

INTERAGENCY AUTISM COORDINATING COMMITTEE

HEALTH OUTCOMES WORKING GROUP

THURSDAY, SEPTEMBER 27, 2018

The Interagency Autism Coordinating Committee (IACC) Health Outcomes Working Group convened in Rockville, Maryland, at the National Institute of Mental Health (NIMH), 6001 Executive Blvd., at 8:37 a.m., David Amaral, Ph.D. and Julie Lounds Taylor, Ph.D., Co-Chairs, presiding.

PRESENT:

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

DAVID AMARAL, Ph.D., *Co-Chair*, IACC WG,
University of California, Davis, (UC)

JULIE LOUNDS TAYLOR, Ph.D., *Co-Chair*, IACC
WG, Vanderbilt University

SHELLI AVENEVOLI, Ph.D., (representing NIMH)

GREGORY BARNES, M.D., Ph.D., University of
Louisville School of Medicine

TIMOTHY BUIE, M.D., Harvard Medical School

JUDITH COOPER, Ph.D., National Institute on
Deafness and other Communication Disorders
(NIDCD)

PRESENT: (continued)

DAN COURY, M.D., The Ohio State University
College of Medicine

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

GERALDINE DAWSON, Ph.D., Duke University

PATRICIA DIETZ, Dr.P.H., M.P.H., U.S. Centers
for Disease Control and Prevention (CDC)

SARAH GARDNER, University of California,
Davis (attended by phone)

DENA GASSNER, M.S.W., Adelphi University

ANTONIO HARDAN, M.D., Stanford University
Medical Center

JENNIFER JOHNSON, Ed.D., U.S. Department of
Health and Human Services (HHS)

JOSEPH JOYCE, M.B.A., Autism Society of
America (attended by Phone)

DENISE JULIANO-BULT, M.S.W., NIMH

ALICE KAU, Ph.D., Eunice Kennedy Shriver
National Institute of Child Health and
Development (NICHD)

CONNOR KERNS, Ph.D., University of British
Columbia

BRYAN KING, M.D., M.B.A., University of
California, San Francisco (UCSF) (attended by
phone)

PRESENT: (continued)

CLARISSA KRIPKE, M.D., UCSF

BETH ANN MALOW, M.D., M.S., Vanderbilt
University Medical Center

MICAH MAZUREK, Ph.D., University of Virginia

DONNA MURRAY, Ph.D., University of Cincinnati

CHRISTINA NICOLAIDIS, M.D., M.P.H., Oregon
Health and Science University

JEREMY PARR, M.D., Newcastle University
Institute of Neuroscience, United Kingdom

KEVIN PELPHREY, Ph.D., University of Virginia

DORA RAYMAKER, Ph.D., Portland State
University (attended by phone)

LOUIS REICHARDT, Ph.D., Simons Foundation
Autism Research Initiative (SFARI)

ROBERT RING, Ph.D., Vencor Therapeutics

SCOTT MICHAEL ROBERTSON, Ph.D., U.S.
Department of Labor (DOL)

MARCELLA RONYAK, Ph.D., LCSW, CDP
Indian Health Service

NINA SCHOR, M.D., Ph.D., National Institute
of Neurological Disorders and Stroke (NINDS)

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

PRESENT: (continued)

STUART SHAPIRA, M.D., Ph.D., CDC

MATTHEW SIEGEL, M.D., Tufts University School
of Medicine

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

SARAH SPENCE, M.D., Ph.D., Harvard Medical
School

JEREMY VEENSTRA-VANDERWEELE, M.D., Columbia
University

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Work, Portland State University, and
Adjunct Associate Professor, Division of
General Internal Medicine, Oregon Health
and Science University

Dora Raymaker, Ph.D., Research Assistant
Professor, Portland University; Co-
Director, Academic Autism Spectrum
Partnership in Research and Education
(AASPIRE)

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PROCEEDINGS

DR. SUSAN DANIELS: Good morning and welcome to this IACC workshop on addressing the health needs of people on the autism spectrum. We are really excited about the agenda we have for today. The IACC has convened a working group on addressing the health outcomes of people on the autism spectrum. And we put together this workshop to start talking about some of the important issues that are at hand that the committee would like to address.

We're going to start out this morning with introductions. I'd ask because we have so many people at the table and on the phone that we would keep these introductions very short and just give your name, affiliation, and your relationship to autism whether you are an autistic adult, a parent, a

researcher, clinician or other person who is a part of the autism community. And I'd ask you to please turn on your microphones before you speak and then turn them off so that we do not get feedback from too many microphones being on.

So I'll start. My name is Susan Daniels and I am the director of the Office of Autism Research Coordination here at the National Institute of Mental Health. Our office manages the Interagency Autism Coordinating Committee.

DR. JULIE TAYLOR: I'm Julie Taylor from Vanderbilt University. I'm an IACC member and researcher.

DR. DAVID AMARAL: Good morning. I'm David Amaral. I'm at the UC Davis MIND Institute. I'm an IACC member and a researcher.

DR. KEVIN PELPHREY: Good morning. I'm Kevin Pelphrey from the University of Virginia. I am a neuroscientist and parent with a child of autism.

DR. TIMOTHY BUIE: Good morning. I am Tim Buie. I am a pediatric gastroenterologist at the Children's Hospital in Boston and work in both clinical care and kids with autism and research.

DR. JUDITH COOPER: Good morning. I'm Judith Cooper. I'm the acting director of the National Institute on Deafness and Other Communication Disorders and I also coordinate the autism portfolio and activities for my Institute.

DR. JEREMY PARR: Good morning everyone. I am Jeremy Parr. I am a pediatric neurodisability clinical academic from

Newcastle University in the UK. I am really pleased to be here. Thanks.

DR. MICAH MAZUREK: Good morning. I am Micah Mazurek. I am at the University of Virginia. I'm a clinical psychologist, a clinician, and a researcher.

DR. CONNOR KERNS: Good morning. I am Connor Kerns from the University of British Columbia. I'm a clinical psychologist, clinician and researcher.

DR. CLARISSA KRIPKE: I am Clarissa Kripke. I am a clinical professor of family and community medicine, director of developmental primary care at UCSF and have multiple roles.

DR. DANIEL COURY: Good morning. I'm Dan Coury. I'm a developmental and behavioral pediatrician at Nationwide Children's

Hospital and Ohio State University. I do both clinical care and research.

DR. PATRICIA DIETZ: Good morning. My name is Patty Dietz. I am an epidemiologist from CDC. I'm the branch chief that oversees the group that does the surveillance system ADDM, and ongoing case control study, SEED.

DR. NINA SCHOR: Good morning. I'm Nina Schor. I am at the NINDS. I am the deputy director there. I am a child neurologist and researcher.

DR. STUART SHAPIRA: Good morning. I am Stuart Shapira. I am the associate director for science and the chief medical officer in the National Center on Birth Defects and Developmental Disabilities at the CDC. I am a researcher on CDC's autism study, the study to explore early development, the case control study that Patty mentioned.

DR. MATTHEW SIEGEL: Hello. I'm Matthew Siegel. I'm a child psychiatrist and researcher. And I'm at Maine Medical Center and Tufts University.

DR. ROBYN SCHULHOF: Good morning. My name is Robyn Schulhof. I am actually sitting in for Laura Kavanagh, who is the acting associate administrator at HRSA, Maternal Child Health Bureau. And I work on autism training programs.

MS. DENA GASSNER: My name is Dena Gassner. I am recovering so bear with me. I am an adjunct faculty member at Adelphi University and Towson University. I'm a Ph.D. candidate at Adelphi University. And I'm here today because I have a 28-year-old son who is autistic, a recent Marshall University graduate after six and a half very long years, yay, after people told me he would

never live independently. That makes me so happy to say that. And I'm also an autistic individual. Thank you.

DR. ANTONIO HARDAN: Good morning. My name is Antonio Hardan. I am a child psychiatrist at Stanford University. I am a clinical investigator as well as a clinician in the field of autism.

DR. DONNA MURRAY: Hi. I am Donna Murray. I am VP of Clinical Programs at Autism Speaks. I head up the Autism Treatment Network and I am also a family member.

DR. SARAH SPENCE: My name is Sarah Spence. I am a child neurologist at Boston Children's Hospital and I run the Autism Center there and do some clinical research.

DR. GREGORY BARNES: Hi. My name is Gregory Barnes. I am a pediatric neurologist from the University of Louisville Autism

Center. I'm also a researcher and a father of a 24-year-old young adult with autism.

DR. CHRISTINA NICOLAIDIS: I am Christina Nicolaidis from Portland State University, Oregon Health and Science University, and the Academic Autism Spectrum Partnership in Research and Education or AASPIRE. I wear multiple hats. I am a general internist, a researcher, a clinician, a parent, and a friend and ally.

DR. MARCELLA RONYAK: Good morning. My name is Marcy Ronyak. I am the director at Indian Health Service for the Division of Clinical and Community Service. I also coordinate all of the Indian Health Service efforts in regards to autism. I am the mother of a proud 9-year-old, bless his heart, who is on the spectrum and also bring a different perspective to this group. Thank you.

MS. ALISON SINGER: Good morning. I am Alison Singer. I am the president of the Autism Science Foundation and a member of the IACC. I have an older brother with autism and also a 21-year-old daughter diagnosed with very severe autism.

DR. DANIELS: Beth, would you like to introduce yourself?

DR. BETH MALOW: I'm Beth Malow. I am a sleep neurologist from Vanderbilt University in Nashville. I also am proud to say I have two children on the autism spectrum ages 20 and 17.

DR. DANIELS: Thank you. Are there other people on the phone that have not had a chance yet to introduce themselves?

OPERATOR: This is the operator. Would you like me to open the lines at this time?

DR. DANIELS: Yes, for the people with the leader code.

MS. SARAH GARDNER: Good morning. I am Sarah Gardner, mother of a 26-year-old son with autism. Our family is also one of the founding families of the MIND Institute.

DR. BRYAN KING: Good morning. This is Bryan King. Sorry I could not be with you there this morning. I am here at the University of California San Francisco where I direct the Division of Child Psychiatry.

DR. DANIELS: Anyone else? Geri?

DR. GERALDINE DAWSON: Good morning everyone. I'm Geri Dawson. I am a professor at Duke University and direct the Duke Center for Autism and Brain Development.

DR. DANIELS: And Geri is an IACC member. Are there any other people who have joined on the phone? I know that traffic was

particularly bad this morning and there were problems with flights due to the weather. We hope maybe more people will join us a little bit later.

Lisa Croen is not able to be with us today due to a family emergency. And Joe Joyce was not able to join us. There are may be some others that may appear throughout the day. If there is anyone just dialing in now, feel free to join the discussion at any time by phone.

With that, we will move to the slides. Thank you. I just wanted to introduce this workshop and how the committee came up with this. The working group, Improving Health Outcomes for Individuals on the Autism Spectrum, was convened by the IACC within the last year. This working group is going to explore ways to support research to better

understand the health conditions that affect individuals on the autism spectrum, many of which have come to light through some of our meetings that are of great concern to the community.

We are going to work to find ways to increase community and provider awareness of these conditions and their treatment. And the working group is also seeking to foster the development of practice guidelines, policies, service approaches, and other efforts that will improve the health and quality of life for people on the autism spectrum.

The working group's scope. Our chairs, by the way, Julie Lounds Taylor and David Amaral - hold on just a second, I'll come back to you - Julie Taylor and David Amaral, by the way, are chairs of this working group who graciously volunteered from the IACC to

head up this working group. The scope of the working group is going to be to cover health and general wellness for people with ASD, co-occurring physical and mental health conditions, premature mortality, patient provider interactions and including medical practitioner training, and parental and family mental health. Those are some of the issues that they would like to cover.

And the last bullet on this next slide is that the working group will be active from September 2018 to September 2019 when this iteration of the committee will come to end. In the next year, this working group will have a chance to address some of these issues. Please go back to the previous slide. There is a lot to do, but these were the first issues. The ones that are going to be on the agenda today are the first ones that

are going to be addressed, including health epidemiology, patient-provider interactions, and co-occurring health conditions.

The working group is aiming to develop a written document to provide an update on issues and to reach certain parts of the community that they would like to inform of what their findings are.

There will be continued discussions on working group conference calls, working group meetings, and/or IACC full committee meetings. And of course, everything that the IACC and its working groups do are open to the public. We will make those accessible by webcast or by phone call.

And then these slides, I am not going to go through them, just list the members of the working group. You will see that there are a number of people who have various types of

experience, parts of the community, including autistic adults and parent and family members.

With that, Julie and David, would you like to make some comments before we open the workshop?

DR. TAYLOR: Hello everybody. First of all, thank you so much for coming out and joining us today. At the IACC meetings, issues around co-occurring conditions come up at nearly every meeting in terms of the challenges that a lot of individuals and families are facing. And so we are really excited to bring together a group of experts both in terms of your academic expertise and also in your lived experienced to really help us think about where the state of the science is at least in terms of the subset of issues that we will be talking about today and what

kind of product can we put together that is really going to be meaningful to people on the spectrum, to their families, and also to providers.

I think the other point that we want to make sure that we make is we know and we are well aware that we are really only talking about a subset of the possible issues that we could be talking about in health and mental health. This is very very broad and there are many many important conditions and issues that we should be talking about. So we really see this as a start of the conversation, I think, and issues like co-occurring mental health problems and other things I think we expect as a working group to move to and think about and address in one way or another. Thank you.

DR. AMARAL: So, I want to also extend my welcome. I am really excited that this meeting is starting. At the very first IACC meeting that we had, I think it was 2015, we were encouraged to think about what is low hanging fruit in terms of helping the autism community. One of the things, as Julie said, that keeps coming up is the occurrence of these medical conditions, many of which are treatable, but oftentimes which families get support to get treated out in the community. I think that this meeting is aiming at really trying to come up with some practical support for the autism community in getting health conditions treated.

And as I see it and this has already been articulated by Susan, the points are what are the medical conditions that are affecting the autism community. How can they

be detected and how can they be treated? And then how do we get that information out to the practicing community? Beyond the academic communities where people are aware and perhaps already treatments are being implemented, but really when you get out into rural communities in all of our states, how do you get the care, the state-of-the-art care to families in those areas as well?

We do hope that beyond the academic discussions that we might have that you will all help us think about what practical advice we can provide to families, to practitioners, and how can we get that advice implemented.

So, again, the things that we are talking about today, gastrointestinal problems, epilepsy and sleep problems, I think are widely acknowledged as being serious debilitating problems in autism. They

are not the only ones, as Julie said. In fullness of time, we will come back to others as well. For those of you who have other pet areas of interest, never fear. We will come back to those. This is a process.

Just to finalize to say that the document that we will prepare, it will evolve what that will be and who that will be directed to. We may start some discussions on that at the latter part of the day today. When the IACC produces the strategic plan, for example, it is really an iterative process that is spearheaded by Susan's team. It does take a while to evolve. We may not have complete notion of what it is going to look like today, but we will over time. And again, I want to emphasize that we want this to be practical. We do not want this to be an academic article going to some journal where

it will die. We want it to be something that community docs are going to have access to in one way or another. We need your advice of how best to do that.

So, again, as a non-clinician, but who hears from many families who come to the MIND Institute for research that they feel that many of the physicians that they deal with really do not understand the complex medical conditions involved in autism. I'm hoping that our committee, this work group, will be able to make some inroads into bettering the situation for those families. So, thank you all for coming. I look forward to listening to you and learning from you. Thank you.

DR. DANIELS: Thank you. And I think that, Jennifer Johnson, would you like to introduce yourself?

DR. JENNIFER JOHNSON: Hi. I am Jennifer Johnson. I am with the Administration for Community Living. I am the deputy director of the Administration on Intellectual and Developmental Disabilities. I am glad to be here. Thanks.

DR. DANIELS: Thank you. Is there anyone else on the phone that wants to introduce themselves briefly before we get started?

MR. JOE JOYCE: Hello. My name is Joe Joyce. I am the board chair of the Autism Society of America and also a father of a young man with autism who is 19 years old, David, and also a son with Down's syndrome, Matthew, who is 22. And I apologize for not being able to attend in person, but looking forward to the day on the webcast. Thank you very much.

DR. DANIELS: Thank you. Feel free anyone on the phone to jump into the discussions as you would like.

And, Louis, would you like to introduce yourself?

DR. LOUIS REICHARDT: Yes, Louis Reichardt, Simons Foundation. I'm on the IACC committee, not this working group.

DR. DANIELS: Wonderful. Thank you. With that, we will have Jeremy Parr come to the podium to give us the first presentation. I am not going to go through his bio, but you have the bios in your packets. They are available on the web for anyone who is listening into this. Thank you so much for being here, Jeremy, all the way from the UK.

DR. PARR: Thanks for asking me to come. It is a real pleasure to be here with so many

of you thinking about this really important issue.

I thought I would do a quick conflict of interest slide. I do not really have any. I've received funding from a number of organizations.

UNKNOWN SPEAKER: Excuse me, Jeremy, I don't think your mike is working or it's not close enough.

DR PARR: Does that help at all? Okay. I have no particular conflicts of interest. The slides are the work of lots of people. I would like to put those acknowledgements out there to begin with, including a lot of people in Newcastle, but also a lot of people whose support is across the UK.

We started thinking about adulthood and aging at a meeting in 2013 where we started thinking about the life course. We sat with

people, autistic people and relatives to work around some research priorities. They very much talked about the need for longitudinal cohort studies. They talked about the need for work around quality of life, mental health, physical health, and very much helped us work out how we were going to engage effectively with autistic people to deliver this program. That is where we started. To some extent, my structure of the presentation today follows that line.

I suppose at Newcastle, we are international leaders amongst others in autism research registers, databases, and cohorts, which we use to support hypothesis-driven research and improve research infrastructure across the UK.

We run large research databases of children on the autism spectrum of over 4,500

parents with children. We have a lot of data on co-existing conditions. And in the last couple of years, we have been working on longitudinal cohorts of autistic adults. We have a lot of National Health Service trusts. That is the publicly-funded health care system in the UK, free at the point of care to everybody, to recruit people and gather data. And of course, we then export expertise to other places and happy to work with people at this meeting and outside to achieve some of the goals that you might that people come up with.

The research program now is broad. It is including ways of looking at more effectively diagnosing people on the autism spectrum and providing post-diagnostic support from the left-hand side, accessing health care for older autistic people and working around

autistic-specific health checks in primary care. I'll refer to that later. We've done a lot of work around quality of life in designing appropriate measures to measure quality of life for autistic adults. We have also been working around mental health in relationship to personalized treatments and for a range of anxiety disorders, but also phobia, in particular, via technology.

And sat in the middle of that, we have the autism spectrum cohort, which of course is supporting so many of these pieces of work. Because of that, we are working now around five of the community top ten priority areas for the UK. AUTISTICA drove this piece of work. This is the UK autism research charity, drove this piece of work with the community to look at what the research priorities of parents of children, of

autistic adults, of relatives and clinicians were, much less so researchers. Researchers have much less of a say, which was very important.

And a number of areas here.

Interventions to improve mental health, interventions to reduce anxiety. How can people be supportive to care for and understand their autistic adult? How can diagnostic criteria become more relevant? What about service delivery and being adapted to meet people's needs? These are some of the areas we have been focusing on in recent years.

It is also important to say that we have been working really closely with autistic people in this piece of work. This is Cos Michael's slide who I have presented with at international meetings previously. She has

been a great help to us in helping us think about how we move forward. These are her words, not mine. Usually I read all of them out, but because of time today, I probably won't do that.

