and we make a big deal of it, you continue to perpetrate the incorrect public vision that autism is a childhood problem.

I am particularly worried that when our lawmakers read of work like this that you do because themselves have a simplistic understanding of this, most of them. They are going to see it as a childhood problem, which is absolutely wrong.

I hope that you can use these kinds of tools to help us answer why are we more subject to diabetes. Why are we more subject to heart - why are we more at risk for suicide? You have a different set of study skills to research that. I very much hope that you will take that as your next step with respect to autism. I wonder what your thoughts are on that.

DR. SCHIEVE: I guess I will start it and everybody can chime in. I really thank you for that comment and couldn't agree more. I do also think as the strategic plan notes, we need to think not just about what are risk factors for ASD, but how can a risk factor work and help us perhaps inform the disabling aspects of ASD so we might limit some of those. I think some of the SEED data is already doing that.

I also think that we are really excited to be embarking on SEED teens because now we will have all of this rich data of children at preschool age and their families and really be able to look at the trajectory of how are they doing. How do some of these early risk factors influence that, but also how are they doing as teenagers?

I did not mention it up here, but we also hope that at the time that we do SEED teen, we are collecting those supplemental consent forms to share their genetic data. But we are also asking the mothers and the children who participate whether we have their permission to contact them again in the future so that perhaps we can track them into adulthood. I will defer to my colleagues at both ends of the table. I do not make the funding decisions at CDC, but I think that has certainly been part of our discussion is

that this is a valuable resource to look forward to those types of questions as well because all of these kids - SEED 1 kids are now just about to turn teenage years. They are all growing up and it is important to track their struggles.

MR. ROBISON: That speaks precisely to why we need to we need to start anew with adults because you have taken ten years to produce SEED 1. And now you say to me we are going to do SEED 2 so in 2030 we can talk adults. That is not acceptable. We have to move faster.

DR. SHAPIRA: John, you made very important points. No one can disagree with the points that you made that we need to have a better understanding of what is going on for adults in order to improve their outcomes so that adults can thrive who have autism. No one disagrees with that.

You are aware that we have some constraints from the standpoint of government funding of what we are actually able to do at CDC with the funds that we receive from Congress because there is particular language in the appropriation law that restricts us to work in certain areas. We would love to work in many areas. We have some restrictions placed upon us. We do the best with what we receive.

And with what we have received for SEED, we are taking it a step further for this longitudinal study, which has not been done anywhere else, that has the rich epidemiologic data from preschool and going into adolescence. We realize that it is not quick enough to answer the questions for adulthood. But with what we receive, we are doing what we can.

We are also learning about issues in childhood that can progress into adulthood. For example, the presentation this morning about GI symptoms and issues in children with ASD and how these may manifest later on. There are other types of symptoms. The anxiety symptoms and so on into adulthood and risk for suicide and so on. We are investigating all of that as part of the SEED team project.

You raised important points. We would love to do everything. We have our hands tied in certain areas. We will continue to work very hard in all the areas that we can in order to answer these important questions and to help folks through adolescence and into adulthood with ASD.

MR. ROBISON: I know you folks believe in what you are doing and you are all committed researchers. Just please remember that folks

like I and Sam are here to offer you the voice of the community and we are the taxpayers who fund the Congressmen who give you folks the budgets. And the reasons those budgets are restricted to children is because we have painted a false picture of autism as childhood disability. We all have to work together to do that so that we can build and restore confidence in our public health system. It is vital to me.

DR. GORDON: Thank you, John. David.

DR. MANDELL: Just a quick follow up to both Alison and John's comments. You do not have to answer this, but I am curious about the CDC review process from manuscripts and how much that also holds up research getting out. Don't answer. But I think it is something that has to be addressed.

With regard to John's point and the relatively limited scope or purview and I

would not call it limited because it is an extraordinarily rich data set that you are creating. It would be interesting to think about what the hand off is for this cohort that you have identified.

If issues related to health in adults with autism is not the purview of this particular study and the CDC is somewhat restricted, there are other funding agencies that are not. And to have this kind of wonderful resources that is so well characterized that could then switch over to another set of studies about those individuals later in life would be an extraordinary contribution to science and the community. But neither of those was my question.

My question was actually for - I think for Dani and Laura about - we certainly do not think about autism as a monogenic

condition. Apply all sorts of more novel statistical techniques to take that into account. Is there a time to start doing that for environment risk as well? Is logistic regression kind of a limited tool for thinking about the idea that there may be multiple environmental hits as well as multiple genetic hits that result in impairment? How do you guys think about that as the next stage of analyses that you might do with these data as opposed to doing sort of individual studies about individual environmental risk factors?

DR. FALLIN: Amen. That is the thing. We have had these working groups that are specific to particular targeted hypotheses. But even in those, as you can imagine, what happens is three of those working groups have to come together because they are all so intertwined. What we have been thinking about

at least in my group and certainly I think in others too is how do you come up with centralizing themes where many environmental factors need to be looked at in concert? The statistical tools of that, I think, are important too.

But we are sort of at the do you conceptualize it around maternal immune activation. Do you conceptualize it around some other thing? And then multiple of the things that we have shown would come together really need to be looked at simultaneously. And then the statistics of is that something like latent class kind of modeling or is that something like just counts. How do you do that I think is why we continue to engage our statistical colleagues to what is the most responsible way to do that. But the conceptualization I think is still part of what I struggle with.

DR. GORDON: Gwen, not to put you on the spot, do you have anything to say about NIEHS' efforts in this area. You did have a workshop that I participated in last year relative to this question.

DR. COLLMAN: Right. We agree and I think that SEED has an environmental piece to it that was described in the opening statement. One opportunity would be to maybe inventory all those measures that have been made using questionnaires, looking at biospecimens. NIEHS has a new resource called the Children's Environmental Health, exposure analysis resource, where NIH-funded investigators who are part of the SEED family could apply for exposure analysis across a number of targeted environmental chemical analytes as well as untargeted metabolomics work. Because the specimens are stored, they would be eligible to do this.

You could create an exposome-type approach for each of the participants and then look at that individually for environmental risk only or do gene environment interaction work. I think it would be an enormous next step to collaborate with us at NIEHS to get that moving. Thank you for raising that.

DR. GORDON: We are running a bit behind, but we will take one more question.

DR. BIANCHI: This relates to the question I have. It has obviously taken a lot of time and effort to create these massive data sets. What plans do you have for sharing the data once your primary publications have been completed? Because I think that would be extremely important. Then NIH and certainly NICHD, NIEHS could work with you to expand the analyses.

DR. SHAPIRA: Yes. You are aware that according to the policy that data sharing is a component of all government data collections. We have reviewed data that had been collected through SEED 1 and SEED 2 and are investigating ways in which we can still fulfill what the participants have agreed to in the consent form and that it does not violate confidentiality or privacy issues in order to be able to make components of the data accessible for other investigators.

DR. GORDON: Sorry. I missed Geri. Did you have something you wanted to ask?

DR. DAWSON: I know we are running late so my question can wait.

DR. GORDON: Thank you very much. Let me just add that I know we are already working with you on the genomics data. If there are other ways that we can help host and/or clear some of these consent issues and take that

data into the NIMH data archive, which of course has a number of data sets relevant to autism, we would be happy to work with you to do that.

We are going to break for 15 minutes and come back at 11:15. Please try to be here right at 11:15 because we are running about 15 minutes late and we want to have full time for discussion of the committee business. Thank you.

(Whereupon, the Committee members took a brief break starting at 11:00 a.m. and reconvened at 11:15 a.m.)

DR. GORDON: We are going to go ahead and get started with our committee business. Susan is going to get us off to a start. But before she actually takes over, I just want to say I know she is going to present the strategic plan highlights. But I really want to thank Susan and her whole team and all of

the work groups who participated because I had virtually nothing to do with this. It is really a wonderful document. You all have it. I have been looking through it. I am going to be looking through it as we make our plans for what initiatives to secure in the future.

We already have some of the points in here.

We have already started working on them. I really want to say thank you to Susan and her staff. It was a long time coming and a lot of work.

(Applause)

DR. DANIELS: Thank you to the entire committee and people who served on all the working groups over many months to get this done. We are excited to have something finally to present to the community.

To get started on committee business, I just wanted to start again thanking the OARC

staff for all that they have done for the documents that we are going to talk about today, the meeting and many other activities related to the IACC.

I also wanted to point out that we have a new staff member, Matthew Vilnit, who joined our team recently. I do not know where he is in the room, but his picture is highlighted below. You can say hi to him and you can be expecting emails from him and so forth with relation to the committee.

We have three new publications to share with you today. The first on the right I have already talked about, the HHS transition report. I am going to share with you our other two new items.

The new IACC Strategic Plan.
Congratulations to the committee on producing the new strategic plan. We titled this one - we did not title it an update because it is

really an entirely new plan following upon the plans from before and updates from before.

This strategic plan provides a blueprint to guide autism-related efforts across federal agencies and partner private organizations. It is continuing to be organized around seven community-based questions related to ASD. This new plan includes 23 new objectives that address both research and services activities in accordance with the Autism Cares Act.

I am not going to go over all of these objectives, but we have in this new document - we tried to make it really easy to access. And in the front, we have tables that just show you all of the objectives lined up in one place so that you do not have to search through the document. They are all listed here.

We put the cross-cutting objective up. It is not really in Question 2. It is labeled cross-cutting, but we put it in the beginning so that people would read it at the very beginning of the plan. They are listed here for people who want to go back in the slide set and read through those and of course in the document itself.

One of the really important things that the committee also decided in our previous meeting was that they wanted to make a new budget recommendation, recommending a doubling of the combined federal and private ASD research budget to \$685 million by 2020. This was a very significant recommendation and is highlighted in the plan and is highlighted on the IACC website so that people can access that information. In the plan is all the background that the committee and OARC put together for that.

I also want to talk about the IACC Portfolio Analysis Report. The 2014 and 2015 Portfolio Analysis Report is also at your desk. We have those available for you.

I have shared the data from this report many times over the past months on previews of the data, but now we have the comprehensive report available for you.

The 2014-2015 IACC ASD Research Portfolio Analysis Report represents the eighth year of data collected by our office and the sixth comprehensive report of the US ASD research funding across both federal and private sectors.

It is also the last analysis that we measure research progress by the objectives from the 2011 IACC Strategic Plan. We are really happy because there were 78 objectives before and now we can measure by 23, which will be much simpler I think in many ways.

The 2014 and 2015 ASD portfolio data are now also available through the IACC/OARC Autism Research Database or ARD. If you go online to the ARD, you can access the actual data behind this report and use it for other kinds of analyses if you wish or see more detail on the projects that were analyzed.

Just a couple of few summary points from the report. Overall funding for ASD research totaled \$309.9 million and spanned over 1400 projects in 2014. And in 2015, it reached \$342.6 million and covered about 1400 projects.

Over the eight years, autism research also showed a general upward trend in funding, increasing by 35 percent since 2008.

We also in this report summarized progress that was made toward completing the objectives that were listed in the 2011 Strategic plan with 97 percent of equaling 76

of the 78 objectives either partially or fully completed. This is a good time for us to move on to a new plan. We will be starting from the bottom again and see how we do.

The next order of business after that is going to be a discussion of the IACC working groups because now that we have completed the plan, we have discussed in 2016 that the IACC wanted to convene three working groups on issues of critical importance to the autism community, but we would begin this work after the completion of the strategic plan.

Before we launch into discussion, I am just going to summarize again what those three working groups are. Health and wellness, safety, and housing.

The health and wellness working group. The title that the committee came up with for this one was improving health outcomes for individuals on the autism spectrum. And the

scope was to cover health and general wellness, co-occurring conditions and preventative approaches to address them including issues such as obesity and many other co-occurring conditions. Co-occurring mental health conditions, premature mortality, and issues with medical practitioners, their training to be able to interact effectively with the autism community and also for autistic adults to be able to interact or the families of autistic children to be able to interact properly with medical practitioners. And parental mental health.

The safety working group. Safety was another issue that the committee felt was important to address in the coming months. The scope of this included the issues of wandering, self-injurious behavior that could be a part of co-occurring conditions as well,

seclusion and restraint, and interactions with law enforcement.

The third topic that the committee prioritized was housing. The committee was interested in looking into research and best practices on housing for people with ASD, implementation of current federal regulations, and housing issues faced by those with ASD with more severe disabilities.

I guess I will turn it over to Josh right now to talk about some of the questions that we have about next steps.

DR. GORDON: You have heard the working groups that you all came up with at the time when we thought the strategic plan would be complete a little bit sooner than it was. But I am glad to say that we can finally turn our attention to these groups.

We want to try to have some discussion today to help Susan and her team to plan the

activities of these work groups regarding three items. One is what products do we hope each working group would develop and that could vary from working group to working group.

Second, the structure, activities and timing in order to develop the products. And then obviously, we would like to be able to wrap up each of the working groups so that we can take any recommendations that they might have and incorporate them into the annual updated strategic plan that we would want to do in 2019 when the work groups would finish their work.

One editorial comment I will make regarding number two and that is that with the staffing burdens that we are facing at NIMH and our inability at the current time to hire new staff, not to mention the budgetary concerns in doing so. Running the three work

groups in parallel might be challenging for us. We were hoping to suggest an overall serial method where we would start with one. And once that work group had concluded the mainstay of the meetings and was working on the final product, we would initiate the second one, giving each group about six to eight months to complete their work and still finishing everything by a year from September.

I recognize that some of you are gung ho to get working on these issues and delaying by even just a handful of months might be frustrating. But I think we could be more efficient actually if we separate out the work that way. I wanted to throw that out there before we begin the general discussions.

With that said, I would like to actually start with the first question because I would

like to hear what people's thoughts are regarding the products of the three groups. Then we can come to the question of how we might accomplish those products.

David, go ahead and start.

DR. AMARAL: Thanks Josh. I would like to speak in favor of the working group on medical care and quality of life or what the new topic is. At the first meeting that I came to at IACC, there was a sense that we should try and address some low hanging fruit and bring some relief to the autism community. And one of the comments that I get most from families of individuals with autism is that my medical practitioner does not understand the challenges of dealing with an individual with autism. We even heard this morning about the prominent gastrointestinal problems. There are a lot of other medical problems that we are aware of, but I do not

think that has percolated down to the practitioner in private practice and in many communities.

I do think this is something that is affecting families all across the United States on a daily basis. And a product that this committee could develop would be first of all to develop a consensus about what are the medical issues facing individuals with autism particularly what are the challenges for them to get adequate medical care. Once we develop that consensus on those issues, develop a white paper that then could be distributed to medical practitioners throughout the United States to help families bring these issues and translate this information to the docs in the street. I do see a practical survey and then sort of a list of recommendations that would be helpful to families seeking adequate medical care.

DR. GORDON: Thank you for that eloquent, not defense, advocacy for that particular group and then also for specifying what the product would be. You imagine that it would be a white paper that we could publish or get published, but that we would also distribute intentionally to pediatricians, to primary care pediatricians so they would have that, which could be done in collaboration perhaps with a professional organization.

I am happy to take more advocacy statements from one of the other groups concurring or disagreeing about what a top priority is. But I also liked that David came back to the product. If there are other ideas about products that a group might put forth and again it could be different with the different groups. Geri and then John.

DR. DAWSON: I would like to follow up on David's comment and I am also very interested

in that work group. Actually, our new autism center of excellence program of research will focus on the impact of co-morbid ADHD on outcomes, which actually has a very significant impact on both early diagnosis as well as treatment and outcome.

One of the ideas as a product as well would be to make recommendations for what might be incorporated in the traditional medical school training. I do think this is an area that is really lacking that people when they are going through medical school that they are not really - either they do not have opportunities to work with populations of people that have autism and other disabilities and that the content of just what are the common issues that children and adults present with and how do you think about treatment. It is just not part of the traditional medical school curriculum.

And the nice thing is that there actually are some really nice papers now that have been written, most of them out of the Autism Treatment Network that have practice guidelines for general pediatricians and general internal medicine physicians and so forth that talk about how you can treat some of these common co-morbidities like GI, like ADHD and others. It would just be great to make those recommendations.

DR. GORDON: John.

MR. ROBISON: I guess I am concerned that we are charged with reporting to Congress and our Congress I believe still labels under the misapprehension that this is a childhood problem. I would like us to think about how we could get opportunities to present the general scope of what we want as is stated in our introduction to the plan in fairly concise forum before the lawmakers who make

our budgets because what I heard from CDC and what will happen to you is unless they understand that, they are going to continue to come back to you with budget directives telling you to spend money on children and ignoring these other issues.

DR. GORDON: Let us just say from the NIMH perspective, we do not get such funding declarations with that great a specificity. However, I do appreciate the sentiment that we need to do a better job of speaking to Congress about the needs in the adults. I think this document, the strategic plan plus the document that report to Congress does that. I think we could think creatively about how to communicate and make sure that is read - say directly on that, David.

DR. AMARAL: John, I agree with you completely. I think we should not lose sight of the fact that autism is a childhood

problem, but children grow up. A lot of the health issues that we are talking about are ones that could complicate later medical care and later health care issues. We have had that lifespan is shorter. Suicide is up. These are all adult issues.

Again, by focusing on health care problems, I think we would want to emphasize that this is an ongoing continuing problem throughout life.

MR. ROBISON: I think so. I think that we need to take it beyond the NIH. We need to insure that they understand this is a lifespan problem so that it does involve Social Security, HRSA, and other agencies.

DR. GORDON: John, I think you are 100 percent correct on that. I do not mean to debate it. I like the fact that David suggests that we make sure that when we address the health problems in that working

group that they address health problems of adults.

I do want to point out that this report to Congress was requested by Congress. There is awareness. That does not mean we don't need to work more on it. I agree with you.