But I think a couple of key points there really are the collaborative working started when shaping the project. Autistic people were not integrated into a pre-designed project. We really were working with people from the very beginning. And autistic people were asked about what outcomes they wanted and what areas should be researched.

Just a quick word about the cohort because the data I am going to show relate to this. We have just more males than females, which is excellent because we have a lot of representation from women. About 30 percent of people need support to complete the

materials that they do. And 130 of the 1,700 people that we have recruited so far are unable to consent for themselves so a consultee consents for them. This is really an important group of people who have often overlooked in research and were pleased to be able to do specific research in that area.

And then there are more than 150 people over age 56 years in the cohort. As you can see, large numbers in these other groups. We have consent to re-contact people over time to update the information that people give originally, but also to go back to undertake additional research projects through the program. Many people have agreed to meet us, although of course not all.

I just wanted to mention this point. Quality of life was pulled out by autistic people as being very important, at the

meeting in 2013. So one of the first pieces of work we did was led by Helen McConachie in Newcastle, was this piece of work with 370 autistic people, looking at quality of life. We showed that autistic adults have lower quality of life than the general population. But actually, we wanted to look at the predictors. We wanted to look at why that was. Negative predictors pretty consistently across the board for the different domains of quality of life were being female, having a mental health condition, having more severe or social communication difficulties. And as you will see, for social quality of life, it was also related to older age. If we think about some of the interventions that we might put forward, some of the interventions might be there to support mental health, for example.

We also did a piece of work to make sure that quality of life measures were really measuring what autistic people need them to. The measures that are out there for use across autism and other conditions are not necessarily valid with the population we are using them with. This is sometimes not very trendy research, but this is research that is really important to get on and do. We are absolutely certain we can measure the important thing. We created nine new items to add to the World Health brief quality of life measure. They are publicly available on our website. I'm happy for you to contact Jacqui Rodgers or I about those and we'll send them to you.

This is my only slide about children. I raise this because we are going to be talking about children today, but also of course we

have the opportunity to study what change, how people change over the life course through this integrated piece of work between our research databases and cohorts. These are data from nearly 4,000 families and children where parents have reported that they have symptoms weekly, often, or frequently. You can see there are very high rates of sleep problems, hyperactivity, injury to the self, anxiety, eating and drinking, feeding, gastrointestinal problems. Four-fifths of people are saying that they have problems in those areas.

On then on the right hand of the slide are these data from a thesis by Beena Koshy. And what Beena showed was these levels of unmet need in relationship to the - unmet clinical need - in relationship to these specific areas. And bearing in mind that

this is in a publicly-funded health care system where everything is free at the point of care. I think that is important that we have it in that sort of context.

And of course, people do not have one of these co-existing conditions. These are data from Morag Maskey's published paper. Only 10 percent of families had no co-existing conditions. Multiple families had more than one. Three, four was the average. And then on the right-hand side, data from Alex Petrou, showing that as you go up in terms of a number of co-existing conditions, the impact on the family becomes greater. Bearing in mind that families might also have autistic people as parents. We have to think really broadly about the issues here for the community.

We are covering large amounts of data from, about mental health conditions through the cohort. Thanks to Alex Petrou for preparing these data. So you can see here the numbers of people in the different age groups in our adult cohort, so 315 young adults aged 16 to 25, 407 people, 26 to 40, and then 408 in that sort of 41 to 60 age group. This is, we have 500 additional people since these data were analyzed. SO it's really interesting the rate at which we are gaining new participants.

So you can see anxiety and depression, high prevalence across the age range. Cause of course, we can use these cohorts either in terms of looking at how individuals change - accelerated cohort and thinking about people in groups as they go through.

But actually in terms of access to mental health services here, we have the proportion here who tried to access mental health services. And then we have the proportion underneath who were actually able to do so. So there is a 30 percent gap between those people, autistic adults, who wanted something and then manage to get it. There are a whole range of reasons for that. I do not have time to go into today.

And then in relationship to physical health conditions, we talked a little bit about sleep problems before in relationship to children. There is going to be a lot more on that today. But actually, autistic adults have sleep problems too, showing that these problems persist through the life course. Children develop anxiety, they develop sleep. They have eating and drinking problems,

gastrointestinal problems. And as David and I were talking about earlier, what happens for children's health when they have multiple of these things simultaneously at age 8 and then that continues through the life course? There must be some impact here in relationship to people's long-term health outcomes and average life expectancy.

These are data hot off the press from colleagues Sam Brice and Sarah Wigham, who has been looking at health care adjustments or you might call them accommodations, so data from more than 600 people. And the data in the middle of the slide really relates to anxiety. So these are examples of what people said they needed most frequently, but were infrequently provided by National Health Service clinicians.

And this, one of the points here really mirrors one of the points raised in the public comments. So, therapists with expertise in autism. Not just expertise in CBT in relationship to anxiety, but actually being able to engage with people because they understand autism and what adjustments therefore need to be put in place. I won't go through all of these, but it is very important that we listen to people to be able to close these gaps in terms of health adjustments.

And I was really interested in this quote at the bottom around diagnostic services. "It was an unfamiliar place in an unfamiliar town, though this was my fault because I tend to avoid going out. Of course, it is not their fault at all. What was particularly hard was that the building had

an outside intercom that, had I been alone, I would not have used. I would have panicked instead and returned home." It is any wonder that people cannot access the health care when these sorts of things get in the way.

So Susan was kind enough to come to Newcastle a year ago for this workshop around autism and aging and health care. I'm not going to read all of these things out, but these were some of the priority areas that were identified and small research projects drafted. But six and seven here were adaptation of online health care toolkit, developed in the United States by Christina and Dora Raymaker for the primary health care of autistic adults and could we use that in the UK. And the development of personalized annual health check programs.

And later this year or early next year, we'll be starting that process, so following a competitive open call for proposals, a group of people were successful from that meeting, including Christina and Dora and Anna Urbanowicz. We have commissioners, managers, clinicians working on this piece of work.

Autistic people involved in the co-design of this research throughout. We will be looking at acceptability and feasibility outcomes, but also health outcomes in utilizing standard NHS data sets. That's one of the reasons the UK is such a great place to do this research because of course we have access to standard care data from primary care.

So to end, some key messages from me. I suppose that we have seen the value of

research programs that build critical mass in autism adulthood and aging.

We've used an integrated research approach where we are using either basic science or improved understanding to design trials, interventions, services, and then think about how to implement change subsequently. And that implementation science element I think as important as the other elements if we are actually going to create change within services.

These longitudinal studies are going to become very valuable to us, I think, across the life course, and enabling us to share anonymized data.

I think access to usual health care, as I said. UK NHS is a great environment to do that piece of work. And also that national and international collaboration will lead to

early results here. Using parallel protocols, parallel measures in research across the international community will allow us to make rapid progress for adulthood and aging.

Thank you for asking me to come. I will leave you with this slide about what we are up to. Thanks very much.

(Applause)

DR. DANIELS: Thank you. So we have time for discussion with the working group.

MS. GASSNER: Dr. Parr

[inaudible comments]

MS. Gassner: Oh, I'm sorry.

DR. AMARAL: Oh, go ahead, please.

MS. GASSNER: I just wanted to point out something that really jumped out to me is how close your gender stats are, that you have 54 percent male and 44 percent female. And in the states, often we hear that is very hard

to find female subjects. I was wondering if you had any insights as to how you were able to recruit.

I know in my research, I look at gatekeepers that hold the access to that community. How are you doing it there, other than using AUTISTICA certainly raises you and elevates your research in our community?

DR. PARR: For our children's databases, it is four to one, as you would expect. We've gone to some efforts to show representativeness with people who don't participate. We're at an earlier stage with the adult cohort. I don't believe that if we were to do a population study of autism in adulthood, in terms of detected prevalence, we would find that the gender split was four to one. I think it would be much closer. I am

not saying it would be one to one, but I think it would be much closer.

Of course, women, I think, have been shown in many research projects to be shown to be much more likely to participate than men. So I think there is that aspect potentially as well.

We do ask people who do not want to take part to give us some anonymized data. There is certainly more men who are not taking part than there are women. But I suppose we can see this as a potential challenge in terms of representativeness or we can see this as an opportunity to undertake high-quality research with autistic women. I've had my eye on representatives all the time, but I also have my eye on the opportunity to get high-quality data.

DR. BUIE: Hi. I am Tim Buie. I am interested as a pediatric gastroenterologist in looking at medical issues in adults in part because for us as a community of specialty people, we don't have adult providers to send our children to when they graduate us. And consequently, I have ended up following many of my individuals well into adulthood. It feels like that creates a barrier toward data collection and understanding what numbers are and who to transition to, et cetera. I know this is partly your experience outside of what you talked about today. Could you talk about how to engage adult providers in this community as a way of helping us gather better data?

DR. PARR: I think these are structural issues for health care providers. And I think

because of, as ever structural issues, there are no easy answers, are there?

We have just finished a two million-pound, five-year research program around transition from children services to adult services. And we found exactly this in relationship to autism, that there were fewer places for people to transfer to in terms of people with the expertise to manage people with autism and co-existing mental health conditions. So in the UK, many people transfer back to their primary care or GP, general practitioner in the UK, rather than to hospital specialists. Then of course, there would then be an onward referral.

If there was a need and there was an onward referral, how much expertise do my adult physician colleagues have in autism? And I think they would stand there and say

not very much. And I suppose it comes back to this point about clinical psychologists and needing clinical psychologists to understand autism as much as they understand CBT. We really do need improved education, but I have no quick fix answers to that. Especially from, and I will say it again, that's from UK NHS versus a different health care system which you have here.

DR. MALOW: Great, thanks. Beth Malow, sleep neurologist. I really love your comments. And I wanted to make two. One was about Tim Buie's last comment that one model that we are exploring in the US and is actually global is like a project ECHO model where you can teach people in the community who are already out there, like family practice people, to learn how to care for adults with autism. They are using this model

in a variety of conditions including - it started out like with hepatitis C. It has really evolved. There is a group of us in this country who are looking at autism throughout the lifespan and trying to train family practitioners and others, pediatricians in caring for these underserved populations including in rural area.

The other comment I wanted to make that I loved about your implementation science is - for example, sleep is a good example, but it also relates to GI. It relates to epilepsy in terms of taking meds. Empowering adults on the spectrum to take their meds or not stay up late or not be on their screens. This whole idea of we know what to do to help people sleep, to improve their diet, to improve GI problems, to take their medicines if they have seizures, but getting them to

actually do it, which is the implementation science, I think is a huge challenge.

So I was wondering if your group was addressing that issue of how do we actually take our evidence-based practices and get individuals with autism to do them. And do the individuals with autism in some way inform that practice?

DR. PARR: Thanks. I think that is a really important point and one of our aims. We set out very much to learn more about the lives of autistic adults. So when we started in 2013, one of the questions was what do people need. What do the lives of the very large number of autistic people look like throughout their life course? And actually, we have a lot of very experienced people in the room. And no one could tell us definitively. Of course, we have learned a

huge amount through this mixed methods piece of work through the cohort so far.

So one of the efforts now is to start to design these interventions. You can see that we have started with the sorts of things that people have asked us to focus on. And I think it is about designing interventions and thinking about novel ways to deliver that. Does this relate to technology, for example, and so on and so on? This is a long game and a need for a large number of clinical trials, effectively, whether it is education-based clinical trials or delivery-based clinical trials, and then implementation subsequently.

I think the worry from autistic people when they ask me about it. This is the pace of research. All of this is great, but actually when they can have progress. But we are not changing people's lives instantly. I

think autistic people really do want that and opportunities for change early on.

DR. KRIPKE: I wanted - I was struck by your comments about including people who need support in your research and, and also the number of autistic parents that you are working with and wanting, wonder if you could talk more about any investigation into the quality of the support and whose voice is really surfacing and working with populations where their primary supports may be also autistic or also have other disabilities.

DR. PARR: So, we are just starting to think about those data. One of the challenges for us is we have a huge amount of data and a huge amount of opportunity. And of course, there is only so much resource to do everything simultaneously.

One of the things I didn't talk about very much at all is the fact that we also have relatives of autistic people's cohort. So 700 relatives of adults on the autism spectrum have joined the longitudinal cohort too. We will be able to look at what those people say about how they are supporting their autistic adult just to figure out exactly what you are thinking about and then marry that up to what autistic people say through either quantitative data or mixed methods qualitative work. So for us, it is a really important target because I suppose support whether it is post-diagnostic support or health care support or everyday life support, opening bills, making sure your electricity does not get cut off. These things are fundamental points for people's lives.

[inaudible comments]

DR. PELPHREY: I noticed when you were showing the regression models that being female was sort of strongest, negative predictor. And initially I thought well of course. But in our samples in the US that tends to be chalked up to having to be a more severe case to, get into, to cross the threshold for diagnostics. You have almost a one-to-one ratio. I could not chalk it up to that.

What do you think is going on there in terms of something that's usually a protective factor for a variety of health conditions sort of turning into the strongest negative predictor once you have that diagnosis of autism?

DR. PARR: I think it's, I think it's a very interesting point and I think it - there

are many potential reasons for that. I suppose I would say that lots of autistic women have a lot of insight into their own difficulties. I think a lot of autistic men have insights into their difficulties as well. But you are asking me to hypothesize. I wonder if autistic women's insight might mean that they therefore, they therefore think, are able to report more effectively around their quality of life or influences in some way. I don't know. I think it is a really important one.

I suppose we are - this is one of the things we are trying to identify by learning about people's lives and looking at these sorts of predictors. We can then work to think about where from now.

DR. DAWSON: I was thinking about the part of your talk that is focused on

implementation and also David's comments about how do we actually make a difference out in the clinics, primary care.

As I am sure many of you know, one of the big movements in health care is integrated health care models where behavioral health specialists, it could be psychiatrists or psychologists, working right in the clinics of primary care. Or it could be in the hospital as well.

At Duke, we have had a very strong emphasis on this. Where we have psychologists and psychiatrists out in primary care or in the hospital.

And there's sort of two ways in which I think that really makes a difference. One is that often the physician is not actually able to complete the tests that need to be done. If you look, for example, in pediatric

primary care and you just look at the number of just well child checkups that are completed, like they were able to look in the ears, for example, they just can't get it done. So even the most basic aspects of health care are not being delivered.

Some of the suggestions that could be made about how you deal with sensory sensitivities or developing communication systems have made a huge impact. But similarly in the hospital, if you have a child who has a cardiac problem and you can't get the leads on or whatever it is, these present huge challenges.

But in addition, by having these specialists integrated, you also are able to address the mental health needs right alongside the physical health needs.

So I just wanted to throw out there whether as we think about the strategic plan that we might actually call for research on the impact of these integrated health care models on being able to impact access to more quality care. Because I've seen it make a huge difference. Yet I don't know a lot of, there is a lot of research on this in other areas like depression, but I have not seen a lot of it in autism yet. I might just be unaware of it.

DR. COURY: I want to follow up on what Geri is commenting on and some of the themes that I am hearing where families, individuals with autism, are concerned that their primary care provider does not know how to manage their autism and the co-occurring conditions, which is what this work group is all about. And seeing the work they have done in the UK

with developing health check, the equivalent of clinical guidelines.

What we have seen in this country and I can give one example with Down's syndrome. As we know about some of the complications seen in Down's syndrome, clinical guidelines are developed so that primary care providers, not Down's syndrome specialists, know when to screen for problems with thyroid, risk of leukemia, atlantoaxial subluxation, and things like that. And if we can develop good guidelines for primary care providers to follow, increasing their awareness of the increased risk of certain conditions happening then that is one step in empowering them to do this.

A second part of this, I think, is another thing that they are doing in the UK, empowering the patient and family to do this

often when they come to the visit prepared and are prepared to discuss this with their provider. It is a way of prompting the provider to become more informed on this, which may be more effective than our traditional ways of publishing, which get buried into vaults.

MS. SINGER: So I agree with Dan and I agree with Geri, but I think we should talk about whether we need to take it one step further and rather than be satisfied with providing additional training to primary care physicians whether we, as the IACC, want to advocate for the development of a new medical specialty that would focus specifically on the complicated and complex needs of people with autism that would encompass the tremendous variety and intensity of needs.

I think the AAP talks and the AMA - they talk a lot about medical home. But I think as our children leave their developmental pediatricians, there is no medical home for them because there is no specialty. I think later when we get to the discussion portion of this conference, that's something that I would like the group to talk about because that is the something that the IACC is able to do. We often talk about what we are not able to do, but this would be something that we could do.

DR. KERNS: And related to that point, I think something that's on my mind in hearing your talk and what everybody is saying is perhaps we could have a discussion about how much additional expertise do we really think is needed for providers to work with this population. So what kind of message are we

sending to providers about here are the skills that you have that really can be applied and could be useful if you can do so in a flexible manner and with an open mind? Then here is the information you really don't have. Here are the treatments that actually need to be done differently with this population or are counter indicated. I am thinking a lot about CBT and anxiety. That's my area.

The truth is that a lot of what works in terms of CBT and anxiety is all of the same core principles. And really what psychologists need to learn how to do is how to deliver those principles flexibly. So stop saying people on the spectrum are rigid. I cannot treat them. They need to look at themselves and say I need to be less rigid and I need to figure out how to deliver these

concepts to this individual by listening to who that individual is and working with them. And when you look at the CBT trials that we are doing in the US now, the truth is that the tailored CBT adaptive, CBT on the spectrum, does work better. But actually, we are looking at some data now that standard CBT can get a lot of kids to a certain level. So I wonder if something that we could do on this committee is trying to sort out some of those questions about telling providers who do not have expertise in autism, what are the basics that they need to know about how to work with this population so that people on the spectrum don't have this really awful experience of trying to get health and then meeting somebody who says I can't help you because you have autism. And then also

thinking about when really a specialist is needed.

DR. PARR: So could I just comment on that? Would that be all right? I absolutely agree, Connor. Jacqui Rodgers, who I work closely with in Newcastle, I know you know well, and I have these discussions. Because we have national guidance in the UK saying this should be adapted CBT delivered to autistic people. But actually, whether these are adaptations in CBT itself or adaptations in delivery or adaptations in adjustments in the way appointments are offered and what the waiting room looks like before people go in and what happens subsequently. I suspect it is not either/or. Probably both of those things that need to happen. I think it's a more sophisticated discussion about what we need.

DR. TAYLOR: Antonio, I had you on the list next. So do you want to have your comment while we get the mike going?

DR. HARDAN: I want to echo what Geri mentioned about the importance of completing physical exams for kids and adults in a comprehensive way. I think we have to think about the motivation of the primary care provider. Sometimes in research we seek it in adults who need to have a physical exam before they enter a study. And then we try very hard to get the EKG, to get the blood work and to be very patient with them to be able to get these tests done. If we don't complete them, we can't enter these individuals in the study. Motivation plays an important part.

For the primary care physician, we need to get an EKG or blood work. If we do not

motivate him or her, they won't be able to push to get that done. In addition to training, I think part of the system, we have to reward them for doing that.

I think, in child psychiatry, in child psychology, we have RVUs or rewards for interactive complexity. So maybe something should be developed for primary care physicians when they have an individual with autism and they need an EKG or blood work to be able to work a little bit harder with the family and the individuals to get this test done.

DR. SCHOR: Yeah, it sounds like it's working. I just wanted to comment on the notion of having a new subspecialty or something of that nature. This issue is not at all unique to the autism population. And for eons, the medical community has trained

people as if we have two discreet and disassociated entities, childhood and adulthood. But as we all know, most adults started out at some point as children and that transition. Now that children with chronic health care conditions are living longer, are living independently, are living out in the real world rather than in an institution. We need to change the medical paradigm to acknowledge that.