MR. ROBISON: We have come a long way with this, Josh. We really have. I just feel like I just have to keep hammering on it. We have to say it as well as ask them to read it.

DR. GORDON: You are 100 percent correct and making sure that the work groups, particularly the health one, straightforwardly deals with adult health issues as important.

Melissa.

MS. SPENCER: I just wanted to add on that I think it is important not to just educate doctors. If you go to the doctor

these days, how many times do you actually see the doctor? You are seeing somebody else, the nurse practitioner, and the physician's assistant. It is the entire medical community.

I know in Social Security I am thinking we do CMEs for the doctors who do work for us. That is not all of the doctors in the country, but it is several thousand that we could tap onto this and educate as well. Something broader.

DR. TAYLOR: I was just going to say that there is some innovative work going on in this area in the adult realm that I think like Christina Nicolaidis, who is here, is doing a lot of that work in terms of how adult providers can more effectively interactive with people on the autism spectrum. I think within the context of this working group, there could certainly be a

nice adult presence that could really focus in on some published work that has been done.

DR. GORDON: I think in terms of thinking about the product again to bring that discussion back full circle. If the product aims to be a white paper then it should be a white paper that we do not just think about distributing to pediatricians, but also figure out how we might reach adult practitioners as well.

I just want to caution. We have been discussing really an issue that the work group can work on. I want to make sure we stick to products. Particularly if you have some creative ideas about other products or ways to work out those products and then we will move on to structures.

MS. SINGER: I think many of us who are at this table have participated in committees here the outcome was a white paper. Those

white papers tend to be very focused on recommendations for what other people should do.

I think one product that we should consider would be to look at what can this group do as a group and what can the members of this group do together to accomplish goals. I think one really good example of where we were successful with that in the past was with the wandering issue where that came to this committee through public comment and we identified that that was a problem. We worked together to realize that the issue was lack of data.

Several of us came together to find the data that was necessary. Then as a result of that data, the CDC was able to help to get an ICD-9 code. We have made good progress. We still have a long way to go on wandering, but

from where we have started, we have made good progress.

My suggestion would be that one outcome be what can we do as opposed to what are we going to ask others to do.

DR. DAWSON: What can we do?

MS. SINGER: It depends on which one we start with, but I think there are definitely things as part of the coordinating responsibility of this committee that we can look at doing together with both the public members and the federal members.

DR. GORDON: As we happen to be on the subject of health, not to keep it on there for a moment, I want to point out that there were important advances made when CMS agreed to fund - to allow billing for both psychiatric care and medical care in the same day as an outpatient. That was a major achievement that was done primarily by

advocates for seriously mentally ill, but also for integrated care in general. If ideas came out of that from the work group in terms of ways to increase - the things that we, we meaning the federal partners around the table, could actually accomplish. That would be a worthwhile product as you pointed out.

DR. RONYAK: Good morning. Thank you. My name is Marcy Ronyak. I am from the Indian Health Service. Thank you for that segue because I was like raising my hand thinking of a product.

Many of us in our agencies actually have the ability to support webinars. If we are doing a white paper and we are talking about reaching out to providers, Indian Health Service has the tele-behavior health center of excellence that we reach out to all of the IHS federal units or tribal communities and it is open to anyone that we also connect

CEUs to. Maybe there is a piece of the white paper that we could set up webinars that can reach out to providers nationwide and be able to support that through our agencies and extend that.

One of the other pieces of that I keep thinking about is the education system. I do have a son that is in third grade that is on the spectrum. I get questions from the special ed folks over and over and over again. I get emails daily of something that he is struggling with in class, and what type of strategies can they use.

I actually asked my case manager and I said do you get education credits where they will send you to the National Autism Conference to have resources, and the answer was no.

If we have educators that have to go on their dime, which we know they are already

struggling with the pay that they have and they are not getting that type of support, maybe there is a piece that we can reach out to some of the national organizations and either have webinars supported for them, education, something of that nature that is actually tangible strategic plans for them to have, tangible items to use.

DR. GORDON: You raise another aspect of another potential product would be actually a curriculum or even perhaps a slide deck or even perhaps a webinar that we could produce. We do not have a lot of resources for that, but it does not take that much to do a slide deck or at least a written curriculum, that could be used for education. Again, I do not mean to - I just want to point out that we have a couple of suggestions for potential products.

DR. RUTH ETZEL: One of the things that still happens is that medical education is driven by the board exams. And having sat on question writing committees for many of the boards, I realize the importance of having pre-constructed questions that can be easily slotted into the board exam.

One very relatively simple product that we could produce is a list of ten questions that could go on both the internal medicine boards, family practice boards and the PEDs boards and they would be welcomed by the board examination committees, I think.

DR. DAWSON: Just wanted to follow up on the webinar idea. In the same way that we vet publications by putting them into the strategic plan or even with our annual - there is a lot of really good webinars out there already. SPARK is doing some very nice, very family focused and education focused

webinars. I wonder whether having work groups really co-write and collect a set of very informative webinars would be a more efficient way of meeting that goal.

DR. GORDON: The question then becomes how do we get them greater uptake. If they exist and already out there, clearly, they are not reaching at least everyone that they need to reach.

We have some good ideas for products. We do not want to define in advance what the work groups are going to consider, but I am glad we have several ideas. We will get those into the minutes and into the charges for the work groups so they can consider what they want to do early on.

I actually like the idea of a white paper because it does provide a statement that we could put out there. But I also like the idea of moving just beyond the white

paper so that we can actually provide something that is useful. Again, I like, Alison, what can we do. And I think the idea that we might be able to actually promulgate a product that would be useful. It would be great.

I want to move on to the second question which is the structure, activities and timing. With the idea that we want to create a product that is on the one hand really an important survey of the field, of the literature, of the science, and the needs, but also perhaps be creative in something that we could actually put out there. And then with my suggestion, if you will, that we might want to stagger these things.

I want to get some thoughts about how we might do this and if we are going to stagger them. We have had one eloquent voice that the health issue should be the first one we

tackle. But if there are other opinions, I also want to hear them.

DR. WEXLER: I do not know how you say let's do medical and not do safety. I am not sure who is going to cut the baby in that sense. We have a saying. Regardless of anything, the school bus pulls up every day. Kids get delivered to schools. There is a lot going on in schools and certainly in the adult world too. I do not know how you vote on this or what is more important. I do not think that the safety is any less important than doing something for medical doctors and medical professionals.

DR. GORDON: Let's just be clear. We are not talking about not doing something, but the order in which we approach them. But thank you. Any other comments?

Given that there are no comments, I think what we are going to do is start off

with the health group. The idea is as soon as we can, shift from an administrative burden in terms of setting up the group and getting it work to a plate where our staff is ready to launch the next one, we will. We are not going to wait for any set period of time, but our target will be within six months and we will start the next one. That we can get all three started within the next 12 months and all of them finished by September 2019.

Activities. Obviously, the first thing is going to be for the group to meet. We have usually done these work groups by teleconferences in the past. We can certainly handle setting up WebEx's so that you can see each other, which I think is valuable.

I just want to point out that sometimes groups will want to do workshops and we could probably accommodate that, but we would want

to be able to plan for it in advance. Do you want to say anything more about that?

DR. DANIELS: Many of you know and obviously having worked on the strategic plan, the typical way we have done working groups is with working groups, we are allowed to have external members from the community that are named. Earlier when we first deciding that we wanted to do these working groups, I did get an initial list of names of external people you would want to add to working groups. It is a matter of if you wanted to run that similarly. For example, if we are going to do the health working group, get the list of names, get more contributions of names and then have that whole group meet to discuss and narrow down some items that you would work on because obviously the topic is very broad. And then work through a set of phone calls. We would maybe decide on a set

of them, but have particular goals for each one so that it is not just an open-ended discussion that does not go somewhere, but to structure that and then structure it toward whatever the product is that you want to do. Is that the way you would like to do it similar to previous ones or would you want to do something different?

DR. AMARAL: I think the way that the Strategic Plan Working Group worked very well. I think the only thing that would probably help is as you say, develop an agenda of items to be addressing on each of the phone calls and webinars so that we bring some closure to that item and then go on to the next one. Write it up and go on to the next one.

DR. DANIELS: And something else that was a possible that we have discussed internally at NIMH was whether we could use part of any

of our upcoming IACC meetings to maybe bring in some speakers for actual discussion around the table, something that is more than a phone call. We could potentially have a meeting, decide who is going to be on it, come up with topics. And then if you thought, for example, the January meeting that you wanted to take on a little bit of that in part of the meeting. We could try to accommodate with that and work with the working group.

DR. AMARAL: Would it be possible maybe to extend to another half day or a half day beforehand a working - I know that complicates things, but just in terms of a face-to-face meeting.

DR. DANIELS: That is pretty difficult in terms of the rules that we have for running these meetings. If you go above a certain cost then you have a lot more approvals and

it is hard to get approved for meetings. We are just within the cost that does not trigger the next levels of approval.

DR. GORDON: I would say if there is a need for something greater than the kind of thing that we had this morning on SEED or what we will have this afternoon on suicide that we would need to consult and figure out whether we could have it at a separate time. I would say it is something that you can think about and if you can justify to Susan and to myself then NIMH could pony up some bucks for it. But we do not have unlimited funds. It does require an approval process. It makes it a little complicated, but we can work on that.

DR. DANIELS: In terms of the timeline, for example, on co-occurring conditions, a while back for some of you that remembered, we did have a workshop and we have done those

all-day type workshops, which can be done, but we need a lot of lead time. Like a six to eight-month total period probably would not work really well for that unless we knew from day one what we wanted for the workshop and could start planning it. But workshops are another way to have a longer discussion.

DR. GORDON: I would say let's see how it goes and identify the need. Like I said, we will try to get each one started as soon as possible as soon as our staff time will allow.

I am hearing sentiment for the health. I am hearing sentiment for a process that worked similarly to workshops and we want to add in the opportunity to have work groups. And we want to add in the opportunity to have at the very minimum speakers and/or discussion time at the IACC meetings so that the broader committee can weigh in and can

hear what is going on, but also so that we can address certain areas where it would be helpful to have experts come in and talk to us on it.

I think the third question sort of answers itself.

Do we have already a chair for the health group volunteers or not yet?

DR. DANIELS: David Amaral had volunteered to be a chair. We usually for these work groups have two co-chairs. We could also consider if there are other people on the committee that would like to co-chair such a group.

Something I wanted to add just so that you know about it with the topic of health. Autistica in the UK is also working on this issue and they just had a recent conference in New Castle a few weeks ago. They are talking a lot about relationships with health

providers and insuring that providers are educated and autistic adults are educated in how to interact properly in the health care setting and talking about adult health issues. There may be ways that we can connect with them and hopefully not duplicate effort, but help each other. That might be something too to try to get people from that effort to come out here and talk with us about what they are doing and if we want to work on this topic.

DR. GORDON: David, are you still interested and willing in serving as one of the co-chairs?

(David Amaral nods yes)

DR. GORDON: Do we have another volunteer for the committee for a co-chair?

(No response)

DR. GORDON: Okay. We will be sending out emails and working with David to form the

committee and we will try to pressure one of you into co-chairing. Maybe someone with a particular interest in adult health.

DR. DANIELS: We also could have an external co-chair as long as one of them is an IACC member if we wanted to add a co-chair who is an external person. We could discuss that maybe once you submit more names and we clarify it. We probably want to keep it to some reasonable number of people. If we have 100 people on the working group, it is going to be a little bit crazy. We want to focus down on people that bring the expertise that will be needed. We can start with that.

DR. GORDON: Then in January, we can have a discussion about which one comes next. Again, we hope to launch no later than six months from now.

DR. DANIELS: Something that would be helpful is with whatever product we are

doing. We are required by law to do a strategic plan update each year. With the 2016-2017, we spent a lot of time on it. It is a combined strategic plan, but you will need to produce one for next year and one for 2019 as well if possible. Whatever we do here if it can be incorporated into that as well in some way that would be helpful.

DR. GORDON: Okay.

DR. DANIELS: Are we ready for lunch announcements? We have boxed lunches that some people ordered in advance. They are in the back of the room from Panera. For those who did not have a chance to order, we have a convenient store in this building on the same floor just across the hall. They have sandwiches and chips and drinks and those kinds of things. There is a deli next door in one of the executive boulevard buildings. And then there is a really nice shopping center

called the Pike & Rose that is around the corner. You would not have time to sit down and eat, but if you could go to the Pike & Rose and pick up something and come back here, you could be back in time. And then we have our next session starting at one.

(Whereupon, the Committee recessed for lunch at 11:54 a.m. and reconvened at 1:05 p.m.)

DR. GORDON: We are going to get started. We are in the Public Comment Session. We are going to go ahead and start with them. As in the past, Dr. Karen Mowrer from the Office of the Autism Research Coordination will present the written comments.

I understand that the first two speakers are speaking jointly, and they are Karla Shepard Rubinger and Dr. Christina Nicolaidis. Please go ahead to the podium.

MS. KARLA SHEPARD RUBINGER: I am thrilled to be here. This is the second time I have attended a committee meeting here and the first one really set me in motion to come back again. Here we are.

I am the vice president of Mary Ann Liebert, Incorporated. We are the publisher of 88 peer reviewed journals. We have been publishing them for 38 years. We create new journals when we see or hear a need. This is a need. We are going to be producing a new journal, launching it now for 2018 on autism in adulthood. As you can imagine, the comments that I heard this morning and heard certainly in July when I was here made it all the more clear to me where the need was.

Our journals are all peer reviewed. They are represented by editorial boards from all over the world. We are the largest, independently owned health and biomedical

publisher in the world. It is not that we are so big. It is that we are independently owned. The advantage of that is we do things really quickly. When I came in July, this was just an idea. We are here now and it is a reality.

It is my great pleasure to introduce Christina Nicolaidis who will tell you her vision as the new editor-in-chief for this new journal.

DR. CHRISTINA NICOLAIDIS: Hello. Thank you. It so nice to be here today. For those of you who do not know me, I am a general internist. I am a professor in Portland State University and Adjunct Associate Professor at Oregon Health Science University. I am the parent of a transition-aged autistic son. I also co-founded and co-direct the Academic Autism Spectrum Partnership in Research and Education or AASPIRE, which is a long-

standing NIH-funded academic community partnership that focuses on participatory research to improve the lives of adults on the autism spectrum.

Obviously, apropos to all the morning discussion, you all know very well that there has been far too little attention historically to autistic adults and the issues that impact them.

Since we started AASPIRE about 11 years ago, I have actually been really impressed with the progress. I am an internist and people would constantly look at me and say, but you are not a pediatrician. It has been really nice to see the growing awareness. I have been very pleased to see how much the IACC has helped with that, how much particular advocates have pushed with that. It has been really nice to see recognition of the importance of including autistic voices

in issues around autism. And then it has been nice to also see more recently, growing interest about transition issues for autistic youth who are emerging into adulthood.

Unfortunately, the parent, the clinician, the researcher in me, knows that we have a really long way to go. But, again, I am really thankful to those of you in the room who have made a big difference in making those changes.

Given this context, when Mary Ann Liebert approached me about the journal, I just could not say no. I really think that this is the right time for having a journal that specifically focused about the issues that are most important to adults on the autism spectrum. I am very honored to have the privilege of being a part of this journal and being able to shape it.

I am envisioning the journal as the home for research and scholarship on autism in adulthood. I am hoping it will bring together academic voices, autistic voices, clinician voices. And our plan is to include original research, in-depth analysis, multidisciplinary dialogue, really about the issues that are most pressing for adults on the autism spectrum. We are really going to focus on things that can provide new insights, new knowledge to guide actual clinical practice in policy.

Given my appointment - I have multiple appointments in medicine, social work, public health. I am really well aware of how different norms can be in different fields. But for this to work, it has to be very multidisciplinary. I am committed to ensuring that the journal is multidisciplinary in nature and is welcoming to authors from a

wide range of professions and a wide range of backgrounds. And of course, if we are ever going to actually have a true impact on the field, we have to include autistic adults themselves.

The one thing I am kind of most excited about and the one thing that probably really pushed me to take a role in becoming editor-in-chief is to really build a new type of journal that can incorporate autistic voices in every way into the academic literature. I am hoping to include autistic individuals both inside and outside of academia.

My long-time collaborator, Dora Raymaker, will serve as the associate editor. Dr. Raymaker brings a dual perspective both as an autistic adult and as an NIH-funded autism researcher.

We intend to include other autistic individuals as some members of our editorial

board, as authors, as commentators, as part of the peer review process.

Finally, the journal has to kind of remember that autism does not exist in a vacuum. As much as we are going to really seek out articles from basic science, clinical science, social services research, we also aim to really include work that addresses the intersectionality between autism and issues such as race, ethnicity, disability, sexual orientation, gender identity, and discrimination, trauma, et cetera.

As Karla mentioned, we are aiming to start publishing the paper in 2018. We are envisioning this as an international peer reviewed subscription-based print and online journal with an open access option.

I am really excited about the potential this journal can have in playing a role with

advancing - really the exact issues that you are talking about here at the IACC.

We are going to need a lot of help. I am actively looking for more editorial board members, for peer reviewers, for authors, for commentators. If you have any interest, please let me know. And if you know of any other folks who might be interested, again, no matter what their role, please pass along the word.

With your help, I really believe the journal can play an important role in supporting the goals of the IACC in advancing knowledge, practice, and policy about autism in adulthood. Thank you.

DR. GORDON: Thank you very much. We have a little time. Before we invite the next speaker, are there any questions or comments that the committee would like to discuss?

I think given our conversations about the importance of transition age and adults with autism, it is really wonderful that we have this new venue for publication of research in that area.

John.

MR. ROBISON: I just want to say that it is great to see that the wider publishing world is seeing the importance of adulthood. We have to keep the word spreading.

If I could say one other thing to you is we always have to keep our focus too on the idea that civil rights and acceptance of autistic people are not mutually exclusive with medical research in solving our problems. We have to always have the message. Do both across the lifespan. I applaud them joining us.

DR. PEÑA: I was wondering if there is a website for the journal yet and when you will be accepting manuscripts.

MS. RUBINGER: (inaudible comments)

DR. GORDON: Sorry, for those of you who cannot hear, there is not yet a website, but there is a draft cover, which apparently, we do not have, but that is okay.

DR. RUBINGER: That is Mary Ann Liebert, whose company this is. And the next slide is a draft of the cover. But we are literally beginning this now and that is what is really important. Our website for the company is MaryAnnLiebert.com. I can share our contact information and emails with you. And obviously, Christina is plummeting the depths of everything that you have talked about.

We will do a preview issue, which will come out next spring. We will start doing publication then and the full subscription

will start out at the end of that year. Thank you.

DR. GORDON: Thank you. I would like to invite our next public commentator, Dr. Micah Mazurek. Hopefully, I have gotten that right. If you would come to the podium.

DR. MICAH MAZUREK: Hi and thanks so much for the opportunity to talk with you today. For those of you who do not know me, I am a clinical psychologist and an associate professor at the University of Virginia, having recently moved from the University of Missouri and the Thompson Center for Autism.

I want to just thank you for this opportunity to share the work that we have been doing to increase access to best practice care for children with autism and their families.

I would like to just add that this work has so far been focused on children, but

certainly has applications for adults. I think you will see what I mean when I share a little bit more about the program.

As you know, children with autism and their families face really significant barriers for accessing high-quality evidence-based care in their communities. Even though most parents will notice early signs of autism very early in life, many children will not receive diagnosis until several years after the onset of symptoms.

In addition to that, that leads to delays in accessing intervention in poor long-term outcomes. Children with autism also have trouble accessing coordinated comprehensive and family-centered medical care in their home communities. That leads to untreated comorbidities, including medical problems and psychiatric problems, which

really affect long-term quality of life and health.

There are many reasons for these kinds of health care gaps and I think this really reflects some of the conversation earlier this morning about the health and wellness work group.

But one of the biggest barriers that we face is the national shortage of health care providers who have training in autism. Many families drive miles and miles to access care. They live very far from autism centers and autism specialists. Those families who live in rural and remote areas and those who do not have financial resources or transportation resources may never access those services. And as a result, significant unmet needs really affect quality of life and health for a lot of the families that we serve.

Even for families who live very close to autism centers, they are often faced with waitlists of months or even years to get in to see those specialists.

Our vision is to really improve the system of care so that families and children with autism can access best practice, high quality care in the communities in which they live.

Over the past two and a half years, our team really been working to test and develop a new model for improving access to care especially for underserved and rural communities.

We based our work on an innovative model called Project ECHO that was initially developed to address hepatitis C at the University of New Mexico. Our tele-mentoring program uses this framework to train community-based providers, including

pediatricians, family physicians and nurse practitioners in autism screening and management of comorbidities. We use high-quality video conferencing technology that is secure to connect these local primary care providers with our interdisciplinary team of experts. We meet every other week for two hours to train them on best practices.

We used a combination of didactics, case-based practice, and teaching providers to implement and practice techniques in their own communities so that they are caring for their patients with the highest quality of care.

The results of our initial pilot study showed significant improvement in provider self-efficacy and in autism screening practices. We were really excited about that and we think that the model has potential to

really spread expertise into local communities.

And thanks to funding from HRSA through the Autism Intervention Research Network on Physical Health or AIR-P, we are currently conducting a large multi-site study to test the model in ten sites across North America, ultimately training 150 primary care providers who provide medical care to underserved children.

We will be able to test the effectiveness of the model through direct chart reviews to see if we are changing practice as well as looking at improvements in provider knowledge and self-efficacy. We hope that the results of this work will continue to guide our efforts to reduce health care disparities for underserved children and families.

We would like to encourage you as researchers, clinicians, and policymakers to consider models like ECHO and other similar training models as ways to disseminate best practice knowledge and to close that research to practice gap to improve outcomes for people with autism. Thank you.

DR. GORDON: Thank you for your comments. Would anyone from the committee like to comment on that or discuss?

DR. DAWSON: It seems very appropriate to our earlier discussion. We should clearly be reaching out and finding out more about the work you are doing. It sounds fantastic.

DR. AMARAL: Just a follow up. Is there some place where we can get information about your pilot program?

DR. GORDON: The written comments contain information about the program and you have a copy of that in your folders. Thank you.

We are then now going to progress to the summary of the written comments. Karen Mowrer from OARC is going to take us through those. Thank you, Karen.

DR. KAREN MOWRER: Good afternoon, everybody. Since the July meeting, the IACC received written public comments from 14 commentators. For the purposes of this presentation, we have organized these under seven broad topics. The committee has provided all of the comments in full, but they will be summarized briefly here.

The first topic we had was the role of the IACC. We received three comments. Ms. Peggy Smith commented that more should be done to prevent autism and to help children and adults with autism.

Mr. Dwight Zahringer feels his comments from previous meetings have not been addressed. He also recommended that the IACC

facilitate a survey of parents of autistic children.

Dr. Eileen Nicole Simon thanked members of the IACC for discussing her comments at the July meeting; however, she asked that more time be allocated for discussion of public comments and that the perspectives of parents of minimally verbal children be represented more.

The second topic we had was autism research priorities. We also received three comments on this topic. Mr. Tom Hess suggested that participation in research studies could be improved by including families as equal partners throughout the research process. He also suggested that research studies focus more on individuals severely affected with autism rather than higher functioning individuals.

Dr. Eileen Nicole Simon asked the IACC to discuss her comments describing potential links between autism and brain injuries resulting from umbilical cord clamping, asphyxia at birth, and prenatal exposures to drugs and infections.

Dr. Gail Elbek asked the IACC to consider and discuss studies on the effect of soy on brain development.

The third topic was resources and support. We had three comments on this topic. Ms. Sarah Williams provided information briefly outlining college internship programs, services for transition-aged students with autism and other learning disabilities.

Mr. Caleb Anderson shared several web resources on mental health and wellness.

Ms. Helen McNabb provided the definition of the term hyperesthesia and recommended it

be used to describe those who are sensitive to touch, sound, smell, and other stimuli.

The fourth topic was heterogeneity in autism. We had two comments on this topic. Dr. Lynn Waterhouse suggested that US science agencies no longer fund studies on DSM-5-defined ASD because the level of heterogeneity within the ASD diagnosis limits the usefulness of these studies.

Ms. Jill Escher shared her commentary on a recently published article about neurodiversity, which she feels does not accurately describe those who are severely affected by autism. She believes a new range of diagnostic terminology is necessary to describe heterogeneity in ASD.

The fifth topic was concern about medical practices. We had two comments on this topic. Ms. Donna Young shared an online petition advocating against premature

umbilical cord clamping and concerns about brain injury.

Dr. Debasis Kanijilal shared several emails he has sent to other committees to express his concern about brain injury resulting from inadequate treatment of hypoxia in newborns.

The sixth topic was vaccines and autism. We received two comments on this topic. Mr. John Best believes autism is caused by mercury in vaccines and expressed frustration that the issue was not being addressed by the IACC.

Mr. Dwight Zahringer asked the IACC to investigate how glyphosate may be affecting children with ASD versus those without ASD. He also asked the IACC to request that Congress investigate the CDC whistleblower issue and to provide a full debrief of the study on autism in the MMR vaccine.

The seventh and last topic was wandering and suicide. We received one comment on this topic. Ms. Peggy Helm-Quest feels that anxiety and social isolation stemming from autism can lead to a desire to escape, which can manifest as wandering and suicide.

That concludes the summary. Thank you again to everyone who sent in written comments.

DR. GORDON: Thank you. Would anyone on the committee like to highlight or discuss any of the written comments?

DR. ROBISON: I just got a text that the online feed is off. Can we have the people check?

DR. GORDON: Can we check to make sure the online feed started up? It is working here, but let's make sure it is working online. Those who are calling in on the

committee, have you been following us and hearing and seeing us?

DR. RING: This is Rob Ring. I lost the feed, too.

DR. GORDON: Thank you, Rob. Anybody else? You heard us because you are telecommed in, but you lost the video feed, Rob?

DR. RING: Exactly.

DR. GORDON: We will work on getting that restarted.

DR. WOLINETZ: This is Carrie Wolinetz. I am on the phone and the feed is working for me for whatever it is worth.

DR. GORDON: And you are on the NIH campus?

DR. WOLINETZ: Yes.

DR. GORDON: Ask if the audio feed is working.

PARTICIPANT: Yes, we are hearing you loud and clear.

DR. GORDON: I am glad. We will continue while we work on this issue. Anyone else who would like to comment on the written comments? John, you also had a comment?

MR. ROBISON: I would like to comment on Jill Escher's comment, which was in response to the recent Simon Baron-Cohen editorial about whether autism is a disorder or a difference and how we should characterize it.

I think that first of all I would say to any parents of kids who are not able to advocate for themselves at this point and also for people who feel more severely impaired than me, I feel like any of us who serve on this committee as autistic people must recognize our duty as autistic people who were appointed and not elected to do our very best to fairly represent the individuals at all points of the spectrum. I certainly always have that in mind. I believe Sam here

next to me does too although I cannot speak for her.

I think that Ms. Escher raises a valid concern that we must be careful in our advocacy to balance our speaking out for civil rights with a similar amount of speaking out for the development of tools, therapies, research that will benefit us. While it is true that there are social problems to autism, it is also true that things like epilepsy, the GI pain, many of these other things are very real medical issues and we must never let the government, the Congress, the senators who watch over us, we must never let them lose sight of that fact.

MS. SAMANTHA CRANE: John is absolutely right, that as the autistic self-advocates on the IACC, we take it extremely seriously our

obligation to speak for everyone across the spectrum.

I will say that when people break us down into functioning levels, it often really obscures the diversity that exists in our community. Epilepsy is not a low-functioning issue or a high-functioning issue. Epilepsy affects everyone across the spectrum. I know quite a few people on the spectrum who also have epilepsy. They all look very different and they all have very different needs. People with GI issues also are all across the spectrum.

I would really caution against the assumption embodied in that comment that if I am here at this meeting then I must not have these other medical needs and I must not understand these other medical needs because medical needs affect really all of us.

We also need to make sure that we understand that civil rights are not for just some of us. They are also for all of us. The people who - I do not need civil rights protections as much as other people in the spectrum do. I have a much easier time advocating for myself. I do not need access to communication supports. I do not need access to significant assistance in living independently. It is actually the people who need significant assistance in order to live independently who we are most concerned about when we talk about civil rights.

DR. AMARAL: I think your points are both well taken. I think Jill Escher - the reason that she brought up her concern is because to the general public, there is an issue of perception. To the general public if the face of autism is represented by the two of you, what happens is they miss the notion or the

reality that autism is also young children who cannot talk, who have intellectual disability, who have terrific GI problems and all these other comorbid conditions.

I think the issue is a balance. As you said before, John, I think we have to never forget that while civil rights is an important issue, we also have a responsibility to represent the entire spectrum of autism and make sure that who cannot speak for themselves have a voice here on the committee. I think that is what Jill was trying to emphasize.

MS. CRANE: I will add that ASAN in the last Autism CARES Reauthorization, ASAN was to my knowledge the only advocacy organization that went to the Hill and said that people with complex communication needs and people who need Medicaid home and community-based services in order to live

independently need to be directly represented on the IACC. We were the only advocacy organization that actually took that position.

I personally hold that belief that we should have people with significant needs on the IACC. I also know that my organization will be taking that position too. We strongly believe that people with significant needs need to be empowered to also speak for themselves.

MS. SINGER: I was going to make a point similar to David's, but just to follow up to what Samantha is saying. Many people with that level of significant needs are not able to come to the table and represent themselves. They rely on their parents, who I promise you do not give birth hoping that one day they will be able to file for guardianship to represent them. My daughter,

for example. There is no way that she would be able to, one, physically sit at this table for more than five minutes nor does she have - because of her intellectual disability, she would not be able to really understand the conversation or advocate in any way for policies that would support her civil rights. There is a large segment of our population that does rely on parents to advocate for them.

Another point that Jill makes that I wanted to point out is that we all talk all day about how heterogeneous the heterogeneity in autism. Does it still make sense for us to use one term, autism spectrum disorder, to describe someone who like the two of you are able to come to the table and advocate for yourself and to use autism spectrum disorder to describe your situation and to use the same terminology, autism spectrum disorder,

to describe the situation that my daughter, for example, finds herself in?

I think what happens is because the media focuses on higher-functioning individuals - we now have two television shows. When studies come out, higher-functioning individuals are always ones who could comment because they have language and are able to comment. Similarly, they are the ones who come to the table to advocate for policy. To use the same terminology to describe those very different clusters of symptoms makes no sense because the needs that my daughter has in terms of services and supports is very different than the needs that I think the two of you. I do not know your personal situation, but just from sitting here and watching you interact, I can see that in many cases the needs would be drastically different, not to say that those

needs are not equally valid, but they are different.

The word autism has now become so broad that I think people who have the diagnosis of autism have almost nothing in common with each other anymore. I think we need to seriously talk about either bringing back the term Asperger's because that did define a clear cluster of symptoms or coming up with a new word to describe the type of autism that afflicts the much more seriously challenged individuals who have intellectual disability, who have self-injurious behavior, who have minimum language who are not able to come here to the table and advocate for themselves because they are being left behind.

MS. CRANE: I have self-injurious behavior. I just want that to be known. In fact, the reason why I often am doing something else while I am at this table is

because I cannot sit quietly without self-injuring myself while doing that. I do not usually talk about my own needs.

When people bring up self-injurious behavior, epilepsy, and even classical autism diagnoses, they often are making an assumption that is not correct. There are people who look like me who are diagnosed with classical autism as children. There are people who look like me who self-injure. There are people who look like me who have epilepsy. There are people who look like me who have GI issues. And there are people who look like me who need extremely intensive supports in order to live at home.

I am not saying that there isn't still a pretty significant range of experiences. But when people have this conversation, it is really important that we not make assumptions

about people's level of need based on how they look.

I think that if we do have people on the IACC who have significant communication needs and people who are on the IACC who have significant independent living support needs, the IACC might look different. I do not think that is a bad thing. The IACC is barely accessible to me frankly as a person on the autism spectrum. I understand that the IACC is not going to be accessible to a lot of people who are not in this room. I would respectfully say that maybe that means we should be changing how the IACC looks in order to make sure that these people are included in conversations that affect us.

DR. GORDON: I just want to point out a few things. First of all, I think this exchange is really important and the importance of the exchange. I just want to

point out is you cannot see it because you are facing the other way and maybe Alison can, how enraptured the audience is in this moment. I think there are reasons for that.

Number one, you are both telling compelling stories about what it is to have the label of autism. And then of course, Sam, coming out with your acknowledgement that you suffer from symptoms, which one might think are present only in more severely affected individuals, points to the fact that unfortunately we have a situation here where we do not know a better way to describe autism except as a spectrum.

Although I was not there in the room when DSM-5 was written and Asperger's was discarded and the spectrum label was selected instead, I would imagine it is because people could not agree on where to carve that

difference anymore whereas in the past they might have been able to.

I think it is important, and we are engaged in it as we go on, to continue trying to do the kinds of research you heard about this morning with SEED where we do more in-depth longitudinal observations in phenotyping so we can get a sense of whether there are dividing lines, whether there are diagnostic differences that could lead to the creation of new labels at worst, and at best, new ways of categorizing and treating people according to not just what they say their needs are, but actually some etiological factors or groupings, et cetera.

Right now, we do not have them and I think that is both unfortunate because it means that we cannot easily pull out who is who, but on the other hand, I guess it is fortunate because we can have these

conversations between people who are affected or their families are affected, in very different ways.

MR. ROBISON: Alison, if I could just say one thing too in response to what you have said. Sam is a little newer than me to advocacy here on the IACC. But you and I have a decade of experience advocating for autism science together. For me as an autistic person, for you as a mother and sibling of an autistic person, we have gotten along okay. We have kind of done the job and we have advanced our causes and we are okay doing that together and we both have a place at the table.

You probably can remember over the years that I have told you about taking part in many studies, looking for biomarkers of autism. And when I take part in those studies, what I learn is that the brain

imaging, the blood type, the genetics at the Thompson Center, all these prestigious institutions, they cannot separate me from an autistic person who is my age, but is seemingly not able to take care of himself, nor can they separate me from children whose outcome is yet unknown.

While it is a great idea to say my autism is different from your child's, we do not know how to separate it. Until we do, I am not sure how we can do better than we are now. I think it is important to remember that I am not your enemy nor am I your child's enemy. I do not think you ever think of me that way, but the wider community needs to know that we are in this together and what we want is maximum quality of life for all autistic people. I think it sucks that because I am articulate person, people think

it makes me a bad representative for autism, but it is the reality we have to deal with.

MS. SINGER: I think using the single term to describe a heterogeneous group does a disservice to everyone. I have talked to several autistic adults who say that they have difficulty accessing services because the expectation is that they are going to be in much worse shape than the way they present when they apply for services.

This is not an issue that is only negatively affecting more challenged people. It is affecting everyone because people get different impressions of what autism means based on maybe the first or second person that they see.

MR. ROBISON: Let us bring Asperger's back. Let us make that a thing.

MS. SINGER: That would be my question to you and to Samantha. What is your feeling

about trying to go back to what Josh was describing, which was a system where we had terminology that was more specific and more descriptive of symptoms so that they were better able to lead to personalized medicine in terms of appropriate treatments.