I think we have the substrate that's really growing by leaps and bounds to do this. That is the Med-Peds trained individuals. It is becoming increasingly popular. It takes an extra year to complete a residency in Med-Peds. And so, you tend because of that to get very motivated people who are willing to invest another year. They're very competitive programs. And really

to train those individuals who are used to thinking of adult manifestations of childhood onset conditions should be much easier than starting with someone who is an internist and has not for a decade or so seen a child in their clinic.

DR. BUIE: I'm a Med-Peds trained physician. I would like to speak to that a little bit. One of the things, certainly, it has helped me because I now still follow many of my individuals into adulthood.

I think when you have a condition with the prevalence that we have, that we are seeing so many individuals. The idea that one pediatric gastroenterologist is sufficient to take care of these kids at the Children's Hospital of Boston is insane. We can't possibly do it. All pediatric gastroenterologist need to become better at

this and need to have a capacity to see these individuals. Likewise, adults who didn't see these conditions a few years ago are in the same boat that we were 15 years ago when we weren't seeing these numbers. We had to learn how to care for these individuals and so do adult internists and adult specialty providers. To narrow it to well-trained Med-Peds people, I think they are wonderful resources and we use them in our community, but I think the numbers are too high.

And the idea that that lets adult neurologists off the hook or it lets general internists off the hook isn't the right pathway. We need to be better about training our medical community across the board.

DR. SCHOR: I couldn't agree more. I think from the standpoint of specialty care, that's exactly the case. And certainly in

pediatrics, you know as well as I, that the situation is the inverse of what it is in the adult world where in fact we have large numbers of primary care people and try and find a specialist on Sunday. There just are not enough of them. And so in the specialty realm, I do think that is critically important.

And child neurology, for example. We do a year of adult neurology and the adult neurologists do at least three months of child neurology. I know infectious disease has a similar thing. But most specialties don't. Most specialties you either do adult or child. And I think fixing that as you say would be a wonderful step forward.

DR. TAYLOR: Nina, before we move on, we are going to do three more comments after this and then I think move to the next

section. I've got Denise, Scott, and Sarah on deck.

Nina, could you just do a really quick definition for those who are not familiar about what a Med-Peds' doctor - what that specialty is.

DR. SCHOR: It is a residency level, primary specialty, if you will. These individuals split their time between pediatrics residency and internal medicine residency over the course of four years rather than three, which is the duration of a peds residency or an internal medicine residency. So they at least have conversance with both populations and often are involved in transitional care, but it is a primary care and not a subspecialty.

DR. TAYLOR: Okay, Denise, did you have anything? Did you have your hand up? Next, we have Scott.

DR. SCOTT ROBERTSON: I just wanted to echo what was being shared about getting info and knowledge when we have good practices and when we're developing better knowledge at scale and disseminated across the board. We'll be mentioning later on what that means in terms of employers and workplaces and how there could be collaboration on that because some folks access either health services or get referrals, some get employee assistance programs, et cetera. As a federal employee, like I also get, for instance, the flu shot and things like that from our federal health service at work.

So just something for folks to think about, and also to think about when we are

thinking scale down the road what it means also across the large swath of the United States including rural areas where a lot of dissemination of some of the knowledge here that we are talking about health care practices is going to take a lot of creative thinking on how you reach these for other areas that we already know from the literature that we already have disparities in, in service provision even for children and adolescents so what that is going to look like for adults on reaching these wide swath of areas across the country.

But I, and I think everything is excellent in terms of what we are focusing on and highlighting a lot of these major areas on health focuses for adults, adolescents, and children is really important for today.

And I look forward to the rest of the discussions today.

DR. TAYLOR: Sarah.

DR. SPENCE: Two quicks comments. One is nothing is going to change in medicine until insurance changes. So, is anybody from CMS here? Sometimes they do come to IACC meetings. So that's something that, I think, this group can look into.

I think the other thing in terms of not letting adult neurologists off the hook. I, we're trying to work with our adult colleagues who are in behavioral or cognitive neurology. There is a subspecialty. And I think the idea that they have a difficult time working with somebody with a developmental disability is quite silly. And I'll use that word because one of the things they are afraid of is this patient cannot

communicate with me in the same way. One of the things they take care of is dementia. I am quite sure that patients with dementia also can't communicate in that way. They take care of stroke patients. They take care of brain injury patients. So I think they have the skills. Absolutely.

I think the idea is - I think it was Connor who said - we have to be careful about telling them that this is a really difficult thing. It is actually not. And so we just have to give them very small pieces of information that I think will make it a whole lot easier.

DR. TAYLOR: Last comment for Christina.

DR. NICOLAIDIS: Thank you. So this is a wonderfully rich conversation and I agree with a lot of what people are saying. I don't think it is a dichotomy. Autistic individuals

need health care. So they need a reproductive endocrinologist. Whatever subspecialty, whatever primary care. We can't let anybody off the hook.

At the same time, there is a utility to a developmental pediatrician. And the truth is we don't have an adult version of that. So those two are not against each other. There are times where we need an adult version of a developmental pediatrician. And then we need all health care providers to be able to actually take care of their patients, whoever their patients may be, whether it is because they are a racial or ethnic minority, whether it is because of a disability, whether it is because of their life trauma. They still need to be able to take care of people who are not our standard patient.

I think the point of having Jeremy here though is largely to think about what can we learn from the UK. And some of what we learn is that even with a somewhat more sane medical system, we still have some of the same problems, which is disheartening.

On the other hand, what we also see is that what Jeremy's group can do and what AUTISTCA's project can do is actually get the tools that do exist to be used.

So I think what we should be thinking of in this group is we have a lot of the - a lot of the things people are saying I know that we and other people in the room are actually doing. Our problem is actually implementation. Our problem is, I am hopeful that, for example, the tools that we have developed to help primary care providers take better care of their patients, are going to

be better used in the UK than they are in the US because they are actually doing it throughout the National Health System. And that is where, I think, we need to be thinking in this group, not so much how do we develop the tools because many of us in the room have them.

It's really how do we get people outside of our little groups to actually use them. How do we focus on dissemination? How do we focus on implementation? And that's what I would certainly like this discussion to come and where I really grateful that Jeremy's group is able to do it on a much larger national scale in the UK.

DR. DANIELS: Thank you so much, Jeremy. It was wonderful to start our conversation around this work and that you were able to bring in both the patient provider aspect and

the co-occurring conditions aspect that we're going to be talking about today. So thank you very much.

DR. PARR: And thanks for inviting me.

DR. DANIELS: Just briefly, I want to say that we have Alice Kau, Jeremy Veenstra-VanderWeele, Sam Crane, and Scott Robertson who have joined us. Do you want to just briefly introduce yourself with your name and affiliation and your relationship to autism?

DR. ROBERTSON: Scott Michael Robertson, autistic adult myself. I work as a policy advisor at the US Department of Labor's Office of Disability Employment Policy on our employment-related supports policy team, which focuses on health care, transportation, other sides of, aspects of being able to work because there are a lot of things that are related to employment that aren't necessarily

the work itself, but things that support the employment's access and I'm our lead on autism and neurodiversity for ODEP, for Office of Disability Employment Policy, as well as like accessible technology, transportation focuses, and apprenticeship. Thanks.

DR. JEREMY VEENSTRA-VANDERWEELE: Jeremy Veenstra-VanderWeele, Columbia University and New York State Psychiatric Institute and the Center for Autism and the Developing Brain at New York Presbyterian Hospital, child psychiatrist, work clinically with folks with autism and do research in the population as well.

And then I'll hand off to Rob Ring since he had the misfortune of just walking in at the right time.

DR. ROBERT RING: Rob Ring. I have my own consultancy practice. I work mostly in the biotech and pharma space, helping companies organize their strategic assessment of the opportunities in autism both on the medicine's development side of things as well as the genetic testing diagnostic side.

MS. SAMANTHA CRANE: Hi. I am Sam Crane. I am the director of public policy at the Autistic Self-Advocacy Network. And I am also an autistic adult.

DR. ALICE KAU: I'm Alice Kau from NICHD. I'm a program director, managing the autism research program for my Institute.

DR. DANIELS: With that, we will move to David Amaral who is going to fill in for Lisa Croen today.

DR. AMARAL: Thanks. We are really sorry that Lisa is not able to join us this

morning. She sent some slides this morning that we will go through and read together.

As an introduction, many of you know that Lisa works at Kaiser Northern California and uses the really rich database of information at her hands to evaluate the kinds of health challenges that people with autism and other disorders have.

And I think, her work is one of the real motivators for this workshop because in general, I think what she has shown is that - she and others have shown that the lifespan of individuals with autism is shorter than typically developing individuals. And that individuals on the autism spectrum actually suffer from many health challenges in greater number than those who are typically developing.

So she sent a couple of slides just that we can go through quickly. First of all, I wanted to thank Jeremy who got us started and really instigated a lot of conversation. I think hopefully that same level of conversation will continue throughout the whole day. And clearly, we will have to get to the implementation component at the end of the day. That will be certainly an aspect that will come back through the work group.

Can I have the next slide? What do I do? Okay, so what do we know? So, individuals with ASD have higher burdens of medical and psychiatric conditions than individuals without autism. So what, I think what Lisa first showed was that it is not the things that we typically think of in terms of autism, but essentially all health care and medical and psychiatric conditions. And that

she can show that higher utilization of health care services and other associated costs.

So the common co-occurring conditions that are seen with ASD are some of the ones that we have already talked about already. So GI problems, sleep problems, seizures. But she also mentioned others. Overweight and obesity, allergy and immune problems. So those are some of the issues that we certainly will come back to in other sessions of the work group. And that there are common psychiatric problems such as depression and anxiety.

But even less prevalent conditions that occur in typical individuals occur more commonly in people with autism. So, she, in her paper, some of you may be familiar with it. She essentially listed all of these

various medical conditions ranging from endocrine to metabolic to cardiovascular. In virtually every case, people on the autism spectrum were more affected and had more prevalence of those non-autistic medical conditions than typically developing individuals.

And particularly I think what was in a sense particularly of interest and of concern is that suicide and suicidal ideation was one of the factors that affected many people with autism particularly females with autism if I remember the data correctly.

So, again, Lisa's work has really identified that for whatever reason, and I think this is one of the challenges, people with autism are having more medical problems. And the question - one of the questions that

we might be able to deal with during this working group is why is that.

She also shows that some of these co-occurring conditions cluster together so things that you might not consider like sleep and constipation, feeding and speech disorders. When you look at them clustered together in particular individuals, I don't think we understand why that is.

Another thing that Lisa's work has emphasized is that conditions emerge over time. So, you do not see everything in a young child. There are different kinds of things that may come out. So, in early childhood perhaps the GI problems may be more evident and they may decrease over time as individuals go into adolescence and adulthood.

Seizure disorders. Actually, seizures - it will be interesting to come back to this. I always thought that seizures were more emergent in later adolescence, but she has it as early childhood.

Sleep problems in early childhood is obviously a condition and overweight and immune conditions. Whereas in middle childhood, the emergence of anxiety is something that we see in our own work as well, is that it is very difficult to diagnose anxiety in a 3 year old perhaps, but you can see it more evidence in a middle childhood individual.

And then in adulthood, these things that at least I had not associated with autism previously, things like cardiovascular disease, diabetes, Parkinson's disease, which now several - I think Jeremy's work has also

shown that Parkinson's and - Jeremy did you just, no, Okay. I forget. There have been a few papers. Joe Piven, I'm sorry. Yeah, Joe Piven. (inaudible comments) I'm sorry?

(inaudible comments) But Parkinson's disease is more prevalent in autism.

And again, the question is why is that. Lisa has provided this. Is the biology that underlies autism, the biology that's leading to these other medical conditions - are there shared genetics? Or are the consequences of these medical conditions - consequences of the core conditions of autism? The fact that a child may not get access to the same kinds of medical care who has autism because of language problems, because of just inability to verbalize their conditions. Does that cascade, as Jeremy was saying, into more serious conditions later on that could have

been taken care of earlier if only had been adequately identified and then addressed? Things like obesity and other kinds of conditions obviously lead to - obesity may be a repercussion of a poor diet of many individuals with autism. And whether there are common environmental characteristics that might be contributing to some of these things as well.

So she asked at the bottom, can patterns of emergence of co-occurring health conditions in first years of life be used as an early warning sign for a screening tool for autism. And, again, I think that that is an interesting question that needs to be asked.

So, again, additional gaps that need to be addressed. What is the natural history of co-occurring medical and psychiatric

disorders among individuals with autism?

Again, her work and a few other studies are showing that if you can do a lifespan analysis of individuals with autism, particularly in a rich, medical care system where you have all the data, you can see these co-occurring conditions. You can ask which ones proceed and which ones lead. But there's not that much data as far as I am aware of addressing these issues. So I think it's something that certainly needs more attention.

And then the health service provision in the end is that once we identify what these co-occurring conditions are, how prevalent they are, how do we do what we were just talking about, provide that information in an integrated system of health care or to again

we rural physicians who can identify these features and try and address them.

So, I guess, the point of having Lisa here, and I am hoping that she will be able to contribute in future workshops, is that she has provided us with the problem in a sense that for whatever reason people with autism are really being challenged by a whole host of medical conditions well beyond the social impairment and repetitive behaviors that characterize the disorder.

And I think it is really a challenge to the field to try and figure out, number one, why is that, but maybe even more importantly to try and convince practicing physicians that these conditions have to be treated regardless of whether the individual has autism or not. And that was part of our conversation already this morning. I think it

is going to re-occur. I hope that we can actually provide - get some advice from you and to provide to others about how we can maybe solve that problem.

I'll stop there. Again, I wish Lisa was here. She can do a much more elegant job of presenting her data, but at least you get a flavor of the work that she has done.

And why don't we continue the discussion of - that we were starting in the last session and just add in some of these conditions as well? Thanks.

DR. DANIELS: Thank you, David.

MS. GASSNER: I did want to - a little bit - go back to prior conversation and then talk in regard to this. In my research that I did before I presented to the IACC a couple of years ago on health care disparities, I used Croen's work and Cassidy's work,

research on non-suicidal self-injurious behavior leading as a gateway to potential for suicide. I used Burke and Stoddart's work on what the barriers are. And there are things like executive function and not making the appointment on time and inability to communicate your needs, an inability to just get passed your phone phobia to make the phone call.

But going back to Kevin's question about risk factors, one of the number one risk factor that the autism community experience is a lack of diagnosis. When you look at the ACE's research by Filetti and you overlap that into our community and you look at a lifelong experience of repeated trauma, when you look at his work, it says it leads to heart disease. It says it leads to chronic health care issues. So why would we think

that the autism community would not be experiencing similar outcomes? This is not a great myth.

And I'm sorry, I don't know how to pronounce your name. Timothy? (inaudible comments). Buie. I totally agree with you. I think that a huge number of autistic individuals present to health care providers not even knowing they're autistic. SO if they just go to any random mental health provider or any random physician or any random person that helps them with their maternal health care and that person is not qualified and they think that autism is something that happens in a silo somewhere else, that person is going to experience repeated medical maltreatment. And what we're hearing from the autistic women who are writing these autobiographical accounts - I'm a social

worker so I look at the soft science and the qualitative work - is they're saying that misdiagnosis was one of their greatest risk factors for long-term mental health issues and exposure to medical malpractice and not in the legal sense, but in the sense of it being ineffective and sometimes damaging treatment.

And so I think I agree with you 100 percent. While there are some things that could clearly be better done with a highly specialized individual, we need to make this accessible.

You know, in my field, I am screaming to the social work community saying if you are working with the homeless population, you're working with autistic people. If you're working in a domestic violence shelter, you're working with autistic people. If

you're working in Veterans Affairs, you're working with autistic people. So the idea that autism happens somewhere in a silo is, is very very destructive to this community.

I think that we can definitely do better if we recognize that these individuals are presenting in every practice, whether it is a mental health field, social work, some kind of medical specialty, and not having intuitively gifted professionals is not acceptable. We have to have more. We have to have people who are qualified from day one. Thank you.

DR. TAYLOR: So I have Christina and then Scott, then Tim, then Beth. And then Antonio.

DR. NICOLAIDIS: Thank you, Dena. Dena actually made some of the comments I was just planning to make so thank you. It was very nice to hear.

There was - when we think about co-occurring conditions, we tend to lump them all together. And I - there was a recent commentary in actually the Journal of Autism by Eric Rubenstein and Laura Bishop-Fitzpatrick, which I found to be really really helpful in making us think about what do we mean when we are saying co-occurring conditions.

And the way they laid it out was thinking about conditions that truly co-occur because of some shared etiology, conditions that really result from autism, which I think is in a way this pathway that Dena is talking about if you think of autism as a social determinant of health and if you think of the various traumas, et cetera, that happen because you're a marginalized population. We already know social determinants of health

predict all of this stuff. That's - that's well known.

Similarly, behaviors that then are hard for you to take care of things because of your autism, which can then lead to these other issues either developing or not being managed well. And then we've got things that are associated with ASD where there is some form of shared risk factor.

It was helpful for me as somebody who focuses all of my work on social determinants of health. I was very keen on thinking of that middle group. But I think when we talk about it, making those distinctions can be helpful because then we're not just trying to find a biologic reason why autism is associated with 50 different things. At the same time, we can separate out that maybe autism is actually biologically linked to a

few of those things. And then maybe there are many other reasons why we develop those things just as people of color and trauma survivors and all the ACEs, et cetera, lead to all of these co-occurring conditions.

DR. ROBERTSON: Just to echo, on - it was mentioned on undiagnosed autistic adults that I think we need more literature and research on there and out there. We don't really know what it looks like on that population group. That is a huge huge huge 800-pound gorilla I think in the room that I've been wondering on that literature base for a while. I do searches every now and then to see if anything comes out. There is really not much there there on folks who are 30s and 40s and older. I know it is hard to find folks after they have left the childhood systems.

It's really really difficult, but I think we need to be more creative on how we are looking at different ways of looking across different systems to see if we can find out what we can be doing for folks who are undiagnosed and then coming into the system and finding out about their autism maybe because of their health care conditions. Maybe they are diagnosed with something else. Or, a lot of autistic adults of course will be able to share stories of just happenstance and finding out about their autism later on in life.

And I do want to completely concur that it sets someone out for a lot of complexity on what that means in terms of barriers on the health and wellness end because you do go for a lot of trauma and stigmatization and - and a lot of major challenges in terms of

being treated as you are growing up as an autistic person. I think that is something that is a lot for folks to consider and cogitate and be able to - to handle without, often lacking support as they are growing up especially for folks who have been missed. So I do hope that we can put that on the radar screen.

That I think, I think if you were to look at folks who were undiagnosed versus folks who have the diagnosis like in terms of look at different age spots and things like that, you are going to find that sometimes some of the health care conditions there is even maybe higher risk for folks when they're not receiving the right supports they can, in terms of being able to get the acknowledgement about what's been - in terms of the lifespan, in terms of going up to that

point. I just want to say that I agree completely with that. Autistic adults' undiagnosed is something that is a major focus that I think we need to incorporate.

DR. TAYLOR: Tim and then Beth.