DR. GORDON: Sam, if you could just answer quickly because there are other folks who have something to say.

MS. CRANE: I disagree that it is specific because when they decided to merge the diagnoses together, one of the reasons why they did so is that by adulthood, clinicians could not tell the difference between people diagnosed with classical autism and people diagnosed with Asperger's as children. They could not reliably tell.

Many people had speech delays up to about eight years old, and then acquired speech, ended up looking exactly like me as

adults. And a lot of people who were diagnosed with Asperger's were diagnosed as Asperger's simply because they had no speech delay, but they had extremely significant needs.

The reason why the DSM-5 now has - the other reason why the DSM-5 now has little spectrums where you can say ASD with this characteristic, with that characteristic. Then maybe they should start using it.

DR. DAWSON: I was just going to make that point. I am not going to try to defend DSM-5, but I will try to explain the rationale, which really was that clinicians cannot reliably make a distinction between the different subgroups that were part of DSM-4. It did not map on to specific treatments or etiologies.

The solution was these lists of specifiers. If it was used properly, it is

supposed to be autism spectrum disorder plus a range of specifiers and those specifiers include intellectual disability, language delay, presence of seizure, early course in terms of regression/non-regression, genetic etiology, and medical comorbidities.

I do think that perhaps even in this group, we might start using that. This is autism and intellectual disability. This is autism with seizures, autism with significant medical comorbidities. And perhaps that would help us to begin to reflect the broad heterogeneity that we see in autism.

DR. GORDON: Are there other comments from anyone else on the committee?

DR. PEÑA: I just want to piggyback on the idea that we should be including more autistic self-advocates across the spectrum whether or not you want to use that term. I do know people who have complex communication

challenges and they use augmentative and assistive technology to communicate. I feel like there should be representation from them.

And while we are on the topic of diversity, it would be really great if we had more underrepresented minorities on this group in particular. I think that this group is not representative of all the people involved in the autism community and we really need their voices at the table.

DR. GORDON: Thank you. We focused most of our attention on the one commenter who discussed heterogeneity. Are there other public comments that people would like to discuss? Thank you. Then we will move on. I appreciate the robust discussion about these issues.

The next item on the agenda and we are just running a teeny bit early, which is good

because that will give us a little bit more time later for some of the other business items we had to give rather short shrift to.

We are next going to enter into a discussion on the science of autism and suicide. Assuming our speakers are ready, we are going to start with Sarah Cassidy, assistant professor at the University of Nottingham in the United Kingdom. We really appreciate you making the trip here.

DR. SARAH CASSIDY: Thank you for inviting me to talk about this very important and very under-researched topic. It is wonderful that it is getting this international attention and international momentum to try and address it.

I thought I would start by telling you a bit about me and what we do in the UK. I lead a research project and group called Mental Health and Autism. And the aim of that

project is to understand and reduce mental health problems in suicide in autism.

Now when we first came to this topic, we were very worried to find that there were very small amounts of studies that have been done in the area of suicidality and mental health in autism. The first thing that we have been doing over the past three years is doing an international priority setting exercise, which is involving autistic people, the autism community, parents, families, policymakers, service providers and clinicians to ask them what should be the top priorities for suicide in autism research to guide what we do. Make sure that it is acceptable and it is impactful.

We have done this with the support of the James Lind Alliance, which is a priority-setting partnership that is part of the NHS, National Institute for Health Research, which

really aims to include patients in the public in driving forward the priorities of future research. It has also been funded by the Economic and Social Research Council and Autistica.

Through this very long exercise, we identified a number of key strategic areas that we should focus future suicide and autism research: assessment and measurement, which is primarily focusing on adaptive tools. How do we measure suicidality in autism? Risk and protective factors, particularly developing new models to explain suicidality in autism. What are the mechanisms underlying this increased risk? Are there autism-specific risk factors, the mean that we have to change intervention and prevention strategies designed for the general population to fit the needs of this group?

I am going to briefly talk about a number of different projects that currently are in progress. I do not have time to go into lots of detail or talk about everything that we are doing, but I am going to try and give you the highlights of it of research that we are currently doing that are trying to develop new adaptive tools to assess suicidality in autistic people and also understand the risk and protective factors for suicidality in autism in order to understand and develop new intervention and prevention strategies. This is a very new and developing field.

A note on language. In the UK, in particular, part of this is what has come out and kind of resonates with the discussion that we have been having a little is how we actually describe and talk about autism.

A large-scale research study in the UK showed that the autism community when they were asked what do you prefer being referred to as, they used a really wide variety of terms to describe autism: autistic, aspie, on the spectrum, person with autism. But on the whole, what has come out of our priority-setting exercise is the autistic person was most preferred by the autism community. A person with autism was preferred by professionals, which is very interesting.

The reason I am bringing this up is for the remainder of my presentation I am going to use the term autistic person, because that is really what we have been asked to do in the steering group and the people working with us.

Why mental health and suicidality in autism? There has been some recent research showing that the majority of autistic adults,

79 percent, meet criteria in their lifetime for at least one mental health condition. And we know from research in the general population that these mental health conditions are a significant risk factor for dying by suicide.

What about suicide in autism is what we asked in 2014. We did the first large-scale clinic study of suicidality in adults newly diagnosed with Asperger's syndrome, which is autism, but without comorbid intellectual disability or language delay.

We asked over a nine-year period everybody who came through especially this clinic diagnosing Asperger's syndrome in adulthood. We asked every single person have you ever been diagnosed with depression in your lifetime. Have you ever contemplated suicide and have you ever planned or

attempted suicide? Those were the three questions that we asked.

We found a really worryingly high rate of suicidal thoughts in this population of adults nearly diagnosed with Asperger's syndrome. Sixty-six percent contemplated suicide. Thirty-five percent have planned or attempted suicide. And 31 percent have been diagnosed with depression. And that 66 percent suicide ideation is significantly higher than the general population of 17 percent and patients with psychosis, 59 percent. It is even higher than the risk groups for suicidality.

We also found that self-reported autistic traits and depression were significant risk factors for suicidality.

And a much more recent and even larger scale study in Sweden showed that autistic adults were significantly more likely to die

by suicide than the general population. The odds ratio was nine.

And what is interesting and very important about the study is that it indicates that the risk factors dying by suicide are very different than in the general population. In particular, being female and being diagnosed with autism without learning disability and depression risk factors. And being female aspect is quite a key finding because in the general population, most people who die by suicide are males. It is a completely flipped over risk profile.

Most of the intervention and prevention strategies in the UK are aimed at men, but maybe we should be thinking something quite different for autism.

There are a great number of counting studies. These are incredibly important

because we need to know the scale of the problem and this is what makes us look at it. But there is not enough about why. We need more about why this is happening, what is driving this, and what can we do about it. That is what I am going to focus on for the rest of this presentation is more about trying to get at the why question.

First of all, assessment and measurement. How do we assess this difficulty in autism? We have a number of challenges that make us question whether the measures that we are using to assess suicidality in the general population are working in the same way or as effective for autistic people.

Difficulties such as alexithymia, which is a difficulty in articulating your internal or emotional experience. It could lead to under or over reporting of suicidality or depression. A lot of the autistic people that

we discussed this with, said the first thing that they are asked in a GP appointment sometimes is how do you feel. That is a very difficult question for them to answer. They say I do not know how I feel. Most of the time that is a really impossible question to answer.

They have mind difficulties. The ability to register or understand the impact of your death on another person. Or are talking about suicidality to another person could affect the way that you talk about it.

Overlapping behaviors such as social withdrawal or sleep problems that are indicators of depression in the general population overlap with characteristics of autism. How do we tease those apart?

There might be unique aspects of suicidality in autism such as rigidity or reduced cognitive flexibility that impairs

ability to weigh up alternatives that could really increase risk.

And what we have been doing is involving the autism community in the development of these questions. How should we ask about this sensibly and in a way that at least more accurately identifies risk and mental health problems?

This is the ESCR grant that I am leading. It has four stages. Stage 1 was a systematic review of what measurement tools are actually available to assess suicidality in adults with or without autism diagnosis.

Stage 2 used a variety of qualitative means, focus groups, cognitive interviews, and an online survey to inform and test the adaptations.

Stage 3 will explore the measurement properties, how robust and useful are these new tools.

Stage 4 will establish the prevalence of suicidality in autistic adults in the UK.

We are about halfway through. I am just going to give you a really brief overview of the key things that we have been finding from our research. We found that there are no validated suicidality assessment tools yet that have been used in autism or validated for this group.

We did identify the Suicide Behaviors Questionnaire-Revised that has been used in loads of research. It is very brief. It is a four-item tool. We have decided to take that forward to see if it can be adapted.

We have four focus groups with a variety of stakeholders, autistic service providers, and clinicians. We asked them how clear are the questions, how important are they and are there any important questions missing.

And then we have two sets, two stages called 15 cognitive interviews with autistic adults. We did it twice, so each person saw the original measure. We made the adaptations and then we did it again.

And the next step that we are going to launch very soon is an online survey to feedback on this candidate tool.

And the whole point of all of this is to say tell me what you are reading and thinking about as you work through the questionnaire to identify the problems, and also to get them to rate how clear all the questions are to really get the meat of how are these things working? How are they interpreted before we do the psychometric measure study?

What did we find? We found real difficulties with language. They also suggested to break up the questions and give few options. Like in the PHQ-9, for instance,

it has a question, something along the lines of do you have difficulties with sleeping, i.e. difficulty falling asleep, staying asleep or sleeping too much. Things like that caused real issues. They just went with the first one or did not take into account the whole question. It led to really different responses and misinterpreted answers.

They talked about difficulties in memory and time. If you asked in the last weeks, have you done any of the following, they found it really difficult to visualize that. They recommended maybe using a diary or a calendar.

Literal interpretation was a massive issue. Exactly how many thoughts. What about when I have accidentally overdosed? But I did not mean to hurt myself or end my life. What do you mean by a plan?

Insensitive language in a lot of the measures such as commit suicide, which has a moral connotation or legal connotation. And they are worried about the purpose of the assessment so things with a lay out like maximum scores were color coded on some of the measures. That was quite worrying and led them to avoid those.

And rapport and trust. If I fill this out, what will happen to me?

That work is still ongoing. We have nearly got our candidate tool finalized, but we are still working on that.

What about risk and protective factors? I am going to briefly cover three studies. One is exploration of autistic traits and the interpersonal psychological theory of suicide. A co-design suicidality survey that we have done in partnership for the steering group of autistic adults. And finally,

preliminary findings from the first Psychological Autopsy Study of suicide in autism.

What is the interpersonal psychological theory of suicide? It is a theory of death by suicide in the general population. It attempts to explain why some people do and don't attempt suicide.

In order to experience the model argues suicidal ideation, one needs to experience two psychological constructs. One is thwarted belongingness, which is I am alone. And the other is perceived burdensomeness so perceiving that you are a burden on others.

And I thought when we were reading the literature on this theory that a lot of the outward indicators that signaled to clinicians that these two psychological constructs at present and signal that the clinician should be worried actually

overlapped with a lot of the challenges that autistic adults were telling us about. For example, social difficulties, social exclusion, unemployment. All of these things are indicative of these two psychological constructs.

As a first step, we wanted to ask are autistic traits associated with experiencing these psychological constructs and then in turn suicidality.

In autistic traits, there is not confirmed diagnosis that we looked at. It is self-reported autistic traits in the general population that differ naturally in the general population. If you report a clinically significant level of autistic traits, you are more likely to have a diagnosis.

We did this study with 163 general population young adults aged 18 to 30 years

old. We found that self-reported autistic traits significantly predicted your likelihood of experiencing perceived burdensomeness and thwarted belongingness over and above age, gender, and depression.

We also found that autistic traits were significantly predicted suicidality through these constructs exactly as the model would predict.

But these models and measures have been developed for the general population and we do not know how autistic people interpret the measures or how much the things that are included in the measures actually apply to autistic people. That is something that we are developing further now.

But another kind of problem approach that we used was a piece of participatory research because there was so little on the topic, but we thought we really just need to

talk to and include autistic people who have experienced these things and asked them what their experiences were and what we should be looking at.

We formed a steering group of eight autistic adults who had experienced mental health difficulties and/or suicidality. We used the focus groups to identify themes, which may increase or decrease risks of experiencing mental health problems and/or suicidality and developed an online quantitative and qualitative survey to try and capture and measure these experiences.

What did the focus group say? The key themes that emerged were isolation, not only social isolation so lack of social connectedness or number of friendships, but also non-social isolation. One person gave the example of not being able to engage in activities that they enjoyed on a day-to-day

basis because they could not say, for instance, get on the bus because of sensory overload, things like that and lots of other examples.

They talked a lot about lack of belonging without being prompted, lack of belonging in an autism unfriendly world, which led to thoughts of leaving, which really resonates with the IPTS that I just talked about earlier. It was completely kind of spontaneous. It was not prompted in any way. They just started talking about it.

They talked about lack of opportunities in employment and education. For instance, having to leave a university or drop out of university because it was quite difficult for them.

Social and communication difficulties and tendency to mask or camouflage these difficulties in an attempt to fit in, which

led to mental health problems and difficulties accessing help. They would present to services and they are so used to masking that they masked their distress and they do not come across as being that urgent.

Lack of autism friendly services in their words. Late diagnosis. Being misdiagnosed. Quite a few of people in the committee have been misdiagnosed with things such as borderline personality disorder before going on to get an autism diagnosis, but there are other examples.

They also found that when they are diagnosed late, there was not any post-diagnostic support. They did not know where to go next.

They also talked about childhood experiences. Not being supported to have a positive identity. Recognizing their strengths as well as their weaknesses. And

they felt that they had a lack of resilience to deal with fewer problems further down the line.

There is an absolutely huge amount of different themes. And now I will cover more, but these are the main ones. We tried to develop a very large questionnaire and we had lots and lots of people take part. We are still analyzing it because we have in some cases 200 qualitative responses to treatment and support. We have an absolutely huge rich data set that we are getting through.

Here are some of the highline results just from the quantitative stats. We had 168 adults that completed the entire survey, 67 males and 101 females and 108 control females. Now, the reason I only have a female group is because no matter how hard we worked, it was actually really difficult to get general population adult males to

complete the survey, particularly the suicidality measures. That is a real challenge for suicide research in the general population.

But we found in autism group - the suicide behavior questionnaire revised was used again out of 10.31, which is massively high. It is significantly higher than the recommended cutoff for psychiatric populations, which is eight. And 69.8 percent of the autism group scored above that cutoff. It replicates what we found in a completely different environment and different method in our first study. But it is significantly higher than psychiatric groups.

We also found that the SPQR in autistic compared to control females is significantly higher. We control for age, education, occupational status, living arrangements, developmental and mental health conditions.

It seems to be over and above those difficulties.

We also found that in the autism group that there were some risk factors that increased that they had higher cognitive SPQR scores if they experienced these things such as history of non-suicidal self-injury, which is a significant risk factor for attempting suicide in the general population.

Having at least one mental health condition. Experiencing unemployment. And also, a possible autism specific risk factor of camouflaging. Camouflaging one's autism in an attempt to fit in in social situations was associated with significantly higher scores on this suicide behavior questionnaire just like the steering group describes.

Now I am going to talk about our psychological autopsy study. These are preliminary results from the first stage of

this study. It aims to establish whether definite confirmed autism or possible autism diagnoses are overrepresented amongst people who died by suicide in the UK.

We also want to look at and compare the characteristics of those with and without autism diagnosis and evidence of autism who have died by suicide.

Full psychological autopsy studies. They involve both analysis of coroners' inquest reports and interview with friends and family of the person who died. At the stage of this study is that we have just taken one section of the coroner's inquest reports so now we have funding to do the next stage, which is interviewing next of kin. That will be happening quite soon. But the idea is to identify targets to prevent suicide in a particular group.

We looked at coroners' records for the period 2014 to 2015, recording a suicide, open where cause of death is undetermined, drug and alcohol related or a narrative conclusion.

We analyzed these records for any evidence of autism diagnosed or undiagnosed. We found over 80 percent inter-rater reliability for evidence of autism.

How we did it was definite diagnosis where clinical diagnosis of autism was noted in the inquest, in the medical records - definite diagnosis. Clinical diagnosis was noted in the inquest - strong evidence of autism, which is possible diagnosis was actually noted in the report. Like this person might have had a diagnosis of Asperger's syndrome in the GP kind of medical record or somewhere else, maybe the family even. And clear indicators when we read about

behavior from various medical records and family's testimony of difficulties in greater or equal to two of these areas. Social communication difficulties, narrow interests, routines, sensory difficulties or special educational needs in childhood.

Possible diagnosis was the same clear indicators and greater or equal to two of these difficulties in these areas, but it was not noted in the record.

Or no evidence where there were no clear indicators of autism.

So far, we have looked at 219 coroner's inquest records, 150 which were ruled a likely suicide according to ICD-10 criteria, and 11 percent of these had evidence of autism, which were significantly higher than the general population rates of 1 percent.

Just to explain this. For the likely suicide, the 150, the majority had no

evidence. 9.3 percent had possible diagnosis. 1.3 had strong evidence, and we only found one record with definite diagnosis. I will come back to that at the end as well to explain a bit more about it.

What are the implications for intervention and prevention from these early results? We know now, I think, that suicidality in autism does appear to be significantly higher than other psychiatric groups. However, because of difficulties in measurements and the types of data that we have had access to, it is unclear whether this is under or over estimated.

Late diagnosed or undiagnosed without intellectual disability, adults without intellectual disability, appear to be most at risk from (inaudible comments) study from Sweden to our study of late diagnosed adults with Asperger's syndrome to the coroner's

study. They are all showing as the same thing.

There appears to be increased vulnerability to known risk factors for suicidality that overlap with the general population, but that autistic people seem to be more at risk for.

Reduce sense of belonging in the world. Isolation. Difficulties accessing support and treatment. Unemployment and comorbid mental health conditions. However, this is not the whole story because controlling for these differences and difficulties, there are still significant differences. And autistic people do still seem to be at significantly high risk than known psychiatric groups. You already have a risk. There is something else going on. It could be the measurement issue or it could be potential autism specific risk factors. And one that we potentially

identified was camouflaging, but there may be others.

What are the implications? Things that we have always been trying to do: timely diagnosis of autism and post-diagnostic support, identifying and supporting the lost generation of autistic adults who have gone undetected, promoting inclusion, independence, and autonomy of autistic people by providing access to education and employment, positive identity and esteem, resilience and sense of belonging.

I would just like to thank you all for listening and also to my collaborators and everybody on the autism steering group who helped with this research.

(Applause)

DR. GORDON: Thank you, Dr. Cassidy.

Next up we have Lisa Horowitz from the Intramural Program at the National Institute

of Mental Health who is going to talk to you about our efforts here to study suicide and its application to autism.

DR. LISA HOROWITZ: Thank you. Thank you so much, Dr. Daniels, for inviting me. I am here presenting my co-PI, Dr. Audrey Thurm, who does autism research in the Intramural Program as well who is not here today, but helped a lot with this presentation.

I am going to focus most - I have nothing to disclose. I am going to focus mostly on youth suicide risk and talk about - give you a very brief epidemiology of that and then talk about the unique challenges of screening for suicide risk in the ASD population and I am also going to talk a little bit about related populations like other neurodevelopmental disorders like intellectual disability.

I am really excited to be here. It is such a privilege to talk to people who are interested to talk about suicide in a group that is interested in autism research. We have a suicide screening tool that we are trying to adapt to be sensitive in populations with autism.

My take home message is really that clinicians need population-specific and site-specific validated screening instruments and that it is really important to use instruments that have an evidence base in the population you are going to use such as in an autism population.

Suicide is an international public health threat. It is actually the second leading cause of death for youth all over the world. And in the United States that is also the case. It is the second leading cause of death for youth 10 to 24. In 2015, there were

over 5900 suicides. As you can see, this is the suicide rate in this country over time. We have not been able to make a dent in this rate. In fact, it just keeps going up.

I am going to use the word yet because I know Dr. Gordon and the National Action Alliance and NIMH is committed to reducing the suicide rate by 20 percent over the next ten years. We have some exciting suicide prevention going on in this country.

But this is really a public health crisis. There is actually more kids that die from suicide than the seven other leading medical causes combined. Just really some stunning statistics.

Suicide is still a relatively rare event. Even more common than suicide is suicidal behavior. That affects over 2 million adolescents who try to kill themselves every year. Some of these

statistics are from the Youth Risk Behavior Survey, which the CDC goes into about tens of thousands of high school students are assessed in schools all over the country. This is self-reported data. They ask about all kinds of adolescent behavior like smoking and sexual activities, substance abuse, but they ask about suicide. Nine percent of high school students report that they had attempted suicide in the previous year.

Even more common than suicidal behavior are suicidal thoughts. And 18 percent of your average high school student has seriously considered killing themselves in the previous year. These numbers are just staggering.

There is also a myth that younger children do not think about suicide, but actually younger children under 12 actually plan, attempt and die by suicide. It is actually the second leading cause of death

for 10 to 14-year olds. It actually just surpassed death by motor vehicle accidents, which used to be the leading cause. It is also the tenth leading cause of death for kids age 5 to 11.

When you look for statistics in suicide in the ASD population, most of the work is done by Dr. Cassidy. But some of the studies especially for youth are very limited. They are very scarce. And they are limited by sample size and the methods vary a lot. And most of the focus is on adults or on people with Asperger's disorder. The rates and the ranges that I can give you vary greatly. It is anywhere between 11 and 66 percent, which is just way too wide a range to know where the true numbers lie especially for youth.

When you look at suicidal ideation and behavior in youth with ASD and this is 16 years or under, about 13.8 percent is what we

can estimate. That is pretty much from looking at again very small studies.

It turns out that people with ASD are at greater risk for many disorders. This is comparing people with ASD to the general population. As you can see, depression, people with ASD have 123 percent higher rates. And then when you look at suicide, it is 433 percent that are the estimates.

These are the risk factors for suicide. I am not going to go through all of them. But the most potent risk factors highlighted are previous attempt. In psychology, we have a saying. The best predictor of future behavior is past behavior. This is absolutely true for suicide. I highlighted medical illness. You will see why in a minute, but that is often an overlooked risk factor for suicide.

And then I also highlighted isolation as Dr. Cassidy told you. This is a risk factor

for people with autism. It is also a risk factor for suicide.

The risk factors for suicide in the ASD population include a higher IQ. Some of the studies showed that people who are suicidal tend to have higher IQs than the non-suicidal youth. Youth with ASD and without comorbid ID seem to be at higher risk. But the findings are very inconclusive and there is more recent evidence showing that people with lower IQs are also at risk for suicide.

There is also comorbid Axis I disorders. Psychiatric disorders are correlated with elevated risk of suicidal ideation and behavior. And some of the estimates again show 67 percent of adolescents with intellectual disabilities and/or ASD who expressed suicidal ideation met criteria for mood disorder.

And then recent psychosocial stressors for those with suicidal ideations include - these are people that had attempted suicide. Thirty-seven percent experienced loss in their family. They had less family and social support. They had greater rejection, stress, and isolation and reported greater difficulties with perspective taking.

Our research group has really been focused on can we save lives by screening for suicide risk. We are looking at the experience that people have in the medical setting. The Joint Commission who is an accreditation board for all the hospitals in the country last year recommended that hospitals screen all patients for suicide risk.

But they did not talk about what screening tools hospitals should use. A lot of hospitals have been using tools that are

not validated. They have been using adult tools with kids. They have been using tools not tested in the population such as an ASD population.

The reason that the medical setting might be such an important key suicide prevention venue is because if you look at death registry studies, the majority of people who kill themselves, have visited a health care provider months before their death. This is actually true for adolescents. That 80 percent had contact with a medical professional three months before their death. The problem is is that these kids are not walking to doctors' offices and saying I want to die. They frequently present with somatic complaints. And if someone does not ask them directly, are you thinking of killing yourself, they may not answer.

We have every reason to believe that people with ASD have higher estimates of suicide risk. Their suicidal behavior and ideation might be overlooked due to diagnostic overshadowing and some communication difficulties.

What are these valid questions that nurses and physicians can use to detect pediatric patients at risk for suicide? I just want to talk about the difference between screening and assessments.

A screening tool is a very brief way to flag someone who is going to need further assessment whereas an assessment is really a comprehensive evaluation that confirms risk, estimates danger, and guides the next steps. And what we are talking about right now is how do you screen. How do you pick out someone, especially someone with ASD? How do you pick out who needs a further look?

I am going to tell you very briefly about our ASQ suicide screening question study. This is where we wanted to create a suicide screening risk tool for pediatric emergency department patients. We looked at three children's hospital in Boston, DC, and Columbus. And what we did was we looked at 524 pediatric emergency department patients. We oversampled the medical and surgical patients because we were interested in occult suicidality in all comers to the ED. We infused the sample with psychiatric patients.

Just a very basic description of an instrument development study is you take a bunch of candidate items and in this case, we took 17 candidate items. They were things like have you ever felt hopeless like things would never get better or do you feel like you might as well give up because you cannot make things better for yourself. You compare

them to a gold standard. In this case, we used the Suicidal Ideation Questionnaire.

Now sometimes people say if you have a gold standard, why do you have to make a new tool? And the reason is is that the SIQ is a 30-item questionnaire and that would never fly. A triage nurse would never be able to administer a 30-item questionnaire. We are really trying to get something very brief and something shorter.

We created the ASQ Suicide Screening Tool. And the questions are in the past few weeks, have you wished you were dead. In the past few weeks, have you felt that you or your family would be better off if you were dead?

In the past few weeks, have you been having thoughts about killing yourself and have you ever tried to kill yourself? If the patient answers yes to any one of these four

questions, they are given an acuity question. Are you having thoughts of killing yourself right now? There are very good psychometrics for this. The sensitivity, which is the true positive rate, was 96 or 97 percent. That means it captured most of the kids that the gold standard captured. And the specificity, which is the true negative rate was also acceptable. We were happy with that.

The results showed that 18.7 percent of the samples screened positive. We were most interested in the medical patients. That was 4 percent. It was feasible. The screening tool took 20 seconds. It was not disruptive to the ED workflow. It was acceptable to the parents. People thought that the parents are not going to let you ask their kids about suicide risk, but they did. And over 95 percent of the patents when asked, do you think nurses should screen kids for suicide,

said yes. ASQ is now available in the public domain. It is translated into eight different languages.

While we were doing this study, I got a call from a psychologist up in Toronto and she said did you include youth with ASD and other neurodevelopmental disorders in your study. I had to tell her we did not. She said I am really worried. She worked in a community health center and she was seeing a lot of youth with ASD who were suicidal. She needed a screening tool.

I spoke with the clinical director, Dr. Maryland Pao of NIMH, and we said let's try to adapt our screening tool for this population. We did a literature research and we found out that not only are patients who present to clinicians are very anxiety provoking for clinicians, patients who present with suicidality, but patients with

ASD present different challenges that needed to be addressed.

We found that youth with ID and ASD were often excluded from research studies. And as Dr. Cassidy pointed out, there are no suicide screening tools that have been created for people with ASD.

We looked into suicide screening and the challenges of screening in the ID population. We also looked in the autism population. We were connected with Dr. Matthew Siegel, who ran the Autism Inpatient Collection. We found out that he had a very large-scale study, multi-site. And he was looking at youth with ASD who presented to inpatient psychiatric units in six different sites. He was giving them all kinds of assessments.

We spoke with him. We said did you ask at all about suicide? He looked through his data and he found there was one single

question on the CASI that he gave parents. It asked the frequency which their child had periods lasting several days where he or she talked about death or suicide. That was one single question.

We were able to look at 107 kids, 10 years or older, with a mean age of 13, an IQ of 55 or greater and they were ADOS-2 positive for ASD. What we found was the majority of them had this - 63 percent had a non-never response. But per this parent report, 23 percent of the youth talked about death or suicide often or very often. Now the problem with this is it talked about death or suicide. But this was the best proxy estimate that we could come up with.

We also looked at comorbid diagnosis. We found that if the child had a mood disorder, they were nearly three times more likely for their parent to report that they talked about

death or suicide. If they had an anxiety disorder, they were twice as likely. In an odd finding, if they had ADHD, they were actually less likely for their parent to report they talked about death or suicide.

We feel like adapting the screening tools really answering a need that previously validated scales may not be applicable. We do not know how the ASQ functions in people with autism. We need to validate the instrument in the autism population.

We have launched the ASQ ASD multi-site instrument development study. And we really want to test and adapt the ASQ for youth and adults actually with ASD.

We were looking at Dr. Matthew Siegel's autism developmental disorders inpatient research collaboration. He has a sample of over 800 youth who are 12 and older, diagnosed with ASD and in inpatient

psychiatric treatment. Again, we are going to administer a bunch of candidate items and then give a gold standard. We are going to do interviews with the patients and interviews with the caregivers.

The other measures we are using are that the creator of the SIQ that I told you about was the gold standard for the original study. He has adapted that measure for the ASD population. I will show you that in a minute.

We are also giving an understanding death assessment, a caregiver questionnaire, and a therapist follow up questionnaire. I am not going to go through all these.

We have five of the ASQ questions and then we added ten more, but just a sample. We have things like in the past few weeks, have you been sad a lot or do you think things will not get better. We added a couple of other additional candidate items.

The suicidal ideation questionnaire, as I have told you, has been revised and we have 17 items. And a sample question is rate how often in the past two weeks I thought it would be better if I was not alive. I thought that no one cared if I lived or died. I thought about how I would kill myself. And the response set was changed from a 7-point Likert scale to a 4-point Likert scale. And the choices are all the time, a lot of time, sometimes, or never.

Just to give you a very brief look at the pilot data. Dr. Rachel Greenbaum, who was the original impetus behind this study. She has just done a pilot test of this. She did it with youth and adults. We are just looking at ten so a very small number, but a very brief preliminary look.

Out of the ten participants, six actually screened positive on the SIQ, the

gold standard. We feel like this is a really good catch because out of these six who screen positive, only one client had reported being asked about suicide in the past and the therapist had not known about this. Only one of them was reported to have a history of suicidal behavior. Four out of the six who screened positive - this was the first time that they were identified as being elevated for suicide risk.

Just to show you some of the items that they endorsed out of these ten subjects. I thought about killing myself. Seven out of ten had a non-never response to that. I thought no one cared if I lived or died. Five out of ten. I thought it would be better if I was not alive. I wish I had never been born. I thought life was not worth living. Six out of the ten subjects endorsed those.

And just as a little check on our candidate items. This column on the right is negative to the gold standard and the middle column is positive to the gold standard. For these modified ASQ questions, have you ever thought about killing yourself, 100 percent of the six subjects that screened positive also endorsed this item. Do you feel like you want to give up on life?

The majority, five out of six, endorsed this item. Has something bad or upsetting happened to you? Again, five out of six endorsed this item. And is anyone else worried that you might hurt yourself? Four out of the six endorsed this item.

When we asked the subjects, what was this like to be asked these questions, this is paraphrased by the research assistant. One said it did not make him feel uncomfortable.

The therapist was not aware of his suicidal thoughts until the screening.

Another subject who was upset by the questions said although he likes and often talks about his feelings, it was clear that he did not enjoy being asked these questions.

And then we asked the therapist for their opinions. And one said I feel it was important that the screening was done. It allowed the client to say something important about how she felt. This in turn may have allowed her mother to treat her daughter's thoughts with more respect.

In summary, we are calling for universal screening for suicide in youth in all the medical settings, but clinicians really need population-specific and site-specific tools.

We need tools for youth with ASD; otherwise, youth with ASD may go undetected. We are going to currently test and then adapt

if necessary the ASQ for better sensitivity in the ASD population.

And then after we do the screening studies, we can have evidence-based guidelines to both detect and manage suicide risk in the ASD population.

There was a big team that goes into doing these studies. I want to thank them and thank you for your time and attention.

(Applause)

DR. GORDON: Thank you, Dr. Horowitz. Finally, we have Colleen Carr, the deputy director of the National Action Alliance for Suicide Prevention.

MS. COLLEEN CARR: Good afternoon. Thank you so much for having me here today. I am delighted have a few minutes with you this afternoon to present on our efforts at the National Action Alliance for Suicide Prevention. We are the national

public/private partnership, focused on championing suicide prevention as a national priority.

I was really delighted when Dr. Daniels asked me to come today because I feel like there is a lot of great alignment between what we are doing at the Action Alliance and what you are doing here at the Coordinating Council. I think we can learn from each other, but also hopefully align our efforts going forward.

I also want to thank Dr. Gordon, who serves on our ex comm on behalf of NIMH, Dr. Ronyak from IHS, and a number of other federal agencies that are both on the Action Alliance and part of the IACC.

We also have a secretariat, and we are supported by the Substance Abuse and Mental Health Services Administration. We thank them for their support.

I am going to talk a little bit about the Action Alliance and then highlight just a few national suicide prevention resources for those who might be interested at the end.

As I mentioned, the Action Alliance is the nation's public/private partnership for suicide prevention. We started in 2010, but really in concept had existed a number of years before that.

In 1996, the World Health Organization issued a report saying any nation that is serious about reducing its suicide rate needed both a national strategy for suicide prevention and a coordinating body to really oversee implementation efforts because there is no one federal agency or one private sector entity that can really tackle this problem on its own.

In 2001, the US had its first national strategy for suicide prevention. It echoed

the need for that coordinating body. And then in 2010, the starts really aligned and that coordinating body was launched, which is what became the National Action Alliance.

To date, we have worked with more than 250 public and private sector organizations to implement the National Strategy for Suicide Prevention.

We use this image to really visually represent and depict what we do. There are so many entities that have a role to play in suicide prevention. As the national strategy says, everyone has a role to play.

At the Action Alliance, we see ourselves as the coordinating body that gets all the fish working together in the same direction so we can align our efforts and really streamline our efforts and do more together than we could do individually even though we each have our own distinct perspective and

approaches and expertise that we are bringing to the table.

Our mission is to champion suicide prevention as a national priority, catalyze efforts to implement high-priority objectives from the National Strategy, which I will talk about in a minute, and cultivate the resources needed to sustain progress.

We have a goal that we adopted last October to reduce the annual suicide rate 20 percent by 2025. We do this along with our other national partners. It really gives us a focus and direction for if we are serious about reducing the burden, how do we align our efforts and really scale up what we know to be effective.

We have our National Strategy for Suicide Prevention, which serves as our roadmap. One of the first things the Action Alliance did after being launched in 2010 was

take on the task of revising the 2001 National Strategy, which at that point was over a decade old. In collaboration with the US Surgeon General's Office, the Action Alliance released the revised National Strategy in 2012.

There are 13 goals and 60 objectives. While we at the Action Alliance cannot accomplish all of that ourselves, we have selected a few high priority objectives that we focus on. We work to create partnerships and engage stakeholders to really advance the entire strategy.

Recognizing that leadership is key to keeping a partnership like this alive and active and robust, we had a public sector chaired by Dr. Carolyn Clancy. She is the executive in charge at the Veterans Health Administration. She has been our public-sector chair for a couple of years now.

At the helm of the private sector is Mr. Robert Turner. He is senior vice president and recently retired with the Union Pacific Corporation. He has been our executive committee since 2010.