DR. BUIE: I just wanted to comment on what Dena had said. A paper that Lonnie Zeltzer wrote who is a pain specialist at UCLA, talked about individuals who showed up in the pain clinic who had chronic pain issues who had never been diagnosed with autism were actually being diagnosed by caregivers in that service in part because they had some background in looking for those conditions. And they were able to come to those families and say, you know what, we think part of this pain sensitivity may be related to an underlying condition.

And so, although I want to advocate for the idea that everybody needs to dig in and participate in care, it comes back to what Alison said earlier that there is some advantage to providing specialized training for how we take care of individuals with autism. My wish would be that that be very broad based because what our mission was in our developmental clinic at the Lurie Center was to take what we did as specialist and bring them to the developmental pediatricians. And we would sit with the developmental pediatricians and talk them through. We want you to look for these things. We want to give you some tools as a generalist to be recognizing these things as they are walking in the door to the developmental clinic. And I think that is the

pathway for general pediatrics for residency training programs.

There is a program in Massachusetts where medical students spend a day with a family with autism so that they really get a perspective on what families are going through and what access to health care looks like and these things. These are phenomenal inventions that have really sensitized physicians to these multiple needs. But, I couldn't agree more with you that there needs to be some specialty training to be able to be alert to those special needs for that unrecognized patient so that you can serve them better.

MS. GASSNER: A lot of autistics are coming up through genetics because of Ehlers-Danlos now. There is a huge overlap, a huge overlap, with Ehlers-Danlos and autism and

nobody is tracking it. Nobody is looking at it, but that is how they are being found. They are presenting with pain and then their inability to communicate the pain sometimes results in this primary diagnosis finally being attained.

DR. MALOW: This is Beth Malow from Vanderbilt. I wanted to continue that discussion too. I think it is such a rich discussion. And I think having Dena and Alison - it's like there is going to be something in the middle that is going to be beautiful. I love the idea of the specialty. I think what we need to do though - I think that would really give us a home.

But then I think we are going to have too limited capacities. So then the specialists would then take the lead in informing all the people. I agree with Dena's

comment. In sleep, I see sleep across the lifespan. And I oftentimes will see somebody without a diagnosis of autism. And I'm like, they're on the spectrum. Or they'll tell me, oh yeah, my kid is getting evaluated next month. Or, oh yeah, I was thinking about I might need to get evaluated. It's very interesting. So I think we have to figure out a way to do both.

And it may be we have - just like we have developmental pediatricians, we have some sort of track for those who take care of teens and adults that's focused on developmental issues, neurology, psychiatry, whatever so those folks feel comfortable. And then they could spear head the education of everyone else getting back to Dena's point that with the prevalence of autism being what it is. Everyone is going to see individuals

with autism. So we can't limit it. I don't want to limit it to just those subspecialists because otherwise we won't reach everyone.

DR. TAYLOR: Antonio and then Jeremy.

DR. HARDAN: Okay, I want to go back to Lisa's presentation. And I think it's great that Lisa was able to show us good signals regarding the high rates of comorbidity. And we have to think a little bit what are the next steps.

I think what we need probably to do is to dig a little bit with regard to the specific comorbidities and to look at the pathophysiological mechanisms underlying these increased rates. For example, if we think it's - if we think about gastrointestinal abnormalities, is it related to a biologic/genetic vulnerability or is it related to core features because of the picky

eating that is leading to higher rates of constipation? Because that's going to be key with regard to how we address that. If it is genetic vulnerability then it has to be systematic evaluation and screening for all individuals with autism. Or if it's related to maybe, related to core features, the approach might be a little bit different.

And that's - I am saying that because I think in the next step of research, there should be some funding mechanisms or some specific RFA that will address these specific issues in the future.

DR. AMARAL: Could I ask that we come back to that when Tim gives his presentation because I'd love to hear what people think in terms of our interim answer to that question? What's driving the GI symptoms? We can hold

off until later, but I would love to try and address that.

DR. VEENSTRA-VANDERWEELE: So this is how it goes when people just raise their hands and get in line, but I am going to go in a completely different direction even though I very much agree with that, but to go to a sort of solution.

Hearing this, many of us around this table are already in high need/low number subspecialties. And then within those subspecialties, autism is - so in New York, we actually have a sufficient number of child psychiatrists. But I still cannot get child psychiatrists to see folks with autism.

I think we can look at what some of our specialties have done though, which is - so for child psychiatry, which I know the best, in New York, we have this CAP PC program that

actually makes consultations available during all working hours of the week for pediatricians who need to be able to reach out and connect with a child psychiatrist. It's difficult to reimburse this with insurance. And so states have figured out systems. Massachusetts has a similar system. And it involves both a phone consultation and then if that is not enough then you can have an in-person consultation.

This makes it possible not just for that kid to be served, but the next ten kids to be served as well because now the pediatrician knows how they are going to manage whatever it is that they are dealing with with this consultant.

I've tried to do something like this in my clinical practice. I primarily do consultations now with the idea that when I

send that letter back and sometimes get to talk with whoever has referred somebody to me, that they are then capable of helping the next five, six people that they were previously uncomfortable helping. And we are actually trying to do this now at the center where we are asking physicians to essentially agree in advance that they will take somebody back and care for them after we follow them and try to optimize treatment for three to six months. Because if we can't, we can never see anyone new. Essentially we fill up.

Most of us in our practices fill up and then we need somebody else. And we are never going to have all of those somebody else's unless we teach them one by one. We can't do that just by giving them a lecture. Essentially, we need to be the Tim Buie who

is taking the 30 minutes to explain to a gastroenterology colleague how you do this.

And then somebody gets comfortable enough, as Connor said, that they realize that they just need to be more flexible. They know how to do this if they can give themselves permission and get a little extra knowledge.

So maybe we have to somehow figure out those mechanisms, which are really about the patient in front a person, not about as much as it is nice to catch someone in medical school, but not necessarily about the knowledge in advance.

DR. TAYLOR: Micah, Clarissa, and then Geri.

DR. MAZUREK: My comment is actually going to piggyback on Antonio's and reflect back on some of Lisa's data. I think it's

important for us to recognize that the importance of understanding co-occurring conditions as we think about etiology of autism and subtypes because what we are learning is that a lot of these conditions are interrelated and they cluster together across the population. So I think it's important for us as we move forward in thinking about autism as a whole how co-occurring conditions can inform our understanding of autism and developmental of more targeted treatments because I think those clusters reflect underlying etiologies that may be similar for subgroups of the population.

DR. KRIPKE: I have three comments. One is that communication is the foundation of patient care. And we have people many of whom have communication disorders of various sorts

or difficulty with getting the support they need to communicate. And that if we want to improve health care, we need to improve access to communication and people skills at listening; and that - otherwise, illness is either not recognized at all or recognized late and isn't treated. Communication is key to addressing the social determinants of health that we have been talking about.

In terms of etiologies and pathophysiology, the newer research that is coming out that is looking at autism from a neurological perspective as a sensory movement issue I think is key to a lot of these issues and that we should take a closer look at that. We can talk more about that when we get into the specifics. But I think if we are going to find pathophysiological roots for some of these problems, then that

research is where we are going to go rather than looking at it as a social and behavioral - primarily a social and behavioral condition.

And then my third comment is that family medicine is the largest primary care specialty. We don't abandon our patients when they hit a certain age. We are widely distributed throughout the community and that definitely need to be activated.

And when we talk about specialty care, this has come up a lot in terms of whether we should have a new specialty or not. And I just want to take it back a step. What we really are talking about is not necessarily needing a new specialty. We need funding and expertise and content expertise. And a new specialty might be a mechanism for that, but there are other ways to do that as well.

DR. DAWSON: So I wanted to follow - were you first? Do you want to go first?

MS. CRANE: Yes, I just want to get in line at some point. Okay, I want to also add an angle that I think we need to think about, which is that a lot of the time when an autistic person comes to a doctor's office, especially people who are not specialists, but even including specialists, sometimes disabilities that interfere with our access get problematized and prioritized for treatment instead of accommodated. If we have a phone phobia like Dena pointed out, maybe it would be a worthwhile long-term goal for us to get better at using the phone or maybe we have decided that it is just not going to happen and we're 40 years old and we still cannot use the phone and we are just not

going to do it, or we're not going to spend our energy that way.

But we shouldn't have to learn how to use the phone in order to get care for our diabetes or our Ehlers-Danlos or a heart condition or whatever we actually need care for. It shouldn't be something that jumps the line over more urgent medical care.

And I think it is especially common in mental health contexts where if we are seeking care for anxiety or depression, everything then gets treated as something to treat, including disabilities that we've been dealing with for a long time and that would not bother us very much if they were accommodated. I think doctor's offices need to recognize that they should be just - if someone cannot use the phone, come up with a

way for people to communicate with your office that doesn't involve the phone.

And I also wanted to back up what others have said about ACEs. I think a lot of people will wonder why is autism associated with depression and anxiety. And I think you are going to see a lot of evidence that depression and anxiety is secondary to the bullying and negative messaging that autistic people have been hearing from childhood about themselves and that is going to be a big part of the cost.

DR. TAYLOR: Geri.

DR. DAWSON: I just want to follow up on this question about health care systems and how we deliver health care to individuals on the spectrum. And I do think the idea of a specialty is perhaps a good idea. We have to be really careful because there is no way

that those folks are ever going to be a medical home for people with autism. There are just literally just too many people.

And I do like, Jeremy, the model that you are talking about, which is a technical assistance model. That is what I was going to bring up too, where the specialists' role is to provide technical assistance to the primary care physicians. Whether it's the family practice doctor or the general pediatrician or the internist or the dentist, right? These models are working really really well.

Massachusetts is one of the first models, but then actually in North Carolina, we have been doing this. It started out where our psychiatrists were contracted really to do this technical assistance for mental health conditions. But we then got a grant

from North Carolina to do it for intellectual disabilities and autism. And it is a wonderful, I think, model to think about being able to provide assistance to a whole lot of doctors throughout the state that just need to ask a question. Should I make a referral? I'm not sure what to do. What are the tests should I do in this case?

And I just think that, I guess, in the end what I would like to see is built into our strategic plan is some research on these different health care models. Whether it is integrated care, which is also another solution, or this technical assistance model and to get some evidence behind this because I think ultimately it does end up usually being government support for this kind of a program.

DR. TAYLOR: We have four people on deck before the break. So, maybe we will cut it off there. We've got Matthew, Dan, Connor, and then Donna. Five people before break. And Greg. And then we will take our break. Matthew is first.

DR. SIEGEL: Thank you. So returning to Dr. Parr's presentation in implementation science, I think we cannot underplay the role that fear and behavioral challenges play for primary care, physicians or mental health providers in seeing people with autism and particularly perhaps those more severely affected by autism. And the reality is that even those of us who run clinics where we are used to the population and like to think that we have all of the communication supports and other things that can make that visit go more easily, we still need a behavioral support

person in the office to get through some of those appointments and have it be successful.

And so, the idea, I think our payment systems for medical care are built on the idea that a perfectly compliant person, young person, older person, is going to come in and submit to the exam and get through the visit is how it was structured and that is not always realistic obviously with our population.

I think we could ask for research to focus on payment structures and systems to - how can they account for in a medical office visit be the complexity, the time, or perhaps most importantly the behavioral support necessary to have a successful medical visit.

And so, as an example, if a nurse comes in and gives a vaccination, there is a payment mechanism for that. But if a nurse

comes in or a medical assistant and provides behavioral support to get through a visit, I'm not aware that there is a payment mechanism for that. And as was commented earlier, insurance and finance drive a great deal of this. I think that is an area we might attend to.

DR. COURY: I want to come back to some of Geri's and Jeremy's comments regarding providing more support to primary care providers. And you've heard Beth Malow earlier this morning mention Project ECHO, which we have been doing. We have enrolled over 150 primary care providers across ten sites where we are providing them teleconsultation and telementoring and managing these complex problems in individuals with autism. We are starting one with transition next. And I think adapting

this model to adult providers would be another way of improving the care to this population.

DR. TAYLOR: Connor.

DR. KERNS: I just wanted to add to comments by Samantha and Dena and Christina and also some data that I do think this issue of adverse childhood experiences is extremely important in this population. There is data from the National Survey of Children's Health that kids on the spectrum experience more ACEs and that is just Anda and Felitti ACEs. It is not actually asking about all these additional types of chronic stress or particular types of traumatic events that people on the spectrum may also encounter in which we could be contributing to these health outcomes. NICHD has actually funded work to try and figure out how to ask about

those different types of trauma. So I think we are going in the right direction.

But I just want to underscore this point that when we are talking about health, we need to be talking about adversity. We need to think about how to consider these issues. And I am not trying to hijack the conversation to make it be about mental health, but of course health is also mental health. The mind and the body are connected. So I think that is why we keep circling around those issues in our conversation.

DR. TAYLOR: Donna and then Greg.

DR. MURRAY: I'll keep it brief because I want to touch on Dan, I think Jeremy, and Geri's comments. I really think that when we think about scalability models, I think it's really important as Dr. Buie was saying is to get this information out. And as Dan was

saying, we do know that there are models that are supported and are effective in providing this mentoring, but the reimbursement is a real issue. I think that we know that communication is incredibly important. When we survey a lot of primary care physicians, it is not a lack of desire. It's a lack of time with RVU requirements and we're not getting appropriate reimbursement for providing the support on either end, the expert team or the receiving end.

I think that we can talk about these models, but unless we really look at the issues around reimbursement, we're not going to be successful because we cannot continue to depend on grant. We have to look at sustainability in our models.

DR. BARNES: Okay, I just wanted to add one more thing based upon our experience in

our state. Besides including research on these different health care models and the reimbursement, I would also suggest that we might also want to include training of professionals that actually work in the medical home. Because it sounds like that we could really help our adults a lot by training our nurses, training our MAs and those people who work in the adult settings to be able to accommodate those specific needs, make suggestions about how to get around the phone issue, all those sorts of practical things that nurses need to.

We've done this with our autism training center in preparing new regional autism center sites. And it's worked very well in the pediatric population for nurses and staff that were relatively unfamiliar with autistic

individuals. So I can't imagine that it would not also work well in the adult population.

DR. DANIELS: Alright. So, we are ready to take a short break. We are going to be coming back for public comment. I would like us to be back in the room at 10:35. And we will start public comment then.

(Whereupon, the Working Group briefly recessed at 10:25 a.m. and reconvened at 10:40 a.m.)

DR. DANIELS: Alright. I'm sorry. It looks like in the packets maybe we did not include the oral public comments statements there, but we did send them out by email and they are on the web as well. So I'm bringing this to you from the web.

Our first public commenter today is Shari Chase. If each of the oral public commenters would go to the podium so you can

use the microphone that would be great. Thank you.

And just to let you know, we are going to take oral public comments first and then Oni Celestin, Dr. Oni Celestin from my office is going to read a summary of the written comments. And you have the full text of the written comments in your packets.

And just on behalf of the committee and the working group, both the committee and the working group were deeply interested in hearing from the community about your concerns, your issues, and your ideas regarding the topics of today's workshop. And so we really look forward to hearing these public comments.

So, Shari Chase, are you here? Okay, it sounds like she might not be here.

Mark Vieth? Please give your name and affiliation.

MR. MARK VIETH: Absolutely. I'm Mark Vieth. I am a consultant for the Phelan-McDermid Syndrome Foundation. It is always great to be the one that gets to go first. So I will try to keep my remarks brief.

I am here today to present a testimony on behalf of the foundation and specifically Dr. William Bennett, who is an assistant professor of pediatrics and an adjunct professor of urology at Indiana University School of Medicine. And what's kind of unique about Dr. Bennett is not only is he a researcher in this area, but he is also the father of a 2-year-old girl with PMS.

What I really want to focus on today - I will read excerpts from his letter. I will not read the entire thing. But our community

has a growing concern about gastrointestinal issues with Phelan-McDermid kids. It was really encouraging to hear a lot of discussion already this morning about gastrointestinal issues or functional gastrointestinal disorders, FGIDs.

Let me just read a couple of excerpts from his letter and I appreciate your attention to this. We are parents of children and adults with a rare chromosomal deletion called Phelan-McDermid Syndrome, which results in a variety of developmental disabilities including a severe form of autism. Many individuals with PMS are nonverbal or have profound communication deficits and 74 percent meet criteria for autistic spectrum disorder. And 85 percent have some autistic features.

As such, most of our children suffer from an array of challenging FGIDs, which are highly prevalent across the autistic spectrum.

Additionally, since autism commonly results in difficulties with sensory processing, many individuals are unable to interpret neural input from their gastrointestinal tract and communicate these sensations to their caregivers. This sensory hypo-reactivity has been explored specifically in PMS and is a common concern for parents across multiple domains, but especially as it relates to stooling and the reporting of symptoms such as abdominal pain.

As a father of a 2-year-old girl with PMS, I, Dr. Bennett can attest first hand to the enormous toll that gastrointestinal symptoms take on patients and their families,

especially in those with communication deficits such as autism.

As a pediatric gastroenterologist caring for a large number of children with autism, as well as multiple children with PMS, I have heard many parents echo these concerns. In fact, at our most recent Phelan-McDermid Syndrome Foundation conference, we had so many questions during the gastroenterology portion that we had to schedule an ad hoc question and answer session that evening simply to accommodate everyone. This speaks to the enormous burden experienced by PMS patients and their families in regards to FGIDs.

Our own data suggests that gastrointestinal symptoms are extremely common in PMS. Seventy-three percent report problems with toilet training, 41 percent

constipation or diarrhea, 28 percent feeding problems, and 24 percent recurrent abdominal pain. This echoes the overall high prevalence of gastrointestinal complaints in autism.

Forty-five percent of children with autism have diarrhea or excessively frequent stools, three or more per day, compared to 15 percent of neurotypical siblings. And 23 percent have high stool variability compared to 0.1 percent of neurotypical siblings.

The gastroenterology community has recognized the need for an expanded body of research on FGIDs and autism; yet, few funding opportunities exist to explore this complex area. While considerable attention has been paid to the overlap between the human stool microbiome and autism and we applaud these efforts, a broader research approach addressing the many complex

interactions between autism and the enteric nervous system are direly needed. Of the 1262 current open RFAs at NIH, only 54 of these have autism mentioned in the program announcement and zero are directed at gastrointestinal disorders. Furthermore, none of these funding opportunities for autism are supported by NIDDK.

Now is the time to act as we have the capable to marry the high volume of clinical data, progress in neuroscience, and vast genomic and microbiome data to create real clinical solutions for the many individuals and families affected by FGIDs in autism. We thank you for your consideration of this important topic area that has been woefully understudied and underfunded.

Investment in research on gastrointestinal disorders in autistic

individuals has the potential to vastly improve their quality of life for patients and families.

And I will just close by saying that not only the autism the community and the Phelan-McDermid community is interested in this. We are reaching out to many rare and neurological disorders where they are hearing similar concerns in their community. We are beginning to form an ad hoc coalition to address these issues, not only with NIH, but also with Congress as well. And I really thank you for hearing Dr. Bennett's statement and I appreciate your attention to these concerns. Thank you.

DR. DANIELS: Thank you, Mr. Vieth. Next is Rick Walba. Is Rick Walba here? Okay, we'll move on to the next person. Annie Acosta?

MS. ANNIE ACOSTA: Hi. I'm Annie Acosta. I am with The Arc of the United States, but today I am here as one of the co-chairs of the Consortium for Citizens with Disabilities Taskforce on Developmental Disabilities, Autism, and Family Support.

So thank you very much for the opportunity to provide comments today. I am here to share some of our top priorities. And due to time limitations, we are only going to four issues. But the first is mental health screening, identification and intervention. As this group well knows, children and adults with ASD have much higher rates of anxiety and depression, which can interfere with their physical health and adherence to prescribed treatments.