We also have approximately 40 to 45 members on our executive committee. We really focus on getting all the federal agencies together. We have the Department of Defense, Veterans Affairs, Education, Justice, Homeland Security, and the various entities of health and human services all coming to the table from the public sector.

And then from the private sector, we have diverse representation both from non-profit entities in the mental health and health care perspective. But the Action Alliance was really charged with bringing nontraditional partners to the table as well. We knew if we were going to tackle suicide

prevention as a national priority, it was not going to be enough to just have mental health and health care at the table. We needed new partners that could bring leverage, influence, and resources to the conversation and help us take this across the nation.

Some of our private sector entities are Universal Health Services, Johnson & Johnson, the International Association of Chiefs of Police, Facebook, Entertainment Industries, Union Pacific, NFL, Kaiser, et cetera. There is really a diverse representation around the table.

We ask all of our executive committee members when they come to the table, they are really tasked with becoming a champion within their sector of suicide prevention and for suicide prevention as it makes sense for the industry in their sector. We see each of these partners as really coming to the table

and starting to own this issue in various ways and collectively make a difference.

I want to go through a few of our early accomplishments and resources we have developed. There are a lot of similarities I think to some of the work of this group. In some ways, we are working from a very similar roadmap.

Objective 12.1 of our National Strategy was to develop a national suicide prevention research agenda. That was accomplished after a couple of years, thanks to the leadership of NIMH. We have a prioritized research agenda with our six key questions. Why do people become suicidal? How can we better or more optimally detect or predict risk? What interventions prevent individuals from engaging in suicidal behavior? What services are most effective for treating the suicidal person and behavior? What other types of

interventions outside of health care systems can reduce suicide risk? What new and existing infrastructure is needed for research to reduce suicidal behavior?

This is our research roadmap. We follow that up with a portfolio analysis of national investments in suicide research both from the public sector and the private sector. Our portfolio analysis covers from 2008 to 2013. This is just one of the findings from our portfolio analysis.

When you look at 2008 to 2013, the average annual combined investment in suicide research is \$71.6 million per year. And when you take out the Army STARRS program, which was a very large project, it averages to \$60 million. That is the current investment in suicide research at the national level. Again, that is public and private.

One of the things that the portfolio analysis was really key is if suicide is the tenth leading cause of death, it is really important to have an understanding the breadth of our activities to prevent suicide and our national investments. Similar to how that has been a tool used by this group, we find it really helpful. If we want to reduce the suicide rate 20 percent by 2025, what are the investments we are going to need to get us there? We will be doing another updated portfolio analysis in the years to come.

We are going to talk a little bit about our priority initiatives. But before I do, I just wanted to highlight two overarching principles that guide a lot of our work. One is reaching at-risk populations. There are a number of populations that increase risk for suicide. We have heard a lot today about individuals with autism. We also have

particular communities and populations that are at great risk. The American Indian, Alaskan Native population, especially youth, veterans and military service members. We also have suicide attempt survivors and survivors of suicide loss. We have formed task forces to really look at all of those populations and see how we can do better to reach them with suicide prevention efforts.

We also have a focus on engaging individuals with lived experience to both inform and enhance our prevention strategies. A lot of early suicide prevention efforts focused on engaging individuals who have lost a loved one to suicide. There was really significant progress at the grassroots level by engaging family members, but more recently we also recognize the need to engage those with lived experience themselves so the suicide attempt survivor who can help us

better understand their experience when they encountered the health system and how can we do better.

I just included a quote here from one of our executive committee members, Eduardo Vega. He really articulates the potential when we engage those with lived experience. We have produced a report, the Way Forward, which is the first report that really pulls the experience of those who are suicide attempt survivors and offers recommendations going forward of how we can do better.

We have three priority objectives that are pulled from the National Strategy. This is building on what Dr. Horowitz was talking about. We know that a lot of people who are dying by suicide are in our health system.

Early suicide prevention efforts really relied on - if we could identify who is at risk and get them into treatment, we can

reduce the suicide rate. But it made the assumption that once we got someone into health care, that health care system was ready for them and knew what to do.

We realized that maybe we needed to take a step back and make sure our health systems were more prepared. This priority initiative, which is Goal 8 of the National Strategy. It is promoting suicide prevention as a core component of health care. It really focuses on bringing all these pieces of our health care system together.

When someone does walk through the door and says I am suicidal or I am thinking of suicide or I am struggling and I do not know what is going on that our health system is activated and can respond accordingly.

The areas of that work include improving acute care transition so when someone is discharged from an acute care setting, they

have the follow up care and the supports needed because that is a very high-risk time for someone is after they have been in treatment and they have been discharged.

We are working to articulate and promote some basic standards of care around suicide prevention because so much has changed in the research over the last 10 to 20 years. We want to make sure that practices in health care are up to date with the best evidence that we have now.

We are also really focused on our clinical workforce preparedness. It is not just emergency doctors and primary care doctors who want to engage. It is actually the behavioral health workforce as well because you can go through training to become a behavioral health provider and not feel confident when someone walks through your door and is at risk for suicide. We are

working to make sure that not only is our primary care workforce and emergency department workforce prepared and confident in what to do, but our behavioral workforce as well.

We are also working to improve crisis services. Connected to the workforce, if someone does not know or is not confident in managing your suicide risk, it might activate a system where hospitalization is the default and we want to ensure those robust crisis services are available so there are alternatives that meet the person's needs at that time where they are.

We are working to improve behavioral health crisis services and then working around financing strategies, particularly around follow-up care and crisis services because they are a little bit outside the normal construct of financing care.

And through all this, a number of years ago, launched the Zero Suicide Initiative, which I am going to talk about in a minute. This is a picture from a meeting we had this summer where we brought all the leading guilds together.

We had the National Association of Social Workers, American Psychological Association, the counselors, the creditors and SAMHSA and HRSA and our federal partners to really talk about how do we better in the space of preparing our clinical workforce. When someone does make that difficult step into care that support is around them.

One of our initiatives under transforming health systems is the Zero Suicide Initiative. This is Objective 8.1 of the National Strategy, which is promoting the adoption of zero suicides as an aspirational goal by health care and community supports.

This was one of the Action Alliance's earliest initiatives and it was built off of models from health systems that were doing this work well, and showing evidence.

Henry Ford Health in Michigan had made Zero Suicide their goal. They took an organizational approach. Instead of relying on a clinician's interactions one-on-one with someone at risk, their organization adjusted to make system improvements to identify those who are at risk and intervene at the system's level.

Using the evidence from Henry Ford, the Air Force model, which had significantly reduced suicide, and Magellan in Arizona would develop the Zero Suicide Initiative. It is a quality improvement approach to improving suicide care within the boundary of health system.

We have a toolkit here. It is in hundreds of health systems to date. And I think it is also a great model where public and private sector have together. NIMH has funded some research to strengthen the Zero Suicide evidence base. SAMHSA now has state grantees that are working with health systems to adopt Zero Suicide. Indian Health Services is piloting Zero Suicide. It is really taking on a life of its own so it becomes standard practice that the responsibility of the health care system is to make sure no one under their care dies by suicide.

Recognizing a significant number of people die by suicide after engaging with the health care. A large number of folks do not. We cannot just rely on improving health systems to reduce the suicide rate. We have another priority about transforming communities.

This is goal one of the National Strategy, which is all about coordinating and integrating our suicide prevention strategies at various levels in between various sectors. This is where we recognize the role of the workplace and identifying who might be at risk for suicide. We have done a lot of work in the construction industry. This is really working with faith leaders to change the conversation. When someone is participating in a faith community, they are hearing messages that are supporting them in their struggle and community supports are rallying around someone who might be struggling with suicide just as they would if they were struggling with a physical illness.

And then we recently released a Transforming Communities' report, which is really meant to strengthen the community response. We are not just picking a few

things out of our toolbox and doing them, but we are really strategically combining and bundling some interventions, which is really the only evidence we have for reducing suicide in a population. It is when we are bundling interventions and taking a comprehensive approach. What can we do at the national level to really support those community efforts?

And then our third priority comes from Goal 4 of the National Strategy and it is all about changing the public conversation about suicide. For a long time, suicide dialogue really focused on the death and despair and the tragedy of suicide. But we were not hearing the stories of people who were struggling, but went on to recover or receive treatment and went on to live a healthy, long productive life.

There is research mostly in Europe that when we have news coverage or entertainment depictions that tell stories of recovery, there is a protective factor in that. If we are telling stories of the death and the tragedy that that can increase contagion and increase suicide in a population level. Our work to change the public conversation is about interrupting some of those narratives that form that might start to normalize suicide and not reflect the full complexity of suicide as an issue.

We work with journalists on how they are reporting suicide and that is mostly focused on training journalists to accurately depict suicide when they choose to report on it. We work with the entertainment industry around accurate portrayals of suicide and those stories of recovery.

We work with suicide prevention messengers. This is what we call anyone who is messaging about suicide. We are doing it in a way that is responsible and helpful to those who are struggling with a very public health approach. We have tried to really shift from stories around death and despair to those that talk about hope and connectedness and resilience and treatment and recovery.

At the Action Alliance, being a coordinating body, one of the things we did this September for Suicide Prevention Month was really try and get all of our partners who were going to message about suicide prevention in September to do so in a coordinated and aligned way. We were not going to all put out the say message because we had different audiences and different

geographic locations, but we wanted to really sync up our message.

We provided a framework of really focusing on how we can be there for those who are struggling. This was messaging that the Department of Defense and the VA had been promoting. It was easily adapted to those who were struggling with suicide themselves or families of how they are supporting each other in grief and loss.

It was a great way to really align efforts without duplicating what each other are doing. We were able to in the course of a month of two get about 60 organizations that committed to this shared messaging framework. We hope to really amplify that in the years to come.

We are really pushing out a few key messages that while we recognize suicide is complex and we need complex system

transformation, there are also really simple things we can all be doing in the meantime to help save someone who might be struggling.

That is a really quick overview of our priority initiatives. As I mentioned, we also have a number of task forces that work to improve population-based approaches whether it is a high-risk community, whether it is improving data and surveillance or research infrastructure.

We are very committed to our goal of reducing the suicide rate 20 percent by 2025. We know to achieve that we need to continue to align and make those hard decisions about where we are going to invest our limited resources.

But I also wanted to end on a note of highlighting some of the national resources that exist for those who might be new to suicide prevention. From a clinical

perspective, there are a number of trainings that are out there to improve the clinical workforce's competence around assessing and managing suicide risk. One is the assessing and managing suicide risk training at the Suicide Prevention Resource Center, which is where our secretariat is housed.

There is also the National Suicide Prevention Lifeline, which hopefully everyone is familiar with. This is the 24/7 free and confidential support for anyone who is in distress or someone who is trying to help someone who is in distress.

And then there are also local suicide prevention efforts and coordinators across the country. One of the benefits of over a decade of investments in state and community suicide prevention is that each state has a suicide prevention coordinator. If you are interested in connecting with your state

suicide prevention efforts, we have a map on our website. It is sprc.org/states. You can get the point person. You can see the state plan for where you are.

And then this is the Suicide Prevention Resource Center's website. And, again, this is the technical resource center that is funded by SAMHSA to really provide resources to states and communities that are working to prevent suicide across the country.

Feel free to connect with us on social media. Thank you.

(Applause)

DR. GORDON: Thank you. If we could have each of the panelists come up and sit at the table, we will have a period of questions and comments from the committee. While they are sitting down, is there anyone from the committee who would like to start us off?

MS. CRANE: I want to say, first of all - John is about to leave, but I am sure he will want to say thank you for this presentation.

MR. ROBISON: That is true -- autistic people pointing out getting me on track here for this. I do want to - I would be with you and I would be my usual, enthusiastic self on promoting the research that you are doing - terrible rainstorms and I have to try to scoot my ass down the road and hopefully I can get home before tomorrow.

I think that it is really important and I am glad to see that here in America we are picking up on the suicide thing. It is a big problem for us. The only other thing I would want to add from personal experience is that I know as an autistic person who has contemplated suicide and who has attempted years before, we can feel isolated and alone. We do not have to feel that we are a burden

too. Maybe that is our autistic nature. But I would not be lulled into complacency that we do not have all of the thoughts so we are not at risk.

I think every single autistic person has had thoughts like me. This is the very same thing as the parents who sometimes say with the best of intentions, but it is just not true that my child or this child has greater challenges than you. People like Sam and I, we are absolutely at risk for killing ourselves just as we are just as at risk for epilepsy and depression and anxiety and everything else that goes with this autism thing. The fact that we are good speakers does not change it a bit. I thank you for doing this and staying on it.

MS. CRANE: I want to add, too, and I am actually going to thank Stuart Spielman, in the audience, for reminding me of this on the

break. This ties in really well with recent Kaiser health news study, which was reported in the Washington Post, showing that people on the autism spectrum who are hospitalized for a psychiatric crisis are being particularly badly served by the hospital system.

I found the comment by - I think that, Dr. Carr, it was your comment that when people do not feel confident that they know how to manage people's suicide risk, they stay in the hospital longer. I am really thinking that that is possibly one of the driving factors, and also what Dr. Cassidy said about people answering very literally, or not knowing how to answer suicide risk questionnaires.

The effort to norm the ASQ for people with ASD is going to be extremely critical in making sure that we have good crisis services

that accurately identify who is at risk and that we do not end up keeping people - we get people back to normal life as soon as possible. Since we have seen that that is actually a protective factor when people are able to return to normal life pretty quickly.

I also wanted to comment on - there seems to be a lot of research consensus that people with ID are less at risk for suicide attempts. I am really wondering if part of the reason why people with ID are seen as less at risk, is because people's suicidal behavior or gestures or ideation is not recognized.

If people have difficulty communicate then they cannot necessarily communicate that they are depressed. And then when they might attempt self-harm, but then that might get confused with other kinds of self-injurious behavior, wandering or risky behavior, with

the assumption that people with ID simply do not realize that the behavior they are engaging in is risky or might hurt them. It might be very difficult for people to recognize when someone is intentionally trying to harm themselves versus simply bolting out into traffic because they do not understand the danger.

DR. MANDELL: Thank you all so much for these presentations. I am struck by the difference in the care system often for people with autism and for people with psychiatric disorders, who are at highest risk for suicide. I wonder what your thoughts are on the implications for how we change practice in those care systems that may not see screening for suicide risk or planning, when suicide risk is identified.

We are talking about mostly school professionals, for example. We are talking

about people in the VR system, as opposed to people in the mental health system. I wonder how you may have approached that in talking about not just suicide screening, but suicide planning in the general populations and what the implications might be for us.

DR. CASSIDY: I did not have time to present it in the presentation, but at the end of our steering group study that was one thing that they really wanted to talk about. They said it is great. Having the opportunity to co-design this questionnaire that we wanted to do something really tangible. We said, what should we do. They all reached the consensus that they would like to develop some guidelines to general practitioners because in the UK the family doctor for autistic adults is probably the first point of contact when they disclose suicidal thoughts.

We developed a training package, like some guidelines for GPs about the adaptations that they can make to how they actually conduct their assessments with autistic people and some videos of autistic people who took part in the steering group actually describing their own experiences and some of the adaptations would be quite useful.

Because I think this was brought earlier about training programs and giving clinicians more confidence to deal with these. It is the most challenging situation that probably a clinician will ever face really, dealing with this. Autism is an added complexity. I think that could help quite a bit.

DR. HOROWITZ: I agree. I think similarly, I had a patient that was in one of our studies who said 20 years ago people used to whisper the word cancer and the same thing is true now for suicide. There is a lot of

stigma around it. I think it is very anxiety-provoking.

We also for kids have gone into - we are trying to implement ASQ, for example, in pediatric practices. We go in and we train the pediatricians. We train the nurses.

We also have an ASQ toolkit and try to take the mystery out of it. If somebody screens positive with a 20-second screen, you follow up and then you give the pediatrician guidelines. Here are the questions that you can ask and then you can decide whether or not the patient needs further assessment.

I think it is exactly what you said, Dr. Cassidy, that if you then add ASD to that, it goes from anxiety to incredible anxiety. If you give guidelines and you give tools and you tell them - if you give them structure, I think, then I think it is more likely to have uptake.

DR. MANDELL: I think that all makes sense. I wonder if we are missing an opportunity here though. If we are talking about a group with what you described as cognitive inflexibility and perseveration on particular suicide thoughts that might make them really sticky that relying solely on the health system for screening and safety planning may be a mistake because of the relative infrequency with which people with autism come into contact with the health system.

But people with autism often are coming to contact regularly with other caregivers, with other professionals. Is there an opportunity for this particular group to rethink how we do screening and how we do subsequent safety planning by enlisting other professionals?

MS. CRANE: What other kinds of professionals are you thinking about?

DR. MANDELL: Well, if I am a child or adolescent, it might be professionals in the school system. If I am an adult, maybe it is my job coach or maybe it is some other professional - contact regularly for some other kind of support or therapy, but someone under whose aegis we traditionally do not see this as falling, but maybe the person in the best position to identify risk and quickly act on it. Sort of like the gatekeeper's approach that has been - but here we have a much more defined population.

MS. CARR: I think that makes a lot of sense and it kind of goes to our efforts around transforming communities and how are we all engaged in making this a responsibility to prevent suicide and

identify and reach out to those who might be at risk.

I think particularly within this population, there are certain as you said gatekeepers or individuals that might be engaged and able to identify either a change in behavior or a life transition. I think across the board in suicide prevention, we look at those life transitions as the jolting moments. That can really change a trajectory whether it is a job loss or a change in family situation. There might be some lessons learned from there that could be a good parallel.

DR. HOROWITZ: As far as for kids, I think you are absolutely right. We do have some studies with the ASQ in the school nurse setting. There are some programs in the country like, for example, signs for suicide where they go into schools and they do teach

not only people like school nurses, but also the administration and coaches and teachers, how to recognize signs of suicide. Then they also talk to parents and they also talk with the kids because there has been some success with they call, peer-to-peer counseling and how to recognize signs of suicide in your friends and then what to do and how to go to a trusted adult with that. I think that makes a lot of sense.

DR. DAWSON: I just wanted to thank you for a set of really important talks. I think the work you are doing is so critical for the autism population. The work group that we are establishing to think about ways that we can improve medical care for people with autism. I do think this topic would fit well in that work group. We would love to be able to call upon you for expertise and materials. I hope

to be able to perhaps work together in the future in that regard.

I did wonder about - as you think about developing a screening tool, a couple of things came to mind. One is that sort of the broader context in which that tool would be delivered to a person with autism or their parents I think needs to be considered.

We are working very closely with the emergency department at Duke. There are about 500 emergency department visits per year by people with autism and their caretakers usually. Just the propensity to respond adequately to a question there like that, it probably depends on just the overall medical milieu and how comfortable that person feels in that setting because there are a lot of changes one needs to make. The lighting. Do you approach them quickly and start saying here is a questionnaire? Do you first

ascertain what is their preferred way of communicating? Just that broader perspective.

And then the second thing is just whether there needs to be some effort into more visual support around the questionnaire because I think even individuals who have pretty strong language capability could probably benefit from thinking about the ways that you can communicate the information in more of a visual or pictorial way.

DR. HOROWITZ: Those are great comments. We thought about using, for example, the pain scale, which has faces for kids and they can point. We did think about adding a component. It is still on the table and something that we may test out as well. That would be how to - again, can you use the ask or do you need to adapt it? I think that is going to be a really critical part that comes out of our study.

MS. CRANE: I will just quickly say that you should check out some of the - I do not know if there is any peer review literature on this, but there is definitely self-reported literature on people having a really hard time with the pain scale when they are on the autism spectrum. We do not understand the pain scale at all. Just FYI.

DR. GORDON: Sarah, I wanted to ask you at this point how strong that data is on the difference in risk between those with intellectual disability and those without or those on one end of the severity spectrum versus the other. We have discussed it earlier, but it was not clear to me how confident we are in that result just yet.

DR. CASSIDY: There is not a lot of literature at all on the relationship between intellectual disability and suicidality. There was one study that I think is published

now that was looking at - similar to your previous work actually I think on talking about death or suicide, but in an ID population so quite similar, but with an ID population. And apparently, they do speak about it and there is a concern for clinicians. But then again, Tattia Study, the Swedish study, shows that those with higher IQ are more likely to die by suicide. That is quite a striking finding.

There could be other things at play like what is maybe ruled as suicide might differ according to presence or absence of ID. I am not too sure about that. More research definitely, needs to be done in that area. There is such a paucity of work.

DR. GORDON: In either of the studies, has there been difficulty in differentiating or dealing with self-injurious behavior as separate from ideation about wanting to die

or behaviors around wanting to end one's life?

DR. CASSIDY: Yes, I think so, but there is such a kind of lack of literature. I think that the paper that I recently read, and I need to actually dig it out because it would be probably useful to share with the committee, is that it was not I do not think minimally verbal individuals, it is the individuals that were able to talk about death or suicide.

That would be a really difficult issue to tease apart because traditionally those kinds of behaviors have been in the context of challenging behavior or self-injurious behavior. It came up a lot when we did our systematic literature review of suicidality assessments in autism. There was just no end of challenging behavior and self-injurious

research studies in autism, but they hadn't considered the suicidality component.

DR. HOROWITZ: I was just going to give a case example, actually. At the hospital at NIH at the Clinical Center, we just implemented suicide risk screening in April with the adults and then we literally just went live with screening the pediatric unit last week.

Before we started with pediatrics, a nurse accidentally screened one of the pediatric patients, a 17-year-old with autism, and an ID component. When I went in to assess her, her mother said I do not think she really understood the question. I do not think she knew what she was saying. So I spent some time talking with her and she did not want her mother to leave the room while we were talking. And then as we kept going,

the mother actually excused herself so that she could have some time alone.

It turned out that she probably was not at risk for killing herself, but she was really depressed. She needed to talk about - she had a debilitating medical condition as well. Someone living in her house with her had been handling her roughly. She actually talked about that for the first time.

While suicide screening sometimes does not pick up eminent risk like someone who the outcome is going to be suicide, it also picks up significant emotional distress that warrants further mental health attention. I think that was a really good example of how this person, because she had an expressive language problem, may have been overlooked and may have not been screened. But because a nurse screened her, she then got some help.

That is a good example of what your outcome is really matters.

DR. TAYLOR: I would love to hear Dr. Cassidy just talk a little bit more about what came up in the focus groups about issues of adult diagnosis and suicidality. It is something that we have thought a lot about in Question 6 of the Strategic Plan in terms of - there is so little research on this on getting diagnosis as adults. Is it valuable? When is this something that is helpful in terms of maybe able to identify or have an answer to your issues?

But if you get an adult diagnosis as an adult and there aren't really any services or supports that come along with that or any follow up, could that be something that could ultimately be detrimental to some people? We have been thinking a lot about this on our

end. I would love to hear what came out in your interviews.

DR. CASSIDY: It is a small amount of interviews and it is kind of a self-selecting sample. But there were just such kind of consensus about what the issues were. Most of our steering group, six out of the eight, were females. All eight of them had been diagnosed as adults. A lot of them had been misdiagnosed with a lot of other conditions, and hadn't actually known what autism was. They described a journey of self-discovery and a massive kind of relief of understanding when they got the diagnosis.

We got some qualitative questions in the survey that ask about experiences of diagnosis, camouflaging, misdiagnosis, and treatment and support, and masking one's autism in an attempt to cope in social situations for all of those years. It really

took a toll, and actually took a toll in their own self-identity. They did not know who they were anymore.

But when they got the diagnosis, they were like I understand who I am now. Then they said that they masked less and they felt a bit more accepted and part of a social group. Their sense of belonging went up as well. There were people in the survey that said once I got my diagnosis, I was much less -- access to treatment and support, my future was a lot less bleak and there is hope. Quite powerful statements are starting to come out a bit.

We wanted to have a look and really explore that in our survey, but our survey kind of attracted and the steering group attracted a lot of people who were diagnosed quite late in adulthood. We still want to explore that issue. I think you really need a

quantitative study comparing kind of early to later diagnosis, and look at it a bit more systematically than anecdotes that we have because that is a big caveat with that.

DR. GORDON: Thank you very, very much to the panelists and to the members of the committee for engaging in the conversation. We are going to take a 15-minute break. We are going to come back here at 20 'til so at 3:40. We will resume with our summary of advances discussion. Thank you.

(Whereupon, the Committee members took a brief break starting at 3:20 p.m. and reconvened at 3:43 p.m.)

DR. GORDON: We had to postpone last time's summary of advances discussion. We have a little bit longer one today and we devoted a little bit more time for it.

DR. DANIELS: We have the nominations in the packet for you. They are listed. They are on Line 2 for anybody who is watching.

By the way, just to mention, we have been having problems with the webcast. We heard that NIH Central is having issues, but everything is being recorded and will be archived. For anybody that wanted to view and cannot view now because of the technical problems it will be online later.

We prepared also some slides with the nominations. I will get the slides to advance here so we can see some of the nominations and then we can have a discussion.

DR. GORDON: You have all of them in the pages. Just remember the idea of is this a preliminary discussion just to confirm that the nominated papers indeed should be held over and then we will have a final discussion at the January meeting with votes to

determine which ones actually get put forth in our final summary of advances.

DR. DANIELS: I have some of the Question 1's here up on the screen. I do not know if anyone wants to discuss those. We can just click through them and you can also look at your list.

DR. GORDON: I am just going to take a moment to discuss that first one and mention if there is time in the round robin, we will talk about this a little bit more. But NIMH really is looking at - with the evidence from this and other studies that the neurobiologic processes underlying autism are really starting to at the evidence as young as six months old to try to develop means of identifying through screening processes children who will later develop or later will be assigned to diagnosis of autism early

enough in the process that we can follow the neurobiologic progression.

This is one of the main studies showing that you can predict with about 80 percent accuracy those who are going to get a diagnosis of autism at two years of age by actually the longitudinal course of structural imaging findings between 6 and 12 months.

PARTICIPANT: (inaudible comments)

DR. GORDON: Thank you and that and the other studies we will talk about later are the product of what has been a longstanding and fruitful collaboration with other institutes predominantly NICHD.

DR. DANIELS: Any comments, Geri, on this one that you nominated, the Hull paper?

DR. DAWSON: I nominated two papers that are reflecting our new understanding that autism is different in girls. One of them had

to do with the sex ratio and that comes later. The idea that we - the diagnosis of autism may manifest differently in girls than boys and may even require some adjustments to our diagnostic methods when we are assessing a girl. I guess for a person who has been in a field a long time, this seems like a really big deal. I want to reflect that in the papers that we nominate.

DR. DANIELS: Any comments on these?

DR. GORDON: Gerri, you nominated the second one. That seems almost like an RDoC-like approach to autism in terms of focusing on one particular cognitive aspect or I do not know if you want to call it social cognitive aspect of the disorder.

DR. DAWSON: I included this one because with the DSM-5, there was a new diagnosis that was created, the social communication disorder. And when it was created, there was

just a lot of controversy about are we really talking about a distinct condition that we should be separating out from autism. It very much reflects our earlier discussion today.

I thought this paper was really interesting because it suggested that this may still be all part of this one continuum.

DR. GORDON: What basis do they make that statement?

DR. DANIELS: This particular diagnosis used to be called pragmatic language disorder. If you think about all the different components of language, vocabulary, syntax, and semantics of pragmatics, pragmatics is the social use of language. It is true that some children present with difficulties in that domain. It was felt that maybe that should still be carved out as a separate disorder. But there was a lot of

controversy about it because that is also a symptom of autism.

We know sometimes kids in terms of the repetitive behaviors, it would also be required. They may not manifest very early whereas some of the social aspects might manifest early so you could be missing some kids.

At the time that it was put into the DSM-5, it was very controversial and now it looks like the data are coming out to suggest that maybe it should be part of that broad autism spectrum category.

Any comments on these?

DR. BIANCHI: The first one is amazing for those of you who did not read it. Who would have thought that it is genetically controlled exactly where you look? It is on someone's face. If you are an identical twin, you are looking - if I am looking at Gerri's

eye level, if I had an identical twin, my twin would be looking at exactly the same place. The investigators originally thought there was a mistake because it was so reproducible between twins. There is an effect with siblings and it is different in unrelated people. It is amazing that there is a genetic control to where you are looking at someone's face. It is really a fantastic paper.

DR. GORDON: Diana, is the genetics - is the monozygotic concordance for that gaze stronger or equal to the monozygotic concordance for autism diagnosis?

DR. BIANCHI: I do not know the answer. It was so striking. It was so concordant --

DR. GORDON: The reason I ask - one aspect of the RDoC hypothesis, which so far has not been proven true, but we are still interested in trying to puzzle out is if you

instead of defining these syndromes, complex syndromes of multiple behaviors, if you distill it down to one particular behavior and then look at the genetics of it, will that yield genetic information faster or is there going to be a stronger genetic signal? Where it has been looked at, we do not see evidence of that just yet. But this could be one area where -

But I am looking at the concordance rate and according to the summary here it is about .9. I am trying to remember the concordance from monozygotic twins with autism. My recollection is it is only .7. I thought it was a little bit higher. It might be that this is one example of where behavior - a specific behavior has a stronger genetic basis than the complexity of the syndrome.

DR. COLLMAN: I would like to talk about the first one. Dr. Manisha Arora has

developed a really interesting way to be able to assess exposures to environmental chemicals and metals and other mixtures by using discarded teeth. When teeth are developing in a baby in utero, they lay down rings according to their growth trajectory. He has been able to take these teeth and find different concentrations of environmental exposures in the different rings of the teeth to be able to more precisely link them to different windows of exposure.

If you think about the whole concept of different windows of susceptibility, defined by when exposures occur. This is a really exciting new tool.

He has used it recently in a study looking at discarded teeth from cases with autism spectrum disorder and controls and found differential exposures to lead during specific prenatal and postnatal periods. It

is not a giant study and it is not a definitive study, but it certainly opens up the door to using new tools to measure this very tricky part of exposure assessment especially when you are working with case control studies where children are diagnosed later in life and you are not able through a questionnaire or even biological specimens, to really capture when the exposure occurs.

DR. GORDON: How old were the children when the teeth were ascertained?

DR. COLLMAN Later.

DR. GORDON: Like toddlerhood, young childhood.

DR. COLLMAN: I do not know exactly in the study, but it is the natural discarding of teeth. It is when baby teeth are getting ready to come out.

DR. GORDON: You can still diagnose with almost - better than trimester accuracy.

DR. COLLMAN: The baby teeth hold that exposure pattern through the rings. And once those teeth come out because we have not extracted teeth in any children in any of the studies that he has been doing.

If you hold onto your teeth like go into night table drawer and find teeth from your children, people do that, but some studies have been collecting them prospectively and then they are able to send them to the lab and to look at these patterns.

DR. GORDON: Diana, you have some studies that are going to be taking advantage of that though.

DR. BIANCHI: I believe we co-funded this study. The kids were around - you can always tell a six-year-old because they are missing their front teeth. These kids were older. They were already enrolled in the study. Their teeth were collected.

DR. COLLMAN: Like years post-diagnosis as well, not just at the time of diagnosis. We think it is a very exciting opportunity. This resource is part of that tier network that I was talking about. This lab is part of that. For studies where these specimens occur, you can get them analyzed for free.

DR. GORDON: I understand you have a teeth bank.

DR. COLLMAN: He has a repository of different studies that has teeth.

DR. GORDON: Like we have a blood and tissue banks now all over, and brain for that matter. It looks a little bit like my keepsake drawer with all my children's teeth in it, except hopefully they are labeled. Mine aren't.

I wonder if you have anything to say about the top one, the joint effect of air pollution exposure and copy number variation.

DR. COLLMAN: This research group is interested in gene environment interaction as a particular set. They have looked at air pollution, especially coming from traffic sources in past studies. This is a continued investigation where they are now looking at copy number of variability as their genetic marker.

It is a small study. It is a preliminary finding. But I think the investigators were anxious to put it in the literature to engender discussion around this and see if others who have access to air pollution data might be interested in replicating it.

DR. GORDON: My understanding was that the air pollution - the evidence for air pollution playing a role in rates of autism was pretty good in terms of zip code localization, distance from highways and that sort of thing. Is that right?

DR. COLLMAN: There are a fair number of studies now where air pollution exposure has been measured in lots of different ways, using monitoring data, using distance from road sites, et cetera. The results are inconsistent to some extent, but I think there is a growing evidence base that people are becoming more comfortable with and there have been some systematic reviews of just that topic. This one in particular is looking ozone exposure, not the full mixture of air pollution.

DR. AMARAL: I can say something about the Pardo et al paper. This is actually a follow-up study to one that Carlos Pardo, who is at Hopkins did in 2005, where he analyzed postmortem brains and had a very small number of cerebral spinal fluid samples. And the outcome of that study was that it looked like the brains were at least - a number of the

brains were undergoing a neuro-inflammatory process and there was some evidence in the CSF for increased cytokines that were pro-inflammatory cytokines. But it was based on a small number. I think only six subjects.

This is an NIMH study that was done partially through the intramural program with Sue Swedo. And it was a much larger study, 60 or 70 autistic subjects who had CSF samples. The bottom line is that it was evidence against an ongoing inflammatory process. They did not see a cytokine/chemokine profile that was indicative of ongoing inflammatory process. I think it is important negative data in a sense.

DR. GORDON: I wanted to say a little something about that first one. It is remarkable in the size of the study. The risk was robustly statistically significant in that study. The challenge to it is that it is

a study that is from - I believe it is from a Finnish data from the national database.

Actually, it was a cohort study, I think, moving forward. I am pretty sure it was from Finland. That is not the reason why it is a challenge. The challenging thing is imagining replicating it and then what to do with it because the odds ratio was small. It was significant, but it was small.

We could certainly think about highlighting it, but we want to make sure to have the odds ratio in there and would want to explain the significance of that.

And the other problem being the population-based study is that of course it is not randomize. We do not know what would have happened to those children if their mothers had not been treated with antidepressants. Although I believe they had some data from untreated mothers in here and

the risk was not - there was no significant risk. I just do not remember the numbers on it.

DR. AMARAL: I thought that it was that the risk was just the same if you had depression untreated. We should get the punchline. At least if it is not this study, there is a large study showing that women taking antidepressants have a slightly increased risk. But if you looked at a population of untreated women who have depression, you also have a slightly increased risk. You could not draw the conclusion that it was the antidepressants.

DR. DAWSON: Thank you, David. I thought that was the interesting thing about this analysis. And partly, I think, it is just a really important story to keep following because I think people in the general public are really interested in it. Whenever you see

a study that has 179,000 and continuing to follow this story, I feel like we need to at least note it. It may not end up on our top list.

But basically, they found that the association appeared to be explained by factors related to the susceptibility of psychiatric disorders rather than the medication use itself.

DR. GORDON: And then what I remembered was incorrect that the control group (inaudible comments) I think that would potentially be nice to highlight as long as we can get the message correct because it does say something about the generic susceptibility risk, which is something that more and more as the geneticists increase their looks, we are seeing more and more genes, which are predisposed to multiple

psychiatric disorders and also that antidepressants actually do not change it.

My concern was if it does not show that nicely, this is something that you cannot imagine ever being replicated. It is so enormous, and it can only be done in a country like Finland where you have these nationalized health records and with research consents basically not being necessary to study it.