A 2015 study published in the British Journal of Psychiatry found that people with

autism and no intellectual disability are nine times more likely than the general population to die young due to suicide, making it the leading cause of early death for that population. The rate of suicide among people with autism and intellectual disability is also considerable.

Despite increasing recognition of the interplay of mental and physical health, practical application in health care settings is often lacking.

Health care professionals need appropriate training in identifying and managing mental health problems in this population. Lack of training results in difficulty for practitioners and patients alike. For instance, providers who are unable to help calm a person with ASD are more

likely to rely on over-sedation for relatively routine testing such as EEGs.

We also encourage the committee to prioritize training for health care professionals and research efforts that examine health outcomes of people with ASD that include social determinants of health such as employment, education, and social connections.

Two, are reasonable accommodations. Going to the doctor can sometimes be a stressful experience for people with ASD. And elevated stress levels may trigger challenging behaviors. There are fortunately a few practices that can help mitigate such events, such as giving patients with ASD the first or last appointment of the day to avoid long wait periods in crowded rooms.

However, the most needed accommodation is additional time for appointments. Health care providers should anticipate the need for flexibility and scheduling.

We encourage the committee to support research in efforts to improve public and private insurance reimbursement policies that allow for extended appointment times.

There is transition from pediatric to adult health care. Autism is more than a childhood condition. It is a life, it is a lifelong condition that requires appropriate supports and treatments, which changes people move through major life phases. This includes moving from the pediatric to adult health care system. This transition is critical to ensuring appropriate treatment for adults.

Youth and young adults with ASD in their families need assistance in transition

preparation, transfer of care and integration into adult-centered systems of care that are less coordinated than pediatric systems.

We encourage the IACC to prioritize efforts under strategic plan question five, where can I turn for services, to implement the six-core elements of health care transition 2.0 developed by the Center for Health Care Transition Improvement with support from the Health Resources and Services Administration.

Four, decision making options for adults with ASD. There are many incorrect assumptions about the needs of adults with ASD for decision-making support. For those who need support, guardianship is often treated as a default option for adults when a less restrictive option would suffice. Parents are often warned that absent

guardianship, they will be denied access to their adult children's health information due to the Health Information Portability and Accountability Act; otherwise HIPAA. However, HIPAA allows the disclosure of protected information when a patient consents. However, parents will seek guardianship in order to go to appointments, schedule appointments, or access medical information.

There is a continuum of options that starts with informal support. Other options include supported decision making, power of attorney and limited guardianship. We encourage the committee to promote health care practice guidelines that provide accurate information about the range of options for decision making authority in health care settings.

Thank you very much for the opportunity to comment. This is on behalf of myself with The Arc and the National Respite Coalition and the National Association of Councils on Developmental Disabilities who are among the co-chairs. Thank you.

DR. DANIELS: Thank you, Ms. Acosta. Next is Dr. Xue-Jun Kong.

DR. XUE-JUN KONG: Good morning. So my name is Xue-Jun Kong. So usually I'm June, like the month. It is really my honor to be here. I am the director for SYNAPSE, an autism research program at Mass General Hospital of Harvard Medical School.

MS. GASSNER: I'm sorry, can you back from the mic a little bit? It's very painful.

DR. KONG: I am a primary care physician. And also, I am a parent of a 21-year-old son who has autism. And today, I am going to give

a few comments. One is just from the parent perspective. I will share a little bit about my son's story and also as a primary care physician as a research investigator, talk about the system. So glad today the discussion is about primary care service and also the model I have been promoting for years.

So first of all, my son was diagnosed at Boston Children's Hospital at age four with severe autism. So he certainly received intensive service including behavior, speech, and everything. And but his behavior could not get improve. He actually could not survive in the public school. He moved to an autism center program. And certainly, I am so glad today that lots of (inaudible comment) there were medical comorbidities. My son has lots of GI problems, also have autoimmune

problems, have endocrine problems, a lot. Over the years, we are addressing these problems with acute progress from being a very severely autistic case and also being outside placed and being life centers by many providers. So we actually, myself, actually, are part of the team. We did lots of medical interventions.

Now, he is a very proud senior, college student at UMass. And this is a long journey. This autism became my lifetime pursuit and passion. My husband quit his job. We have been working as a team.

Along with all these years of journey and by talking to other parents and being a provider myself too, I deeply understand the system. I have lots of challenges. Not only just autism itself. It is so complex medical condition. It is called medical syndrome

instead of disease with lots of psychological and neurological and medical comorbidities. And so it's very hard. Not too many trained providers understand the systematic approach. And also the provider being so much in shortage. As parents, we actually know. It's a long waiting list. Also, you get a different opinion from different providers. It's very hard to find a provider who gives you the right message. It has been a long struggle for parents not only physically, emotionally, and financially, to suffer from this. I want to pass this message.

Also being a primary care physician and certainly I think the systematic approach is the way to go. And because nowadays, the psychiatrists, neurologists, and the primary care role is really little. And I think that that is the thing - I am so glad we discussed

this today. And I think the primary care being center to screen the disease, to have a diagnosis, to address the medical issue, to better coordinate specialists, and also coordinate with school, coordinate with the community service and to deliver best care and improve the outcome of this population. I think this is so critical. I want to posit that comment.

Over the years, I teach Harvard Medical School. We teach lectures about this model. We call it the SYNAPSE. Also, I named my lab SYNAPSE too, called a "Systematic Network of Autism Care Services". I think this is very important to implant. With the right team, the team is a primary care team plus we see all the behavior, all the committee people, with the therapists, together have these function team. And also closely working

together with the specialists with the right protocol for the early screening, for the adulthood transition program. For this, we have been talking to my colleague, actually Dr. Spence here, for years regarding the transition program. Also, with the - particularly medical comorbidity issues, the medical treatment. This is so important.

With this system, certainly the primary care should play more role and talking about subspecialty, I think it is more than the primary care training and the awareness, have an autism-minded primary care physician. They can know how to triage and what they can do, what they can work closely with specialists address the medical use because addressing medical use make a huge difference on this group of people.

And certainly, by implementing that, they still have a lot of challenges. We need support and medical funding and policymaker insurance coverage and also the medical team and the protocol implementation.

Thank you so much for your attention. I am so glad to be here. Thank you.

DR. DANIELS: Thank you, Dr. Kong. Is Shari Chase or Rick Walba here? Then we are going to move to the written public comments to hear a summary from Dr. Oni Celestin from my office, the Office of Autism Research Coordination. After that, we will have a few minutes for the working group and committee to discuss the comments.

DR. ONI CELESTIN: Good morning. The IACC Health Outcomes Working Group has received written public comments from 17 commenters. For the purposes of this presentation, we

have organized these comments into four broad topics. The Working Group has been provided the comments in full, but they will be briefly summarized here.

The first topic is medical practitioner training and patient-provider interactions. There were eight comments received on this topic. Ms. Lauren Agoratus believes that all medical practitioners who work with patients with developmental disabilities need to be trained to do so. She is also concerned that there are not enough practitioners trained to treat individuals with both developmental disabilities and other mental health conditions.

Ms. Jacqueline Murphy is concerned about the lack of psychologists with expertise in ASD for both children and adults.

Ms. Maureen Callahan wrote about the need for an increased awareness of autism symptoms in hospitals, especially in emergency rooms and in other situations where autistic behaviors may make medical procedures more difficult.

Ms. Shannon Des Roches Rosa believes that it is imperative that autistic individuals receive proper and sufficient health care. She recommends that autism-informed health care policy be facilitated by participatory research and be better integrated into medical practitioner training.

She expressed the need for more practitioners qualified to treat the range of symptoms of ASD and about the need for all medical professionals to treat autistic people with respect.

She also wrote about the need for increased practitioner awareness of atypical reactions to medications and unpredictable side effects in autistic people.

Ms. Marian Dar expressed concern that many practitioners do not consider the insight of the family members of their autistic patients when providing care.

Dr. Linda Papadimitriou-Varsou believes that increased mental health services are needed to reduce the rate of suicide in autistic individuals. She also believes that medical practitioners need more training on non-pharmacological methods for treating people with ASD. She encourages a more holistic approach to treatment.

Dr. Colleen Kraft on behalf of the American Academy of Pediatrics wrote to provide examples of AAP practitioner training

programs. She encouraged the Working Group to engage primary care providers in their discussions. She also emphasized the importance of a medical home as a critical element of coordinated and high-quality care for autistic individuals.

Ms. Anna Seahorn wrote of her experiences with autistic patients as a nurse in a rural hospital. She expressed concern that these patients are often misdiagnosed due to a lack of practitioner awareness of some autistic behaviors. She feels that education is critical to better serve autistic patients.

The second topic is co-occurring physical conditions. There were six comments received on this topic.

Dr. Eileen Nicole Simon encouraged the IACC to investigate several factors that

could be contributing to autism symptoms such as autonomic functions and metabolic syndrome. She expressed concern that long-term use of antipsychotic or anti-anxiety medications could lead to metabolic syndrome in autistic individuals. She also urged the IACC to address language difficulties that individuals with autism often face.

Ms. Marie Ciriello would like to learn more about the links between ASD and congenital heart defects including differences in treatment plans.

Ms. Angie Hughlett believes that the gastrointestinal health issues of adults with autism deserve more attention.

Mr. Ben Furlow expressed general concern about health issues affecting autistic people.

Ms. Denise Lombardi is interested in the intersection of autism, intellectual disability and epilepsy. She cites several research articles exploring the links among them. She believes that there should be a shift in research focus in order to better understand and reduce premature mortality among individuals with these disabilities.

Ms. Marian Dar is concerned that subtle differences in the immune system of infants receiving inoculations as well as prolonged antibiotic treatments may contribute to the gastrointestinal issues in autistic individuals. She also proposed that Vitamin D deficiencies may be contributing to autism symptoms.

The third topic was service needs, resources, and policy implications. There were five comments received on this topic.

Dr. Eileen Nicole Simon requests that the IACC set standards for caregivers who work in community group homes. She also recommends mandatory family involvement in creating treatment plans for health, education, and ongoing development of community group home residents. She is concerned that trauma-informed care is too widespread.

Ms. Cynthia Reed encourages advocacy for improved statewide data collection on people with ASD and co-occurring conditions in order for states to better plan for long-term health care and housing needs.

She also believes that improved data will help identify the proper qualifications for group home workers and thereby increase the quality of care.

She also suggests that it may be more efficient for group home residents to receive routine medical care from a mobile unit rather than having residents leave for a health care facility.

Ms. Shannon Des Roches Rosa advocates for investment in a health passport system similar to one developed in the United Kingdom that would help improve medical experiences for autistic individuals.

She would also like to see widespread adoption of toolkits designed to improve medical interactions for individuals with disabilities.

Additionally, she expressed concern about Medicaid funds being available for conferences that present information on treatments without a strong scientific evidence base.

Finally, she wrote about the need to address disparities in autism care due to gender, geography, socioeconomic status, or race.

Ms. Elizabeth Moffit expressed concern about the lack of Medicaid covered speech therapy services and long waitlists in her county.

Dr. Linda Papadimitriou-Varsou recommends increased resources and counseling for parents of children with ASD. She is also concerned about the effect of poverty on individuals with ASD and their families. She encourages federal agencies to implement policies that will reduce poverty.

The final topic was co-occurring mental health conditions. There were three comments received on this topic.

Ms. Kim-Loi Mergenthaler is interested in research on autism and co-occurring mental health conditions including anxiety, depression, PTSD, and the increased suicide risk in autistic adults.

Ms. Gilda Sanchez is interested in more research on deep brain stimulation in autistic individuals with co-occurring obsessive-compulsive disorder.

Ms. Jaqueline Murphy is concerned that untreated depression and anxiety lead to a higher rate of hospitalization and a failure to thrive or live independently in autistic individuals.

This concludes the summary of the written comments. Thank you again to everyone who submitted comments.

DR. DANIELS: Thank you, Dr. Celestin. We have time now for discussion among the Working Group members and committee.

MS. GASSNER: I just wanted to thank Annie Acosta for discussing the rather heavy-handed use of guardianship in situations where supported decision making could be successful.

The flip of that though, I apologize for trying to get through today, is that these individuals who are not externally expressing in their disability are often sent into government systems like Social Security and food stamps without any support. I work in my private practice facilitating social security reporting with adults who have autism and transition age teens and youth.

I can tell you that I have 100 percent success rate at getting people through after

the first appeal. It isn't because I am a wizard. It is because I understand how social security makes their determinations. I know what the categories are that they consider. And I know how to teach people how to report their symptomology within the framework that Social Security uses.

Providing systems navigation support to families and individuals affected by autism is crucial and it is again another non-billable service. First of all, these systems should be frankly more accessible. It shouldn't be a game of do you know how to figure this out. It should not be a money-making opportunity for attorneys, not that they are not worth their money at times, but this system is supposed to be accessible to people who are inherently struggling to communicate their needs. By using probative

interview technique, we are able to get these people to not just turn in the report, but a seven-page report, a document of their reporting of their challenges. This is a teachable skill set that we can provide to providers anywhere to teach them how to do this.

But the process to do this with an individual with autism takes me between 7 to 14 hours just to get the reporting. And then I have to create the document. And then I have to go to their provider and say you know that narrative you wrote. It's totally useless in reporting to Social Security. Can you please give us the narrative information within their categories? They do not have any way to do that. Psychologists that I work with, psychiatrists, medical providers. They do not know how to change how they report to

meet Social Security standards. We can fix this. That is something IACC could help facilitate. Thank you.

DR. MALOW: Beth Malow. I really, those comments that Dena just made are really relevant I think to what we were talking about earlier. From a provider perspective, I will just wear my provider hat. One of the reasons that I get frustrated when I see this population is because I cannot help them in ways that I feel like I need to. And I think that may be a message for this idea of trying to build capacity because it's so frustrating when you do not have the time and you also do not have the resources. Finding ways to help providers navigate that, like even having the insurance companies, the MCOs, hook them up with resource navigators who can then - they can just say to their adult with autism or

the family member, hey, here is a number you can call. Here is somebody who will help you get what you need would be huge.

I think that in addition to fear and not understanding needs and lack of training, I think this idea that you are going to open up Pandora's Box and then you are going to as a provider have to figure out how to help someone navigate when you do not know how and your insurance claims are denied on a daily basis is one of the pieces of the puzzle to I think increase in capacity.

DR. ROBERTSON: I just wanted to say that the comment that was made in the - I think it was the written comments about poverty, so that economic end really resonated a lot with me, especially since folks who are more in the challenges on social economic end already are going to struggle more in health then. We

already know that for the general population that folks are going to - outcomes do not look as strong there. I think that is something to make sure that we do not leave out from the conversation. Sometimes our approaches tend to be more focusing on folks who are already in the middle class at times. Those are folks who could have better access to the Internet and information and stuff like that.

I just want to make sure that that stays on our radar screen. It was something, the poverty economics, self-sufficiency kind of end. Not only relates back to employment, but it was something when I was on the Hill working for Senator Harkin. We worked on a report at the time on barriers that all folks with disabilities kind of face as far as the economic end. This is something that is also

sparse on the literature too is that autistic adults - there is not a lot on the economic end.

We don't - even a lot of studies like on the employment are not looking at the income end of things. We do not necessarily know. We know it is pretty significant. We do not know what the economic complexity looks like and the challenges and barriers for autistic adults and family members and supports and stuff as folks age through life. I think we need to see more of that because it is going to be really impactful as far as what we are looking at on the health care end. And then also folks who are in poverty may not - who knows what insurance and things like that looks like for folks because they may not have insurance or they may not have strong plans, access to health care services. There

is a lot of intersection there on the economic end of things. I hope that stays on our radar screen as we keep on the discussion. Thanks.

DR. HARDAN: It was great to hear the public comments. I want to make two quick comments and two things that I actually liked. One is something that I think definitely the focus of this committee here is regarding how we can sensitize medical practitioners to better care - provide better care for individuals with autism and intellectual disabilities. I think there should probably be some strong recommendations regarding what is the best way to do that.

I am thinking about the books that we look at. I am not sure if in primary care books, there is a chapter on how to assess

the medical needs of individuals with autism and intellectual disabilities. I am not sure if in primary care they have just a lecture, just a general lecture, on how to assess an individual with autism or with intellectual disabilities. So that is one part in terms of, I think something that we can make a big difference in terms of making recommendations and see what is the best strategy to push this message.

The other one that I liked is the medical mobile unit. If you can imagine that in the DC area or in the New York area or in the San Francisco Bay area you have teams of expert like a primary care physician who can assess who has the patience and the support financially and team watch to be able to go from one area to another and do comprehensive medical evaluation. That's a neat idea.

DR. AMARAL: Can I just ask Antonio a question? In terms of your first comment on trying to instruct primary care providers, something that we have talked about is the possibility of creating some kind of videos of webinar kinds of things. Do you think that actually would work? Do you think people would make access of those?

DR. HARDAN: I was thinking about that. I was thinking about videos would be a good idea. I think we want to empower parents and encourage parents to encourage primary care providers to look at these videos. Because as a primary care provider when you have 10 to 15 minutes to see a patient, it is unlikely you are going to go watch a video at home regarding how to assess individuals with autism.

I am thinking even before that in terms of traditionally part of their training to include something like that. If we look a little bit at general psychiatry training, 20, 25 years ago when I was trained, we had very limited number of lectures on autism and intellectual disability. Fast forward to now. It is part of the main curriculum to get lectures on autism and intellectual disability.

I think it will be nice if we could have something like that in general practitioners - part of their curriculum to do something like that.

DR. SCHOR: I have to say in listening to the public comments, one of the things that struck me in a very positive way is the concordance between what the public identifies as the problems and issues they

would like us to address and the problems and issues that are highlighted on the program and in our discussion today. I dare say that that isn't always the case at the IACC. The danger that we have - I can't tell you how many times I have said to families that I am going to talk to you about the major issues in whatever disorder their child has. They look at me kind of blankly and say but that is not the real practical problem for us at home. I think the value of the public comments is that it forces us and allows us to think about not just what we as professionals think of as important, but what the public thinks of as important.

Here, I was just struck that the same issues were identified in both cases. So, I guess I am feeling a little more optimistic than usual that we will address something

that is of critical and practical importance for the public.

I want to make just a very brief comment about the notion of introducing primary care curricula, introducing something on autism or mental health, behavioral health. I think that there are from the standpoint of putting curricular elements in. There is already a lot out there. It may not be disseminated as well as we would like. The American Association of Family Practice has a curriculum. Many of the pediatric developmental and behavioral pediatric elements include transition to adulthood and so forth.

But I honestly do not think there is any substitute for having an actual hands-on rotation where you are actually in there in sight to working with patients and families.

I applaud the efforts to have lectures and didactic elements. They are necessary as an introduction. They're certainly better than nothing. But there is no substitute for taking a medical student or a resident and saying these are your patients for this month. I just think we need to recommend that.

DR. TAYLOR: We have Tim, then Sarah, and then Jeremy.

DR. BUIE: I was fortunate enough to be supported by Autism Speaks to do a series of videos to talk about a variety of gastrointestinal issues in autism. They were really geared. They were short, seven-minute sessions, talking about particular topics in autism. They were intended for families to see them so that they could go to their

primary care providers and discuss those things.

I think there are a lot of resources out there that provide some of that information. Marvin Natowicz at Cleveland Clinic did a beautiful series of videos that is part of the CME that is still available on the Cleveland Clinic CME that was sponsored by one of the autism organizations. I am sorry that I am blanking on it. But that's a series that you can get continuing medical education credits to go and see about gastrointestinal issues, seizures, metabolic disturbances in autism, et cetera. They are out there.

I think there isn't a repository that makes that information available. Where do I find these pieces of information? That would be tremendously useful.

I think the series that was done by the NewsHour several years ago that involved a number of specialists talking about autism is rich for new families to experience the overall discussion about autism. There's a lot of information out there. It's providing some tool to post that and make it known where people can seek some of those resources.

I want to say one other thing. I wanted to thank Dr. Bennett for the discussion about gastrointestinal issues in Phelan-McDermid. I have to say that I am fortunate to follow a number of kids with that genetic syndrome. It is a little easier when we talk about genetic syndromes to look at those medical aspects as being part of the syndrome. As with Down's syndrome, we know a number of kids have a

variety of known GI conditions that we expect to look for.

Now that I have seen a number of kids with Phelan-McDermid, I know that those kids have severe very refractory gastroesophageal reflux and constipation. I have the vision that their underlying phenomenon is a generalized motor disorder that is accounting for that. I think it is part of their genetic syndrome.

I think as we start to peel out some of these genetic conditions and we recognize that they used to be part of the rubric of autism, Rett syndrome, et cetera, we now can recognize differences in those select communities and think about them really differently. I don't think we are able to do that for the general autism community right now. We are still seeing mostly common

conditions and not able to sort of characterize them beyond saying you've got constipation or you've got reflux.

But I think part of the reason that there is not an enormous amount of funding is that a lot of the care providers haven't been able to figure out how to seek that funding. They are still providing clinical care for most of those people. It is coming that that might be something that we could come together with. There is now a known list of kids with Phelan-McDermid that we might be able to pool the kids together and do a study. Many of them are not kids. They are young adults that are diagnosed and have been carried as to autism for many years before they get their genetic diagnosis.

DR. SPENCE: I think the ideas that have come up so far have given some action items,

pulling together things, thinking about ways to train. I think the only thing that I would add to that is that from a systemic point, we could actually develop competencies, right, for training. That is something that - it is not a curricular issue. It is actually a competency issue. It would be a requirement that in order to get your credentials at your hospital, you have a competency in working with individuals with neurodevelopmental disabilities because they're in your hospital. This is something that I think this committee could actually do.

DR. PARR: Thanks. Nina has said a lot of what I wanted to say which is that real similarity between the public comments and what was discussed here. But I also wanted to bring up the perspective of the UK. I think if you had asked that question to the UK

population, we have actually - you would have gotten the same sort of set of comments as well. That is sort of suggests that is not a US-specific or US health care-specific problem. This is a worldwide problem probably.

In that context, I think the lessons that are being learned in research in one health care context are very likely to be able to inform others. Let's not repeat research in separate settings. It is not a good use of resources, which are built on the results and effect change from that.

DR. MALOW: I just wanted to piggyback onto the comments about the video training and how we can get people to do it. The other thing we have done - we had a video series in Tennessee. We partnered with Medicaid TennCare. It was interesting. We had all

these primary care providers watch our videos. It is on reducing psychotropic medication use in individuals with IDD. I was an actor in it. It was really kind of fun. But I don't think people watched it because of me. They watched it because they got this gold card from our Tennessee Medicaid. Basically, they did not have to fill out as much paperwork if they wanted to prescribe a psychotropic drug. I am serious.

It was really interesting because as a result of that, all these people watched the video. Now, I am not sure what they got out of the video. I am not entirely certain that they did not watch the video while they were cooking dinner, but they did watch the video. They did get privileges from our Tennessee Medicaid to not have to do all this paperwork. It is an interesting idea.

We talked about insurance earlier and thinking of ways that maybe we can actually get them to respond to the video, make sure they are learning from the video, but then have some sort of carrot with insurance.

DR. TAYLOR: Connor and then Clarissa.

DR. KERNS: Just to add to that, I think we do need to focus on requirements and training, if we can make that push just because I know there are a million videos I should watch and I really desperately want to watch to enhance my own training, but the truth is you answer some emails. You go to some meetings. You see some patients and then the day is gone, even those of us with the best intentions.

But I also know like clinical psychology programs care a lot about their site reviews and their accreditation. I am sure it is very

similar for medical schools. There are also continuing education credits and things like that. If we really want people to do this, I think there needs to be some kind of requirement because even those with the best intentions are just probably not going to get to those videos otherwise.

DR. KRIPKE: I have a lot to say about training medical providers, but I am going to save it for a different time. But I wanted to echo the comments about how congruent we all are about what the issues are and how much of our discussion today and the public comments were really about systems issues and about policy issues and about funding issues. When we think about writing this up, we had a framework that we started with that was about provider interactions and co-occurring conditions. But given the emphasis of what we

are talking about and how congruent it is, I think we should rethink that framework to include a stronger emphasis on social determinants of health and systems issues.

MS. GASSNER: And please on these videos, can we include autistic people instead of it just being people who are providers? because a colleague of mine, Chloe Rothschild, who will be joining on the Board of Directors for The Arc. She is a young 20 something year old autistic woman who uses a combination of verbal language. But when she is in pain, she has to use her augmentative communication. She made a video with the University of Michigan Hospital showing hospitals how to be better at working with people like her who really need childlike specialists, but they age out of that support.

You are talking about needing them to have face-to-face contact, but that may not be possible. But even if they can just get a snippet of somebody, it might be informative in some way. Thanks.

DR. KERNS: Can I just jump on with one thing too? There are a lot of specific populations that need care, right? I think there could be many different committees for many different disorders. But we are talking about a really high prevalence disorder here. In that way, I feel like we have a really decent argument for this and that this needs to happen that this is part of the population that providers are going to see.

DR. AMARAL: I just wanted to comment, an observation, from listening to folks that one of the issues might be that it's hard to get funding for these integrated approaches.

Regardless of whether you are trying to do the basic research on GI problems and autism or you are trying to do an integrated approach to treatment.

What happens at NIH is that you have to go across institutes and you have to find the right institute who is willing to support that particular component, but they might say I don't deal with gut problems even though it is a psychiatric disorder, but we do not deal with the gut problems.

I think not necessarily at this meeting, but at some point later on, it might be interesting to have some of the NIH representatives talk to us about how we might facilitate or integrate a funding mechanism so that we can do a whole person approach to autism and disorders like autism.

Anyway, just the kind of thing - I know I've heard people tell me from my own institute that I can't get funding to do immune problems in autism because I cannot find the right place to pitch the grant. Something to deal with later on.

But I think that one of the take-home messages we are all getting is that we have to take a whole person integrated approach to autism and we need to figure out how to do that.

DR. ROBERTSON: I wanted to concur both with the integration on funding and then making sure that as we work across silos that we look at where the real barriers are in terms of what's hindering in terms of research or practice development.

I also particularly wanted to echo the comments and making sure the autistic adults

are not only involved in terms of being featured in the videos for education and training and informational materials, but are involved in shaping the narrative and information, et cetera, that happens in every step of the processes were as folks were looking at innovation and practices, knowledge, dissemination, et cetera, and outreach and technical assistance, et cetera to health care. I think that that is just strongly important is making sure that folks hear it first hand and also the wide breadth of diversity of autistic people, folks who are augmented alternative communication users in terms of devices and systems, et cetera, and other kind of cross sectionality on economics and diversity on backgrounds, ethnic, racial, women, men, et cetera. I think that is just tremendously important

when we are thinking on the health care end is to making sure that autistic adults of varied backgrounds are involved at every step of the process and providing input all across the board.

I think that, for instance, how ASPIRE does with the CBPR model on having autistic adults heavily involved - it could provide some input on how autistic adults could also be more involved more broadly when we are thinking on policy and systems and practices and disseminating knowledge, et cetera, and making sure that that - it is just something we have at the forefront and it is constantly on our minds as making sure that autistic people ourselves are the ones who are actively involved alongside providers and families and others and can also share directly were some of these barriers are that

sometimes folks are missing out on some of the co-occurring conditions, some of the neuromuscular that have been raised are specifically sometimes because autistic adults have brought it up. I just want to make sure that that stays of major importance because I think it is tremendously important. And sometimes it has been a historical thing for autistic adults often - not sometimes, very often autistic adults have been left out of the conversation. We do not want to see that for the health care end too is to make sure - we want to make sure the autistic adults are involved everywhere for the whole process on innovating health care services. Thanks.

DR. DANIELS: Is there one more? Kevin. Oh, and then Micah next and then probably close.

DR. PELPHREY: I wanted to make a suggestion that may seem absolutely outrageous because we've talked a lot about funding for the type of care that we would like for our children and our family members and our friends to get. And we've thought about ways to encourage government funding. We've thought about ways to encourage other sorts of funding, how to kind of figure out the insurance system.

But I wanted to make a suggestion around what about the movement in the US towards concierge care. I googled it having kind of thought of this. I'm aware of it in terms of family/doctor approaches, but I wasn't aware that there is any sort of pediatric form of it. For example, there is a nonprofit in Seattle. This is not an endorsement. This was just me finding it on Google. It sounds

really interesting because they are doing exactly as a pediatric practice what we are suggesting is needed. So same-day appointments, everything that is needed for really thinking about the individual, calling and scheduling appointments with specialists, following up.

It looks like their funding model is one where when people can afford it. It is about \$1,500 to \$2,000 per year. For those who cannot, they do fundraising. It is a bit like how a lot of our kids end up going to summer camp. We go to a fundraiser. We buy something for a more expensive cost than we would normally buy it in a raffle and a kid goes to camp.

At that level of cost, leveraging the existing Medicare and insurance systems, you could rapidly get a data quick back of the

napkin type calculation to concierge care for every person with autism in our country.

Quite, quite rapidly for less than some of the government programs that we develop that we are not very happy with. And you could imagine that there could be a gigantic profit motive here, where somebody could make being a concierge pediatrician as attractive as being a dermatologist. And now our very best medical students in the world want to be developmental peds as opposed to being dermatology residents.

It's just kind of a plug for maybe thinking outside of the current silos that seem to be kind of knocked down and have to be built back up every four to eight years, from kind of a government point of view to more of a could we solve this as a community of parents and a community of individuals

that are directly affected by autism. And it would be a topic that I would think those groups would be readily able to work together on.

DR. DANIELS: Micah.

DR. MAZUREK: I just wanted to reflect back on some comments that we have made earlier today and on the public comments that I know we are focusing mostly on physical health today, but mental health keeps coming up as a primary concern of the community and of folks around the table today.

I think when we are thinking about training providers on recognition of symptoms and co-occurring conditions, it is also important to think about cross training, physicians to be aware of the impact of mental health on physical health and vice versa so that if a child comes to a

behavioral health provider with challenging behaviors, they are also aware that there may be some potential medical conditions that could be contributing like sleep. If a child is not sleeping, they are likely to be irritable the next day. And so you want to be aware of that as a behavioral health provider. Just putting a plug in there for that intersectionality between mental and physical health.

DR. DANIELS: Thank you and thank you to all our commenters today and for this discussion.

I want to take just a moment to introduce Denise Juliano-Bult. Do you want to say something about yourself? We missed you earlier.

MS. DENISE JULIANO-BULT: I am Denise Juliano-Bult and I am a program officer in

the Services Research and Clinical Epidemiology Branch here at NIMH. I have the portfolio on research on services for autism for adults. My counterpart is Denny Pintello, who handles the child services portfolio. It has been an excellent, very informative discussion so far today. Thanks.

DR. DANIELS: Thank you. I would like to have Dr. Shelli Avenevoli introduce herself.

DR. SHELLI AVENEVOLI: Hi everyone. I'm Shelli Avenevoli, the deputy director at NIMH. I just want to thank you for being here today and look forward to your comments. I apologize that I will be in and out of it today.

DR. DANIELS: Is there anyone on the phone who has come in later and has not had a chance to introduce themselves yet? No.

We will move on to the next session, which is on epilepsy in individuals with autism, the state of the science. We are going to have Dr. Gregory Barnes and Dr. Sarah Spence talking with us about this.

DR. BARNES: I would like to thank the IACC for picking this as a topic to discuss by the committee. This is a population that I and certainly Sarah and others have advocated for a long time. But there really has been a lack of research and study in the area of epilepsy and autism. Autism studies oftentimes exclude epilepsy patients and epilepsy studies oftentimes exclude autism patients. I thank the committee for helping us think about how we can move the research and the knowledge forward in order to be able to help our patients.

This is my disclosure. If you guys want to talk to me later about the clinical trials I'm doing in this space with GW Pharma in autism, I would be glad to talk to you about that.

If you really look at the one thing that we have established over the last couple of years - over the last five years, it really is that ASD and epilepsy are highly related. They are certainly highly related genetically. It seems as if that most of the relationship really occurs by the occurrence of intellectual disabilities occurring in the population with ASD and epilepsy. That's probably genes, but it also could be other risk factors for intellectual disabilities as well. You can see epilepsy and autism outside of intellectual disabilities, but it's fairly rare.

This slide is just to emphasize to us. This is data on the Vineland scores, the Vineland Composite scores in the agreed population. What this is meant to drive home is the fact that if your scores are less than 70 that there is a three-fold increase in the amount of epilepsy versus those whose scores are over 70 so again suggesting in these multiplex families with a genetic component that intellectual disabilities needs to be present in order to see epilepsy.

This is really our summary slide for the whole presentation. This is how you can really conceive of and how ASD and epilepsy occurs in a single patient. You have your genes that on your left and those code for proteins mainly within the connection between nerve cells, i.e. the synapse. These can either be structural proteins or they can be

proteins that controlled the excitability and inhibitory ratio.

Those probably have a large effect upon the outgrowth of the tracks that we see both within the local tracks and the developing brain as well as the long-range tracks. Those of course are all seen in the setting of the variants that at the bottom, which besides intellectual disabilities include the common genetic variation, epigenetics, random events, and environment.

And then what's meant to be seen on the right is showing the different developmental trajectories of symptomology. Whether you are talking about restricted interests, repetitive behaviors or you are talking about communication or social skills. What you have is a trajectory over time that ends up in that green circle that is ASD.

The rest of the presentation is going to be a summary of basically of the shared neurobiology that we see both in the ASD field and the epilepsy field. Both disorders are largely involving the connection between cells, so-called synapses. Both are disorders of activity-dependent pathways.

Interestingly, activity including seizures can regulate these autism-related protein cascades. There certainly is evidence for epilepsy in human autism syndromes and animal models. Both occur in critical periods and both disorders have an emerging, similar neuroanatomical and functional alterations of shared brain circuitry. In yellow, we are going to talk about the first four.

Possible mechanisms that would lead to excitability. Number one, autism has an involvement of these cell types that are

listed on the left. It includes excitatory neurons and inhibitory neurons. Also it includes serotonergic neurons as well as cholinergic neurons and cerebellar Purkinje cells. Alterations in those cells each can produce autism-like behavior in animals.

Early life epilepsy. We know certainly from human models and some animal models can also produce epilepsy. We think in the majority - the speculation has been that in a majority of the humans, that this altered organization of many columns associated with defects in GABAergic circuits and GABA-A receptors in a setting of ID may contribute to both ASD and epilepsy.

I don't want to take credit for some of the visual effects here. I want to thank my engineering colleagues for that. I'm not that talented.

Neuropathological findings in autism.

What is a minicolumn? A minicolumn is a vertical arrangement of neurons in the developing cortex that grows towards the cortical surface. What you find in postmortem specimens and autistic individuals versus controls is that there is an alteration in the thickness of the columns themselves. This data was originally publishing by Dr. Casanova showing thinner minicolumns. It turns out that if you look at data across ages, what you find is that overall on the far left in blue, at early ages, the minicolumns are actually expanded, which may explain some of the increases in gyrification and surface area that you see in the MRIs of younger individuals with autism.

This complicated mess. I am going to try to explain this real quickly because it just sets the stage for our discussion about GABA. On the left, this is a figure from a paper by Lowe and Broward. In that paper, they looked at the 500 to 1,000 genes that have identified in the Autism Sequencing Consortium and the Simons Simplex Consortium.

Essentially, what they did was they mapped gene variants to the genes themselves and then genes to pathways and then pathways to biological conditions.

What I want to point out here is that if you take a bird's eye view of what all the genetics look like, you have two major themes, one of which is the neural wiring and morphology that is on the left side and the synaptic transmission that is on the right side.

That is really, really interesting from an epilepsy point of view. Let me tell you why. There is a wonderful neurobiologist whose name is Richard Tsien. He just published a study postulating that in fact autism was a disorder of homeostatic regulation. Let me explain it to you this way. The figure on the right there is really quite informative.

The change in the excitatory and inhibitory ratio really represents a change in calcium dynamics, mainly in the calcium channel system. That essentially is your sensor in the system.

What your sensor does is that it then in turn impacts upon the effector. In a house, it would be the furnace or the air conditioning. In cells, it would be nuclear events. And then what it does is it goes

through. The effector in turn goes through the membrane. It goes through the ductwork. It goes through the axons and the dendrites. And then it affects change, i.e. does it affect the way the synapses actually impact upon the cell or does it affect the firing rate of the cell, i.e. controlling the variable in the system, which is analogous to the temperature in the room. It is a really interesting idea. And certainly for a dynamic system where you have epilepsy developed, it might actually have some plausibility.

Just to remind ourselves that in the genetics, there are some genes that have large effect size. These are the two autism and epilepsy models that have been studied the most. One is in tuberous sclerosis and the other one is in Fragile X syndrome. Not to get too bogged down into the slide, but

essentially what this slide is trying to communicate is that it can change things at the synapse, i.e. in the dendritic region, which is in yellow there, such that it impacts the other parts of the system. That all can happen in GABAergic cells.

Now, if you look at a lot of the genes that are involved in the GABAergic synapse, essentially you have a lot of different genes and some of those are listed here on the left side. In fact, there is probably about greater than 25 genes that are just in the GABAergic synapse alone.

Secondly, if you look in animal models, what you can do is - you can actually do a drawing between GABAergic dysfunction and then how the cells are - those impact the cells and then that in turn affects the micro-anatomy and the neuro-circuitry

structure. That in turn impacts the oscillations. In this case, we're talking about gamma oscillations, for instance, if you are talking about parvalbumin neurons.

In that case, those are parts of the neural network that mediates a variety of autistic type behaviors, which are on the right side of the slide.

We have two other things to talk about in the shared neurobiology. One is the critical periods. We all know about there are critical periods in the developing brain. I have actually listed some of those in humans. I am sure that there has been some refinement of that. I apologize if I have not gotten those exactly right. But certainly in humans, social skills, intellectual skills and cognitive skills have a critical period, the need to be effective before two years of age.

Hearing, you actually need to be effective before age 7 and vision you need to be effective before age 8; otherwise, you can have a dysfunction of the actual, in this case, neural circuit.

Over there on the right is a picture of a synapse that is in the auditory pathway. This is from a paper that was recently published by Frances Jensen. What she had found was that in the normal tonotopic organization of the auditory synapse in the auditory cortex in the rodent, there is this critical period between days 13 to 15 postnatally.

If you give it the appropriate stimulus, i.e. a seven kilohertz stimulus, you develop appropriate tonotopic map in the auditory cortex. And what that does is that essentially at the top there is the normal

maturation of the synapses. The synapses are normally silent with just NMDA receptors in it. But when presented with a stimulus and the tonotopic map organized then the synapses become functional and they have AMPA receptors.