DR. DAWSON: In fact, the last line is based on these findings, the risk of ASD in offspring should not be a consideration to withhold treatment with commonly used antidepressant drugs from pregnant women. Maybe that statement is a little too strong, but I think it is a strong statement in the direction of this is not the reason why there is an increased risk is the medication use. Again, these are kinds of things that I think

the general public really is interested in hearing about.

DR. DANIELS: Any comments here?

DR. GORDON: The measuring developmental outcomes in autism - this is the only one I am singling out. I have to give Larry a hard time every now and then. Is that an advance or an interesting use of a tool?

DR. WEXLER: It is pretty much a predictive tool. It is a tool that has already existed. I would not consider it a major advance. I tried to be responsive to Susan's plea for articles.

The one I would actually like to - is the strain one, which is two or three down. It is the four-year follow up. This is an advance in the sense that there is very little evidence that inclusive education for kids with disabilities in general is

effective. It is just taken on faith. It is a more of a civil rights assumption.

Phil Strain, who did a terrific randomized trial on a particular intervention, which is to an inclusive education model, the LEAP model, which has a huge research-based tool, got funded for a follow up. He found that, number one, decisions about where kids get placed have nothing to do with their needs. They have to do with the model that the particular school district uses.

But number two, the kids who were in the inclusive settings for a number of years, their outcomes were significantly better. That is in our world of non-biological interventions. That is a really big deal. I would ask for that to be included. Plus Phil Strain is absolutely hilarious himself.

DR. DAWSON: (inaudible comments)

DR. GORDON: Not necessarily. When we go for voting in January, we tend to not consider reviews very strongly unless a systematic review or meta-analysis that they really reveal something that was not or conclude something that was not strongly concluded before. You will probably want to comment on those in January.

David is not here. I would like to hear about that first one. Does anyone know? Actually, you can go ahead and look ahead and see if there is any you want to talk about. You all have this in your folders.

DR. DANIELS: Any comments on these?

DR. DAWSON: The second paper I submitted on behalf of David really. This is David Mandell's analysis of the cost offset that was associated with delivery of early intervention. And the fact it is early start Denver model, I do not think is the critical

point here. But so far, there have been no economic analyses that have not more been just modeled on hypothetical data.

This was a randomized clinical trial of early intensive intervention. The intervention was provided for two years intensively so 15 hours a week for two years versus community intervention. There were effects on IQ and so forth.

Then what happened is the children were followed for two years after receiving intervention. And just the parents chose to do whatever they wanted. And then every service that was received was monitored over that two-year period and costs were associated with that.

What David was able to show - first of all, the kids who received early intervention went on to use fewer special education

services and fewer one-on-one services. We are much more likely to be in general ed.

After three years, you had fully recouped the cost of doing the early intervention because of the reduced need for services. I just thought it had pretty important policy implications and had never really been done on real data before. That was David's analysis of the existing data.

DR. GORDON: What age does this model start at?

DR. DAWSON: In this particular study, the children entered in between 18 and 24 months. They received intervention to age 4. And then they were followed until age 6 so two years post that period.

DR. GORDON: That is interesting because that 18 to 24-month period - it means that probably a lot of them are identified through screening.

DR. DAWSON: Yes, probably.

DR. GORDON: Which would be nice to know. We have talked about it in the past and we will talk about hopefully at the round robin that we are really trying to figure out how we can get screening to be recognized by the USPSTF and this would be one way to do it.

DR. DANIELS: These were both nominated by David Mandell, who is not here. And then this one was also you, Gerri.

DR. DAWSON: I just think this is a really important issue to keep front and center is the fact that we see this huge disparity in access to treatment services and diagnosis among ethnic minority families. I thought this paper, which is published in Pediatrics, did a really nice job of identifying several barriers that exist that help to explain why we are seeing this disparity. I thought it was very well done.

DR. GORDON: I think it might be useful if we at least have one or two lines in here about what those reasons were. I think it does mention English proficiency or limited English proficiency as one. If there are other ones, it would be nice to highlight.

DR. DAWSON: We have English proficiency obviously. The other was the level of knowledge about autism in the patient population themselves and then actually provider trust. Those were the three. I am thinking of the table. I can see it visually. But the top three were those three.

DR. GORDON: Great. They are in there.

DR. DAWSON: Yes.

DR. TAYLOR: I want to say a little bit about some of these studies. Advances for Question 6 have been fairly incremental let's say. I want to pull out a few that I at least, thought were interesting for

consideration and then where they fall as we move forward and would be up to the committee.

The Ditchman article is using - we have a large database to look at what are the specific services provided by rehab, but support employment. That in and of itself is not particularly innovative. Some other studies have done that.

But what they did was a little different and I think kind of neat is they used social network analysis to try to identify groups of services that might cluster together, which is more realistic to how services are actually administered. It is unlikely that the effects of these services in a vacuum are going to really give you an accurate look of what is going on.

By doing that, they identified six services that seemed to work together to

promote employment within vocational rehab. Services were not a big surprise. Again, I think this is a fairly incremental improvement. But I thought that the way that they analyzed the data was innovative in a way that services data is not typically looked at. I thought it was kind of neat.

I did somewhat sheepishly nominate one of my studies. I think adult research needs to - most of the employment work looks at employment at one point in time and that gives us a really limited look at what is going on.

We had a fairly small sample, about 36 people, but we followed them over three years. We looked to see what percentage of people had job loss or had to drop out of college within about two and a half years after leaving high school. And what we found was that most people transitioned into

something, which is different than I think what we typically see. But half of the sample had a disruption, meaning they had to drop out of college. They got fired from a job in this relatively limited timeframe.

The other thing that I think was important about this study is that the factors that tend to predict people getting jobs -- higher adapted behavior, fear of behavior problems were not related at all to having one of these experiences of instability. In fact, it was characteristics of the family.

What this suggests to us at least is that the factors that promote sustainability and employment might be entirely different from the factors that predict getting a job in the first place. It is small, but I thought it was interesting. I am completely unbiased of course.

And then this last study I thought was also interesting. Looking at the relationship between social media use and friendship quality among adolescents on the autism spectrum and typically developing adolescents. And what they found was that social media seems to work a little differently.

It was actually more social media use was related to higher friendship quality rated by parents and the adolescents themselves among the adolescents with autism, but there was no relationship between social media use and friendship quality among typically developing adolescents. Just sort of provocative and interesting.

DR. DANIELS: Question 7.

DR. GORDON: I think it would be interesting to consider the larger study here of socioeconomic, racial, and ethnic

disparities and compare it to the earlier ones, Gerri, that you nominated. There was the Hispanic one you discussed and I think there were one or two other ones as well that dealt with disparity issues.

The advantage of the large studies is one could be confident that the results are generalized. On the other hand, though I do not think we are learning much about why in that study. I think that might be a more significant advance in the sense that we knew these disparities existed or at least we had a high likelihood of thinking that they do whereas - to the wise is going to be important if we are going to try and address them.

DR. DAWSON: Totally agree and I do not think necessarily we have to put this on. I think the reason why I put the geographic patterns on - it is a relatively large

sample, 13,000. But almost everything we know comes from the CDC sites. This was another look at this.

I was really struck by - for example, in the Southeast, children are half as likely to have autism. It is not like we are seeing small variations, but really dramatic geographic differences. It could be diagnosis. It could be environmental risk factors. I think it was more that it was a completely different methodology than what we have seen before. I agree that it does not completely change the picture either.

DR. GORDON: I was actually thinking about that first one, but I am glad you brought up the second one. We have a number of these to think about in terms of what they add to the discussion.

The geographic patterns that control for race?

PARTICIPANT: (inaudible comments)

DR. GORDON: Thank you. Any other comments?

DR. WEXLER: The last one that Gerri submitted on the male-to-female ratio was a very - it is a meta-analysis, but it is a game changer in terms of expectations and everything we know about autism. I think that should be given due consideration.

DR. GORDON: Thank you everyone. We had requests in advance. We will proceed with those first and then we will move on to other matters.

Larry, go ahead.

DR. WEXLER: There were a number of requests for some clarification on the Department of Education - rollback of rights for kids with disabilities. I could read you a long talking point explanation that I have, but the bottom line is this was much to do

about nothing. I would suggest that you take a look at disability scoop today. The department clarified what certainly we knew that maybe it could have been a little clearer. These are all guidance documents, policy documents that are simply no longer in effect or no longer relevant.

An example would be when IDA was reauthorized in 1997. It took effect immediately. We provided a lot of guidance to states and districts around what you ought to be doing to make that law happen. Once the regulations were passed about nine months later and issued, all of that guidance was mute because the regulation supersedes the guidance. It was pieces like that that were rescinded.

There were no rights rescinded. Nothing that really will affect families. I was reading some of the press actually at the

break and various national stakeholder organizations are in fact saying now that it has been clarified, however, the department could have rolled it out a little more considerately. I am not commenting on that, but that is just an assurance that this is not a rollback of any right for any child or family.

DR. GORDON: Thank you for that clarification. We have asked Dr. Alice Kau to talk about the Autism Centers of Excellence, which is a program that is a collaboration of multiple institutes in the NIH, most prominently NIMH and NICHD. Or I should have put the order in the reverse really.

DR. ALICE KAU: Good afternoon. I am here to give you a very brief update on the NIH Autism Centers of Excellent program. Autism Centers of Excellent program, all of the ACE programs, supports very large research

projects. And a goal of this program is to understand the underlying biological mechanisms and to develop a novel intervention.

The program encourages innovative, multidisciplinary research. Awardees are required to submit all data to NDAR and also to collect a common set of measures.

There are two types of ACE centers, which is typically located at individual institutions and ACE Networks, which are multi-site collaborations.

I am happy to announce that NIH awarded nine ACE awards in September of this year so just a few months ago. We are very excited to report that we founded five centers and four networks. These are new awards. Total funding of almost \$100 million for the next five years.

This initiative is a collaborative funding among five NIH IACC. They are NICHD, NIDCD, NIEHS, NIMH, and NINDS. All the directors of these five institutes are members of IACC.

This is a map of the nine principal investigators and also the collaborating sites. I am happy to see we are moving into the middle part of a country as collaborating sites, which is very exciting.

As you can see, three of the PIs, Dr. Amaral, Dr. Dawson and Dr. Pelphrey, are also members of IACC.

Here are the five centers of new ACE centers. The Center awards need to have three highly meritorious R01 levels of research projects. They need to be synergistically related among themselves. There are highly innovative. We have Dr. Amaral's center, looking at - I think it is a follow up of

your phenotype project, phenotype studies, focusing on - you were trying to improve the treatment based on symptoms and the features.

Dr. Bookheimer will continue to study the heterogeneity of autism. One of the projects they were looking at is comparing different genetic risks and their impact on brain development.

Dr. Chawarska was examining development of functional brain connections. And Dr. Dawson was studying the impact of having comorbid ADHD symptoms on the diagnosis and treatment of ASD.

Dr. Klin continues to study the social interactions to identify the early signs of ASD. This project definitely has a potential to help us in lowering the age of identification and screening.

Here are the four new ACE networks. I want to follow up on Dr. Gordon's comment

about how we might be able to address the higher priority evidence gap identified by the US Preventative Services Taskforce. The first two networks are continuing networks. They have been funded in a previous iteration of ACE. Dr. Pelphrey, of course, will continue to study the female protective effects of autism. And Dr. Piven will continue the tracking of those babies who were recruited in infancy into school age.

Dr. Robins and Dr. Wetherby's studies are the ones who are addressing directly about the evidence gap, identified by USPSTF. Dr. Robins will compare two-time points of autism screening, one at 18 months, and the other at 48 months. And then to compare whether early screening improves the early initiation with early diagnosis and early initiation of intervention and therefore better outcome.

Dr. Wetherby's ACE network will compare two low-cost, unstructured social communication interventions for infants who are screened for high risk for autism at 18 to 24 months. In Dr. Wetherby's network, the toddlers will be identified in low socioeconomic very diverse ethnic communities. And the intervention she is testing will require very little professional continuous assistance. It is very needed to address the evidence gap and hopefully will help us - will be able to meet the expectation of a taskforce.

I think that is all I have.

DR. GORDON: Thank you.

DR. KAU: I think many of the investigators from the ACE programs have presented at IACC. I am sure Dr. Daniels will invite the new cohort to come and present new

projects. We are excited to monitor and watch how the study unfolds.

DR. GORDON: Are there other folks? We will start down here on the right side. Who would like to give updates from their organizations or agencies? How about coming down the left side from the far end first?

DR. COLLMAN: I just wanted to remind the group that NIEHS has been committed to an ongoing funding announcement. We participate with the other institutes on some of the broad autism-related research and we collaborate on things like the Autism Centers for Excellence, but we have spearheaded one in particular, related to environmental exposures.

And the reason is that because we have found that they were not getting their due diligence and fair shake in some of these other programs. We felt like we would be

missing important research if we did not call it out and have a special ongoing program announcement. These are also in collaboration with NIMH and NICHD.

Last year we made \$15 million of awards from this program and we are committed to keep it going. Over the last few years, we have funded jointly over 29 grants. They target a diverse set of exposure, autism relationships, air pollutants, as we talked about earlier, laminated, chlorinated, fluorinated compounds, pesticides, fungicides, herbicides, and androgen active compounds. Also metals, infectious agents, pharmaceuticals and preventive nutritional supplementation have also been part of the cohort that we funded.

Some of them are looking specifically at immune outcomes and many of them have also

included things like metabolic outcomes and neurological comorbidities.

Also, the full range of study designs and types, mechanistic work all the way up to epidemiology studies. We are committed to keep going. We know that our partners will stay with us through this. We have really, I think, stimulated a good group, especially of young investigators who see that there is lots of benefits to studying these questions, working with communities, both scientific and environmental justice communities. These communities are quite interested in these neurodevelopmental outcomes in their children.

DR. SHAPIRA: In previous IACC meetings, I had mentioned that this was coming down the pike. Today CDC announced and this was today, the availability of a new free app for IOS and Android devices called Milestone Tracker

app. This app makes it easy for parents to track, support, and celebrate their young child's development by providing a way to track developmental milestones to recognize delays in development and the ability to share the information with their health care provider in a more easy fashion.

And the Milestone Tracker app was developed by CDC's Learn the Signs, Act Early program, which I have presented on here previously. This program helps parents and early care providers and early education providers and health care providers to track developmental milestones in young children and to recognize problems early. We are very excited about having this app now available.

DR. GORDON: Sure, Laura. We will come around again. I think there is time.

MS. SINGER: The Autism Science Foundation is currently accepting

applications for pre-doctoral fellowships, postdoctoral fellowships and medical school gap year research fellowships. The deadline is December 1. The full RFA is on our website.

Also, we will be announcing next week, but I will announce it now, the date for our sixth annual day of learning is going to be on April 11 and one of our speakers will be the IACC's own Dr. Taylor.

DR. GORDON: Geri.

DR. DAWSON: Putting on my International Society for Autism Research Board Member hat along with David, I wanted to mention a really phenomenal meeting that we had in Africa. INSAR has chosen to fund these regional autism meetings in areas where people could not come to the regular meetings, which typically are in Europe or in North America. We had a very successful one

in Shanghai a couple of years ago and this year in Africa.

There were 25 countries mainly from Africa represented there. David and I both spoke. We learned so much from the people there about issues that related to how do you address needs when there are very low resources. I always feel like when I go to a low-resource country like that that I learn so much about what we can bring back to the United States in terms of new strategies and collaboration. It was a great meeting.

And then I also want to mention that the next meeting of the International Society for Autism Research, the regular meeting, will be in Rotterdam on May 9 through 12. Registration is starting to open up for that if people are interested in going to that. It should be a very good meeting.

MS. CRANE: ASAN recently published the funding from the Golden Gate Regional Center in California, a toolkit on addressing communication needs in autistic children and adults. The toolkit is based on the available data for research and also clinical best practices that we gathered from clinicians in the field. It gives pretty clear guidance to parents, professionals and service providers how to recognize when there might be a communication need, what to look for in a good communication evaluation and what to look for in a good communication intervention.

Much more importantly because we are a policy shop more than we are a science shop, it goes into pretty good detail on sources of funding for communication, evaluations and communication supports including IDEA funding, Medicaid funding, vocational

rehabilitation funding, private insurance, anywhere that you can find money for communication support. We put information on that in there. If you want a link to the toolkit, just give me your card. I will send you the link.

DR. GORDON: Laura, did you want to --

DR. MAMOUNAS: Just briefly, NINDS along with NIMH and NICHD, is organizing a workshop that will be held December 7, 8, and 9. It will look at biomarkers that could be used in autism-related neurodevelopmental disorders such as Fragile X, Phelan-McDermid syndrome, tuberous sclerosis. There will be a lot of autism people there as well.

It will focus on neurophysiological and functional biomarkers that could be used in clinical trials to stratify subjects or to give us an early indicator of treatment response. There will be a lot on EEG and

imaging and other functional measures. We will have a white paper. I am sure Walter can update you all.

DR. GORDON: I did want to give one update to an NIH-wide initiative that we are working on as I mentioned and as we heard presented. We have some studies trying to look at the efficacy of screening in the 18 to 24-month-old range in terms of improving outcomes later.

But we also recognize that that is probably not early enough. We are embarking on a multi-step process to try to figure out if we cannot develop methods that would be amendable for screening in the first year of life. And the first step in this process is we will be holding a workshop in the spring in March. It is not determined yet. We are working on the dates. But we look forward to bringing the results of that workshop to this

group probably in the spring meeting so we can talk about what we plan to do in that area.

Thank you very much everyone. There are no further comments. We look forward to seeing you January 17.

(Whereupon, at 4:35 p.m. the meeting adjourned.)