In the case that you actually have early life seizures before this critical period, you actually insert AMPA receptors into the synapse so the synapse is prematurely functional. As a result of that when you present the stimulus, there is no change in the tonotopic map has messed up.

There has been a suggestion in autism that autism may be a disorder of the critical periods. And certainly the premature activity might impact these critical periods. It may be precocious. It may be delayed. It may never open. It may never close. As a result,

a brain that is too plastic at the wrong times could result in a noisy and unstable processing. A brain that lacks plasticity early in life might remain either hyper or hypo connected and unresponsive as a result to environmental changes early in life.

These mechanisms can either be GABAergic or excitatory. A large number of reported in the animal literature actually are GABAergic in nature.

And then finally, let's talk a little bit about the neuroanatomy and functional alterations of shared brain circuits. This was a really interesting study that was published by Ingrid Scheffer from Australia. Ingrid is an epilepsy researcher. What she did was she did a meta-analysis of MRI studies. What she looked for was she looked for studies that had both tasks involved in

facial and emotional recognition or theory of the mind, both in people with epilepsy versus age-appropriate controls or ASD relatives versus controls. This was really really, some interesting findings.

First off, the people with epilepsy certainly had defects in both theory of the mind and facial recognition tasks, which are tasks that test social circuits, greater than typically developing controls. These deficits and the people with epilepsy were actually less than the deficits of the ASD relatives. Both groups were free of intellectual disabilities.

What was interesting about the findings of these tasks were that the deficits and the people with epilepsy were actually independent of the epilepsy characteristics. That was very very interesting. That

certainly might - might tell us something or a little bit about how these disorders can develop in the same person.

In summary, the shared neurobiology. Both disorders involve the synapse. They are activity dependent. These seizures can regulate activity dependent on protein cascades. They may share critical periods. They may share similar findings both neuro-anatomically and functionally and shared brain circuitry. This is all in the setting of course of shared genetics. Thank you very much.

DR. AMARAL: Greg, why don't we go on and let Sarah talk and then we can open it up to general discussion about both presentations? Thank you.

DR. SPENCE: I want to echo Greg's thanks for putting this as an agenda item. I also

want to thank him for doing all the hard work because now we are actually going to talk about the clinical aspects. He got to do the hard neurobiology.

I have no relevant financial disclosures. I will - since I am a clinician, I want to apologize in advance for using person first language to those who are autism self-advocates and like to have the autistic first. But in medicine, this is the way we are trained. I will try to do a good job and go kind of both ways.

We have talked about this already that there is a big association. It really -we have also talked about the major impact on quality of life and the idea that this could be common neural mechanisms. This is really why we're talking about it. I think the phenotypes that we are talking about are

behavioral, they're language and communication, and their cognition. As Greg was talking about, I think a lot of this is driven by intellectual disability, but I will point out not all.

I think the other main question that I've always had is is there any causal relationship here. As we talked about this morning, with three separate categories of truly shared mechanism or having one thing leading down the line to another thing. Or is there kind of more epi phenomenon where the brain of an autistic individual is the brain of an autistic individual and that gives you the increased risk of having epilepsy?

The rates of epilepsy are actually highly variable. Most people will tell you that it is 30 percent. It's probably actually lower than that. I point out kind of why this

is because you would think this is not a really hard question. It turns out that it matters where you get the sample. If you get the sample in a neurology clinic. Who goes to neurologists? People with epilepsy. If you get the sample in a population-based sample, there is where you get the lower and I think probably the truer rates.

The other is age. We have a bimodal age of onset in epilepsy. I think, like David had mentioned earlier in Lisa Croen's slides, I had always thought that it was more with the younger ages. David had thought it was more with the older ages. I think it is probably about half and half. Patrick Bolton's paper a few years ago actually said just over 50 percent had onset in the later adolescent.

One thing that is important to note is it's not actually puberty. This doesn't seem

to be a hormone thing. Many of the older adolescents are 18, 19, 20, 21. This is not an onset of puberty.

We have a lot more epilepsy in what we think about as kind of syndromic autism or non-idiopathic autism or we have known cause. And then IQ and language skills seem to be a predictor.

This, I want everybody to memorize. No, I am kidding. The only reason I put this up is this comes from a review that we did a few years ago. It just points out some of these issues. Here is the effective ascertainment. If you look here, this is one of the highest rates that has been published, 46 percent. It's clinic based. That is going to give it to you. Here are some of the - not all, but just a few of the population-based samples, much lower.

Here is effective age. In population that includes adults, you have much higher rates than in populations that have only included kids because you have not gotten that second 50 percent.

And then we have the effect of the comorbidity or the syndrome or the ID. I would point this out because I think there are a lot of people who think it is just intellectual disability. With and without. Without intellectual disability, the rate is 8 percent. The general population risk of epilepsy is 1 to 2 percent. There is something about autism, regardless of intellectual disability, that does increase your risk.

We, as neurologists, know about this because there is a lot of overlap between certain epilepsy syndromes and autism.

Infantile spasms are a relatively common way of presenting with epilepsy in the infantile period. It has high rates. If you have infantile spasms in follow up, you have high rates of intellectual disability. It turns out if you really look at kids with spasms, the social communication difficulties are worse than you would predict just from the developmental outcome, which is interesting.

If you look at all the kids with spasms, 10 to 15 percent of them will go up on to develop autism. And then if you look at kids with autism and epilepsy, many of them had a history of spasms in their past.

Greg mentioned Tuberous Sclerosis Complex, which is one of our animal models and human models of this association between autism and epilepsy. We have very high rates of epilepsy and TSC. We have very high rates

of autism and TSC. And the autism is higher in those who have the epilepsy and intellectual disability.

I got interested in this after a 20/20 broadcast when I was a medical student with Landau Kleffner Syndrome. This is very rare epilepsy. It is very rare where you have completely typical development and overnight you lose your language. You have this massive regression. You have behavioral changes. You sometimes develop epilepsy. The epilepsy is not actually the big problem there. We know in autism that there are kids who have a language regression. They have behavioral change. There is this overlap about whether kids with autism have Landau Kleffner or not. I think, in general, they are two separate things, but there may be a continuum.

Very unsatisfyingly, there is no single epilepsy syndrome in autism. It would be an interesting thing if you said if you have autism then you are always going to have this kind of seizure and it is going to happen at this time. That just doesn't happen. We see generalized convulsive seizures. People will call it grand mal seizure. We see partial or focal seizures and we see absence or what people call petit mal seizures.

What I will say and I think one of the points of this meeting is to talk about how we get access to health care around some of these issues. Seizure behavior in kids with autism is a little hard to discriminate. As an epilepsy person or a child neurologist, we will say seizure behavior's unresponsiveness sometimes with focal seizures that can have eye deviation. You can have some repetitive

behaviors or kind of what they call automatisms. I will give parent talks and I will hear kind of 17 people line up who say my child is seizing all the time because they are not answering to their name. They're peering out of the corners of their eyes and they have stereotypies. I think it is very important. Even some of the best epileptologists actually can't tell what is seizure and what is not.

One of the things that I think I like to say to people is watch for whether you think this is voluntary or not. Make sure that when you see your child being unresponsive, they are really unresponsive. Get in their way and do something to them that maybe is not so fun, which we talk about like touching their nose. If somebody else touches your nose, it's really annoying. It does not hurt, but

it's really annoying. If they do something, that is a purposeful movement. That is not a seizure. You cannot stop somebody's seizure by touching their nose. Simple things like that to really distinguish between is this unresponsiveness or not. We think about some of the autism behavior as being more voluntary, being more purposeful. We think of the seizure behavior as being not.

What do we know about the epilepsy other than there are multiple seizure types? All different seizure types. Multiple seizure types in the same person. Treatment refractory epilepsy may actually be common. This was a paper done at NYU. I was thinking Orrin Devinsky was going to be here. This is his sample. They found in the sample at NYU that over 30 percent had really refractory - treatment refractory epilepsy.

This second point of increased mortality is a very scary thing for families. I will tell you. This paper was published by Jane Pickett from the Brain Bank from the DDS California data. It is a five to six times higher mortality in those with ASD with epilepsy than ASD alone. I will tell you that it's lower than epilepsy alone. Many people with very severe epilepsy have an even higher mortality risk. Autism in that setting almost seems to be protective.

One paper that was published a few years ago and I haven't seen a lot more since is that it may actually predict the outcome of early intervention. I think this is the thing that we really - this kind of sent fear through my heart as a clinician of thinking we're doing everything we can for the kids. If the presence of epilepsy is actually

getting in the way of the therapy that we are giving then this is a reason to really think about this disorder.

Here are some risk factors. We talked about the intellectual disability. I made the comment that it absolutely increases risk, but it's not the only thing. The comorbid conditions. It turns out that girls have an increased risk of epilepsy over boys. I don't think we have teased out whether this is because many of the girls that we have ascertained so far have been associated with more intellectual disability.

There is a big question about developmental regression. I told you about that. Landau Kleffner disorder. If you have this regression, do you have an increased risk of epilepsy? There have been really some

very nice papers. About say yes and half say no. I can't really answer that question.

And then there are some of the really nice population-based data that show some pre and perinatal factors. Prematurity, birth weight, low APGAR scores, the things they give you as the baby is born.

We know a whole lot less about the relationship between epilepsy and the actual ASD clinical profile. I think this is an important thing as clinicians and as we talk about access to improving health outcomes, it would be really nice for us to be able to say, okay, if your child has autism and you develop epilepsy, this is what the autism is going to look like. I think we cannot really do that.

I found a couple of papers. I know of one that is actually under review right now

that's a large sample. But it turns out that the epilepsy people don't really look as hard at the behavior and the behavioral people do not look as hard at the epilepsy. There is really a whole lot less known about this.

There is a great paper out of the UK where they found more motor, more adaptive behavior deficits and then one item on a big long three-hour interview called the DISCO in the non-verbal communication realm where the kids with epilepsy had "stares too long and too hard." I do not know whether that really means a whole lot to the rest of us. But these are the kinds of things that I think we need to be doing.

The question is are these associations independent. Greg, I think, mentioned the AGRE sample, which was a large, shared, genetics database started by Cure Autism Now

and then taken over by Autism Speaks. Emma Viscidi took data from AGRE, took data from the Simons Simplex Collection and the Autism Consortium and really wanted to look at the clinical characteristics. Now, this is a sample of convenience. Right? She did not design anything. She just knew that these data were out there.

The strengths of the data were very good autism samples, really good behavioral data. The weaknesses were only so-so epilepsy data. And the initial analysis showed significant effects of whether or not you had regression, whether or not you had language deficits, IQ, adaptive function and the severity of the autism. Unfortunately, most of the effects - there is the original, these nice healthy P values for those of you who are statistics geeks. And then when you adjust for IQ, it

kinds of all goes away. Again, this idea of the intellectual disability really driving this association.

If we think about treatment, we treat all kids with epilepsy if they have ongoing seizures. We use - there are a number of anti-seizure drugs. We used to call them anti-epileptic drugs. That is actually a misnomer now because it does not prevent the development of epilepsy.

We really treat dependent on the seizure type that the person has, on the side effect profile, and then even things like practicality. If you can't take a pill, you cannot take that particular medicine that only comes in pill form. If you need a liquid medication then you need to go that way.

If you need to get frequent blood draws for monitoring some of these medicines that

might be a medicine that you can use in a given population.

I think we need to think about the fact that all seizure medicines have behavioral and cognitive side effects. The practitioners need to be really really careful.

I am going to bring this up mostly because I think Greg and I should talk a little bit about it, but there is a lot of cannabis interest out there right now mostly from the epilepsy community, but also in the autism community. There was a trial using cannabidiol just CBD, which is the part of cannabis that does not make you high. It is purified and made into a medication called Epidiolex. It's about to be available. It's already been approved by the FDA. It really showed improvement in some very difficult to treat seizure patients with a disorder called

Dravet syndrome that has a high rate of autism as well.

But there is also a lot of interest in using cannabis for behavior in autism as well. There is no clinical data so far in that although there is a paper that - a project that is going on in Israel right now.

Greg is actually doing a trial at the University of Louisville, looking at the safety and tolerability of a slightly different agent and in kids with both autism and epilepsy. He's going to look at the behavioral outcomes.

In reality, there are probably multiple different kinds of epilepsy in autism. When the early onset seizures actually maybe contribute, change the brain in those critical periods, when these other disorders co-exist and then true idiopathic autism and

the comment is whatever that means. When I was in medical school, we learned that idiopathic meant that we are idiots and we do not know the pathology.

For those who do not EEG, this is a nice epileptiform discharge on EEG. Greg and I actually came up with a few things to launch some discussion, having been here all morning. I think we do not need any.

I think the only one that I did want to talk about was this idea of the data are not out there yet because of the disparate fields of investigation. These are both very heterogeneous conditions and we have behavioral science people, basic science people, neurologists who are the epilepsy clinical people, and I think we have been siloed for too long. This is a nice way to think about moving forward. Thanks.

I am going to whip through these last slides because I know they actually come - I did want to mention just because AUTISTICA came up this morning. There was a lovely lovely collaborative workshop that they did a year and a half ago maybe where they were looking at autism and epilepsy. Here, for people to just have to look at, these are some of the questions that came up from parents, clinicians, autistic individuals, and researchers.

DR. DANIELS: Thanks very much both Sarah and Greg for your presentations. We now have some time for discussion among the Working Group and Committee. We can start over here. Dena.

MS. GASSNER: I just wanted to ask given that we have already heard today that we are seeing four to one in early childhood, which

I kind of wonder about a lot and yet when we get to adulthood, Jeremy is telling us that disparity shifts quite a bit. I am wondering if the reason you are finding more girls is because the epilepsy brings them to you as compared to an individual having autism. And then the other thing is they may come in having epilepsy, but they have no idea they are autistic and then through this process very much like this study we talked about earlier. Do you have comments, insights?

DR. BARNES: It's most likely an ascertainment bias I think as you alluded to. There still are a lot of genes that cause autism and epilepsy that's on the X chromosome. If you actually have two different - if you have a dosage of two rather than one mutated gene, it certainly is

possible that some of this may actually may be genetically based as well.

DR. REICHARDT: I was curious about your thoughts of whether the numbers are there for looking at the range of epilepsy when you look at the different sub-cohorts of individuals that have identified genetic lesions. Part of the reason for this is the definition of intellectual disability - how susceptible you are to it not only depends on what has happened to your brain. Is it a result of something maternal or genetic? But also how smart or how intelligent your parents were on average. It's clear that these genes differ in their impact on IQ, for example, and so whether this correlates at all.

DR. SPENCE: I think that's a really really fascinating question. To my knowledge,

I am not sure that there are data that are out there looking at the sub-cohorts. In other words, I think what you are saying is how different is the rate of epilepsy in tuberous sclerosis versus Phelan-McDermid versus Fragile X.

What I can say is that epilepsy is very high in TSC. But there are people with TSC who have no intellectual disability. I'm not sure that the data are out there to really say that. They should be. In other words, many of the family groups - we have big registries now for many of these individual genetic disorders. I think we could really look at that.

DR. AMARAL: I have a comment and two questions. My comment is that it was interesting when you said that community-based samples of people with autism tend to

have a lower rate of autism. That is certainly what we found. We have an autism phenome project going on for now over a decade. And the number of kids that we see with autism early on is really small, which sort of surprised us, but it is consistent. I am sorry. With epilepsy. Kids with autism who have epilepsy. Sorry. That is consistent at least probably with the literature.

I have two quick questions. Number one, oftentimes medications that are used for whatever in typically developing individuals do not work as well or work too well in individuals with autism for the epilepsy or the seizure medications. Is there any evidence that that is the case or is the efficacy basically the same?

DR. BARNES: The efficacy itself for seizures is probably the same. Do you know of

any data? I don't think so. There is no difference in efficacy per se for the seizures themselves. Both in clinical practice and at least in one paper, there is some data to suggest that you ask about if you suppress the discharge, does anything change in the autism core symptoms or the behaviors? The answer to that is usually no. There is 8 to 10 percent of the time maybe you will have something that will change, but usually not.

The other question is, was the change that you saw due to sleep. Rather than, are they sleeping better now?

DR. AMARAL: But the bottom line there is that if you can reduce the seizure, you still do not see much of a change in the autism symptoms.

DR. BARNES: Yeah, in general, that is true. There are some patients though. It's really really interesting. Parents will do various things with the anticonvulsants. Sometimes they will drop them. Sometimes you will actually get them to wean it. But anyways. And then they will come back and they will tell you this behavior is different. This attention is different, et cetera. And then you recheck the EEG. The discharges are back. And then you suppress the discharges again. By the way, they also had seizures. You suppress the seizures again. You suppress the discharges again. Things go back to the way they were.

There are some patients in the epilepsy population that definitely are sensitive to either seizure or spike suppression or both and that we just don't know.

DR. SPENCE: I agree. I think you can say as a general statement that if you treat a person with autism's epilepsy, you do not take away their autism. I think we can say that. I think that probably the seizure burden may be the background. Epileptic discharge burden has something to do with certain behaviors maybe with language, maybe with cognition, maybe with behaviors. That's the part that I think we do not know as much about now.

DR. AMARAL: So my last, I don't want to capitalize - take the entire question and answer period, but I just have to ask. There was a notion years ago that if you could treat occult seizures or occult epileptiform activity that perhaps you could prevent or avoid some of the autistic symptomology. Did that ever go anywhere?

[inaudible comments]

DR. AMARAL: Oh, it's going to go somewhere.

[inaudible comments]

DR. BARNES: She will talk about it, but probably not.

DR. SPENCE: There is actually a trial right now. This was one of our questions. Would early treatment in epilepsy actually reduce the idea for the kids who had infantile spasms say where we know there is an increased risk? Would that reduce the risk of developing autism later on?

This trial right now called the PREVeNT Trial is enrolling. It's in kids with Tuberous Sclerosis where we know there is a high risk of infantile spasms. We know what the EEG looks like. They're actually putting these kids on a medicine that for whatever

reason in Tuberous Sclerosis, this particular medicine, which we don't use otherwise, is exceedingly successful. You get a 90 percent rate of recovery or cessation of seizures. They're putting them on as soon as they see any EEG abnormality. They're not waiting for them to develop spasms. They're going to look at outcomes. That question is actually going to be answered.

And my guess would be, and in an animal model, it does work. So if you prevent the epilepsy in an animal model, you prevent the behavioral cognitive side effects, not side effects, outcomes in animal models in TSC. I think they are going to try it in humans.

DR. MALOW: Thank you, Greg and Sarah. I have a question for each of you, which is the - in addition to the seizures, all the other comorbidities we see in autism like let's OCD

and anxiety and others, is there anything based on your work, Greg, that would allow us to understand which kids, maybe kids with epilepsy, have more of these brain-related conditions because of the synaptic connectivity. That was one piece.

For Sarah, the social determinants of health. In other words, if a kid with epilepsy isn't driving or their parents are really scared that they are going to hurt themselves and have a seizure and they don't get to do the summer camp and all the other stuff that a typically developing kid would do, just that whole idea of how much of some of the disability is related to those kinds of issues. Those would be my questions for both of you.

DR. BARNES: I will take the first one. There are some animal studies that suggest

that if you do have epileptiform discharges in certain pathways that you could put - that somebody would be at risk for having exacerbation of anxiety or repetitive behavior or whatever. Of course, we've had these discussions at Vanderbilt. I've had these discussions at University of Louisville about children with uncontrolled seizures. Their behavior is usually worse, not always, but sometimes they are.

The animal data would suggest that there is possibly propagation of those discharges into the behavioral neural circuits that may actually make things worse. That certainly is a possibility.

DR. SPENCE: I think the question about the social determinants of health is a very good one. I don't think we know the answer for sure. But I will tell you that from a

clinical standpoint, my experience has been that for the patients who develop epilepsy later in their life, the epilepsy is really devastating to the parents. This is a family that has really done a remarkable job on working with the autism and all the challenges that the autism brings. And then one seizure happens and the whole family falls apart. I say to them no, no, no. You can handle this. You absolutely can handle this. You've handled way more than this for this child's whole life. You can handle this. But there is a real fear about seizures. And I think that that's...

Now, I will make one other comment, which is there is a real fear about seizures in general. There's even more I would say nowadays because there is a lot more work and communication being done around sudden

unexplained death in epilepsy, SUDEP, which is something that as a neurologist we didn't talk a lot about for a long time because there was not a whole lot we could do about it and we did not tell people that there was a risk of death in epilepsy. But that, the families have spoken and said that was absolutely the wrong move and that we ought to be talking about it.

I think that that raises another level even though it is a relatively rare occurrence. It raises another level of fear in families.

DR. TAYLOR: I have Scott and then Antonio, then Sam, then Jerry. Scott is first.

DR. ROBERTSON: I was just wondering about related to this also on the genetics and families also is for parents who have

epilepsy in terms of that link also back to autism among their kids. It makes me think about, makes me want to have another conversation later on with my parents at some point because I remember my mom saying at one point having seizures as a kid and being on an anticonvulsant. She was on the one that I think eventually - one of the ones that turned out cause birth defect type issues. She was taken off it long before having me. She went off it before she had my older brother. It just makes me think on family history on the genetics on that.

Is there any more research that has come out recently in terms of what it looks like if parents have epilepsy and what that looks like in terms of population rate among their kids as far as what the rate on autism looks like and then maybe the rate of autism plus

epilepsy, like autism with and without epilepsy among the parents who have epilepsy?

DR. BARNES: It's a really interesting question. It turns out that the odds ratio is about 8. It's fairly high actually. If you have ASD, you are at risk for epilepsy. And then if you have epilepsy in the family, you're at risk for ASD. So it's actually bidirectional. The odds rate for autism and epilepsy is 28.

It is really suggesting that at least the condition of autism and epilepsy seems to be maybe a little bit more genetic in nature than just autism alone. It's really quite interesting.

DR. HARDAN: I have two questions. The first one I think - Greg mentioned that there has been limited research in this area. Despite that, there is interest in funding

studies looking at epilepsy and autism. Is there anything that this group can do to facilitate more funding or more research in this area? That's one question. You can think about it.

The second one is I have been practicing for about 20 to 25 years, seeing kids and adults with autism. And one of the most challenging patients to treat from a psychiatric point of view is the individual who has a severe seizure disorder. Over the years, I 've tried you name it in terms of antipsychotics, anticonvulsants and in some occasion like very limited benefits from any of these interventions. I don't know if you have insights into this clinical problem.

DR. BARNES: I'll be glad to answer that by illustrating a story. It was actually Dr. Malow who sent me this - there is a 12-year-

old patient who was resistant to everything behavioral wise. This kid had not had a clinical seizure. She asked me, she said, do you think he has an epileptiform EEG? We did the EEG. Yes, it was epileptiform. I went ahead and started some Lamictal. In the meantime, he actually developed generalized tonic-clonic seizures. He was a kid who never slept as well. I put him on Zonegran at night, suppressed his spikes at night. He slept well at night. I don't know if you know that family if the kid has had another seizure again. Anyways, all of a sudden, all the behavioral meds started working all of a sudden. My point is that of course that is something that we see with clinical practice.

Now, why is it? Is it due to depletion/alterations in neurotransmitter systems because of the epilepsy? Is it

because the wiring is just wrong? Who knows?
But this is something that we see in clinical
practice. Do you have anything to add?

DR. SPENCE: Yeah, I think, the only
thing that I would add is that the
individuals with really intractable epilepsy
tend to be on multiple drugs and many of the
medications that have the worst behavioral
side effects. So the medicines - if you get
the epilepsy well controlled with a single
medicine then they are not your patients.
Your patients are the ones where they have
tried probably ten different medicines and
are on still five of them and still seizing.
And those five have a lot of behavioral side
effects themselves. So whether it is the
epilepsy or whether it is the medications
that they are on for that bad epilepsy. Is, I

think you are dealing with both of those things.

DR. BARNES: And they also have of course severe intellectual disabilities as well. That is another complicating factor.

DR. TAYLOR: Sam and then Geri.

MS. CRANE: I want to go way back to a previous question about effectiveness of medications because Dr. Barnes had said that medication effectiveness is not necessarily different between people with epilepsy alone and people who have both an autism and epilepsy diagnosis.

But I want to clarify. Is that that we don't have evidence of difference of effectiveness or that do we have actual evidence of equal effectiveness? Because -

DR. BARNES: We don't have actual good clinical trial evidence of head-to-head

comparisons. No, we don't have that. This has been an observation that's been made and published among many different sorts of clinics that have taken care of autism and epilepsy patients.

MS. CRANE: Because in the autism community, there are people who feel differently from that. I think it would be interesting to have an actual head-to-head study to analyze whether or not it is actually true.

DR. SPENCE: I think one of the things that Greg mentioned earlier is and we have talked about is the silos of investigation. Right? The people in an epilepsy trial are probably not going to enroll a person with autism. I think those data would have to come from big registry data would be my thought, which are flawed in some other ways as well.

But I think that is the reason that we do not have those data.

DR. DAWSON: I am sorry if you covered this. I had to step out for a clinical call. But, I'm wondering about the role of technology and engineering in this field and whether there are really new things on the horizon that could help with either early risk detection. I know that there's a device now that Affectiva developed that is apparently helpful in possibly preventing SUDEP. I just wonder what's going on in the field in terms of bringing in new technologies for telemetry or anything like that that might improve our ability to detect or prevent the consequences of having epilepsy.

DR. BARNES: With regard to new technology, besides obviously some of the

newer anti-seizure drugs that are coming on the market, there is a new emphasis on essentially making our devices that we do have like, for instance, the vagal nerve stimulator to make it much more effective. The models that now detect tachycardia and a certain threshold above baseline really are giving quite a bit more seizure control versus the old models.

There is also a talk with Medtronic of using some extra cranial sensors as well to try to detect seizure activities. There are a number of things that they're doing for the vagal nerve stimulator. That's the first thing.

The second thing of course is we still do use although very rarely, but we still do use epilepsy surgeries. That still can be

effective for the epilepsy population under the right circumstances.

Thirdly, there is a renewed interest in using deep brain stimulation. In particular, looking at the centromedian nucleus of the thalamus for generalized seizures. And of course there was an approval for focal seizures for the interior nucleus of the thalamus for deep brain stimulation. That's coming around the corner.

Pediatric centers of course have been a little less likely to develop the deep brain stimulation because there is always that risk of hemorrhage although all the hemorrhages and the deep brain stimulation trials have been asymptomatic, but neurosurgeons are still nervous about that.

And then there is finally a device that's called NeuroPace. I do not know if you

have heard of this device or not. It's an interesting concept. The idea is that let's just say that you can't tolerate medications and you may have instead of one area of the brain developing the seizures, you have two areas. Okay? You can actually take subdural electrodes and actually place them on top of where they generate those epileptic generators are, usually on the same side of the brain.

What it does is that the device will - the device is implanted in the head. The device will record electrical corticography for a month and then you will kind of get an idea of how you are seizing from those foci, et cetera. And then there is programming done to give stimulation directly to the epileptic generators.

We actually recently did this in one of our children who had a very large - was not autistic - that had a very large left frontal parietal cortical dysplasia. That child has done very, very, very well. It can be effective in some situations under certain conditions.

There is great interest in the epilepsy field in looking at stimulation from a variety of standpoints and stimulating a variety of structures just beside the vagal nerve stimulator.

DR. DAWSON: Are people using the Affectiva device that looks at galvanic skin response or electrodermal response?

DR. BARNES: I think that is a model that is relatively new now. It's just now getting used. I know we have implanted some. I know

we have at it the University of Louisville.

We have a very active --

DR. DAWSON: I think this is just a wristband. FDA approved.

DR. BARNES: Oh is this the wrist? You're not talking about the ASPIRE. Okay, alright.

DR. SPENCE: I think people are using it at least in Boston because it was actually tested out in Boston. So at Children's, for people who do not know what this is, it was a device that was developed at the MIT Media Lab that really was developed around autism to see whether we could determine whether any changes in behavior were coming from looking at heart rate and changes and kind of autonomic responses.

But then I think the story goes that somebody wore it when they went in for their epilepsy and monitoring and it changed right

before. Oh, no, I know. I have heard Roz give this talk. She said she was looking at it. One of her research assistants had let her brother with autism wear it and had seen a big change in the output and said what happened here. She said he had a seizure. Right before, there was a big output. So they went into the seizure. The epilepsy monitoring unit at Boston at Children's and started putting it on along with the scalp electrodes to see can we see it and it does seem to come just before the seizure, the autonomic response comes just before the seizure. (inaudible comment) Yup. So, yes, I think people are using it. I think it is hard to get insurance to pay for it so people are paying out of pocket for it, but yes. I think in the epilepsy clinic, at Children's at least, we are seeing it get used.

DR. DAWSON: Right. Just for the IACC, two things come to mind. One of the reasons why I thought of this is because it reminded me a little bit of the wandering and the fact that there was no medical code to pay for the tracker for kids who were wandering.

If this is an FDA-approved device and I have not done a deep dive into the scientific literature behind this, but I assume if it is FDA approved, it must have some validity. It is a device that can be worn that could detect when a seizure is happening particularly at night and could prevent SUDEP.

Then one of the things we could do as we did before is make a recommendation that this actually have a code that could be reimbursed.

And then the second recommendation would be thinking about again the strategic planning is what is the role of technology and being able to enhance whether you are talking about things like deep brain stimulation or other kinds of even non-invasive trackers or things like this that might be able to help us detect seizure early in life. I just feel like this is potentially an area that could move the field in some innovative ways that could have some real-world benefit.

DR. DANIELS: Last comment.

DR. SPENCE: The other thing that Geri mentioned is is there anything that we are doing in the epilepsy monitoring units. I think very low tech is better behavioral supports. People are foregoing care because they think maybe they are having seizures and

they don't want to go in for the epilepsy monitoring. They don't want to go in for the EEG. Many, many places are developing better care.

We are actually doing in our simulation lab at Boston Children's - we are doing a study looking at whether just bringing the kid into the sim lab to practice getting the EEG because you can't do that in an actual EEG lab. They want to get you out very quickly so they can come in. They can spend a whole hour. They can play with the leads. They can do all of those kinds of things and whether that is actually helpful for the day of the real EEG.

DR. DANIELS: Thank you everyone for a really robust discussion, so robust that we have gone over our time into the lunch hour.

I would like for the Working Group to step into the next room, which is the quiet room. By the way, I did not announce that earlier, but it was on our announcements for the meeting. We have been trying out having a quiet room available for people. If anybody does need that, it's there. But we would like everyone on the Working Group to step into there for a photo.

And then we have the boxed lunches that people ordered in advance available in the cafeteria. You can bring them back here or you can eat in the cafeteria.

We'd like to keep the session on time for us to start at 1:30. But if you still have lunch, you can keep eating while we move into the next session so that we can make up for the time. Thank you.

(Whereupon, the Working Group recessed for lunch at 12:50 p.m. and reconvened at 1:34 p.m.)

DR. DANIELS: Our next session today is going to be on gastrointestinal issues in autism, which is a topic of perennial interest with the autism community. We really look forward to hearing from Dr. Tim Buie.

DR. BUIE: Good afternoon. I'm so grateful to be here to talk to this group. I was very fortunate to be invited to come with the last gathering of medical specialties, which I am reminded was now three years or more ago. I looked back at my slides to that session. I feel like progress is being made. That makes me very happy. I want to talk a little bit about that today and talk about some new issues.

Here is my slide to talk about general progress. 1998 was an interesting year. It was a year that gastrointestinal issues sort of hit the map as an idea of being a major problem in children with autism. That was the year that Dr. Horvath talked about GI findings and the possibility that secretin might be something that could be offered as a therapy to treat autism. That was a hypothesis that was vetted and there were a number of studies that didn't support the idea that that was helpful, but that was the year that launched that.

Interestingly, during that period of time, a lot of families were seeking him out and seeking out the limited number of GI people that were seeing large numbers of kids with autism. There weren't many people doing that.

Also, in 1998, there a number of papers that came out from Andrew Wakefield, talking about the finding of colitis and this condition of lymphoid nodular hyperplasia and ideas around what might be causing that.

Interestingly, that was the year of the explosion of clinic visits for children with autism to seek gastroenterologists. And most of us were utterly unprepared for that.

There had not been a significant amount of training for that. There was no general sense for what was going on with those individuals and why it was a value for most of us to see these kids. But kids kept coming. And kids I think drove the idea of evaluating these gastrointestinal problems in a way that work ups happened.

When I started looking at the medical literature at that time, I found that I

didn't get a lot of guidance about what I should be doing, what I should be saying to patients, what I should be thinking about in terms of taking care of these individuals.

A lot has changed. In 2018, 20 years later, we now really accept that gastrointestinal problems are common and in fact maybe one of the most common comorbidities in the diagnosis of autism. It seems to be likely more common than the general pediatric population.

We are going to talk about a paper that we published that didn't show a significant amount of differences in the population of kids with autism to kids who are not on the spectrum. But we didn't find - we found things. We were looking for things. We were considering gastrointestinal issues. We didn't find that there weren't these

problems. We found that they were very similar to the community.

I think that with all of this progress, one of the dilemmas for families is that pediatricians have been made aware of this. Gastrointestinal doctors have been made aware, that we really feel strongly that these gastrointestinal problems exist, but they might not still be confident about providing care themselves. I think that's the progress that we talked about earlier today. How do we get the idea beyond a supported piece of literature and become active caregivers about these issues in the community.

I want to start by saying you can find quotes that talk about gastrointestinal issues all over the place. There's a paper early on that talked about 8 percent

prevalence of GI issues and a paper that says it happens 90 percent of the time.

And now when you read newer papers, they reference this broad range as if it has any value. I think one of the things that we have learned over time is that we have to get better about really vetting the data.

And one talk I gave a few years ago to our LADDERS conference was to try to talk to families about how to critically read the medical literature. That was the biggest flop I ever had as a speaker because if I was critical of a topic that was near and dear to someone, I seem to be discounting it when what I was really trying to give people some guidance about was how do we value what information is out there so that we can really be good informers to the community. I think that is the problem of Google

University. I can find something on Google that will support my position, but it may not be meritable. I think we really have to help the family as advisors.

One of the things that I think is important is we have to say yes, I'm aware that these ideas are out here. But here is why I can't advocate for that idea yet. Here's why I'm not willing to support that this hypothesis has come to be. I think that is where that confidence has to come. Pediatricians do not feel like they have enough information to feel confident about talking about that.

As we narrow in on better literature, we can say with several studies that the prevalence of gastrointestinal issues is pretty dog gone common and is more common relative to the general pediatric population.

One of the first papers that said that was the Valicenti-McDermott paper that talked about 70 percent of children with autism had gastrointestinal symptoms compared to 42 percent of children who had other developmental disabilities and compared to about 28 percent of children with typical development.

I'm going to refer to a bunch of papers as a way of making the case. I'm going to try whenever possible to show you the reference of some of these papers because I know people will want to go back and look at this. That's how I am going to present some of these ideas.

We became really involved in this during this time as well. I certainly saw a big spike in the number of children who needed to be seen with autism in that 1998 period of

time. I had just moved from private practice into the LADDERS program, which subsequently became Lurie at Mass General. And the day I moved was the day before the Dateline NBC video showing secretin and Dr. Horvath's work. And the third day I worked at Mass General my clinic was full for the next nine months of people who wanted GI evaluations. It really brought me to saying I need help. I need to try to get help in evaluating this literature.

In 2008, we were able to bring together a consensus group of researchers, sponsored by Easter Seals and the Autism Society of America, the Autism Research Institute to try to get a consensus on the literature that was available at the time. Those consensus meetings were condensed into a couple of papers that were published in 2010. There is

the link that you can go directly to those papers. I think they are still relevant and I am going to explain why.

Since that time, other people have supported what we said in those papers that gastrointestinal issues are common. One of the papers that talks about that was the Emory paper, Barb McElhanon's work that showed that there were common gastrointestinal symptoms that were seen in the autism population. Diarrhea, constipation, abdominal pain, acid reflux were the most common things that they saw. Those are the most common conditions that we see in the general pediatrics population.

When you look at the prevalence of those conditions in children with autism, the numbers are about right too. Constipation is by far the most common. That's now been

supported by the Autism Treatment Network's papers and other papers.

What they found in their meta-analysis, which was an analysis of multiple papers and bringing together a larger patient population by doing that was about a 3.2-fold increase of gastrointestinal symptoms in children with autism.

I think the newer data depending upon which papers you might include, we can pretty much support that somewhere between 50 and 70 percent of children with autism will have times at least in their career of gastrointestinal symptoms. They may not be present over the life of their care. We have kids who we have seen over the years who had severe diarrhea, severe abdominal symptoms as younger children. And when we see them later,

they come back with other symptoms or they have cleared those symptoms.

I think that the idea of assessing longer term symptoms and that longitudinal tracking of these individuals is going to be very important as we characterize the conditions.

When we looked at why people felt that children had gastrointestinal issues, there were early hypotheses and there are subsequent hypotheses. One of the early hypotheses was this idea that products in food, gluten and milk, in particular, might have a chemical property that looks like opioids in the brain. If the gut is not healthy, those substances can get to the brain and cause brain dysfunction.

I would contend that that literature has pretty much been excluded at this point. That

there is no link of opioid receptors in the effect of autism. There is a lot of literature that suggests that there is increased permeability of the gut in these children that might set these children up for these peptides to get to the brain. But individuals who have these high peptide measurements who have celiac disease don't get brain dysfunction or autism as a result of having these circulating peptides. We don't have a great way to tie that theory up. I think we should look to other issues.

Increased intestinal permeability may have bearing in other ways. That chemical byproducts of bacteria or other things might get across the gut line and may get to the brain. I think that is extremely relevant.

The idea of colitis or an autistic enterocolitis was also one of the early

discussions. I think that it is easier to suggest that at this point, we do not think there is a very characteristic colitis in these individuals. There are certainly some individuals that we find in the process of our work up who have colitis or who have other inflammatory type of conditions. I think it is really important to investigate for those possibilities. But I don't think that is a distinct entity and I think that has been fairly discounted at this point.

What we think is true that holds up is that there are a variety of conditions that now continue to have a number of papers pointing to them. Chronic inflammation in the GI tract is common. One of the evaluations that looked at that was Dr. Horvath's paper way back when. That's one of the very few papers that showed a very high frequency of

esophagitis and inflammation in the esophagus likely from acid reflux.

More recent papers have also suggested inflammation in the upper GI tract from a condition called eosinophilic esophagitis or allergic esophagitis. There are now several papers that suggest that that's common and maybe more common in this population than the general population.

There are several studies that show increased intestinal permeability in a variety of settings. We did a study where we looked at intestinal permeability at the time that we were doing endoscopy on patients and interestingly the increased permeability did not correlate to the presence of inflammation or the lack of inflammation. Those patients who have permeability problems may not be defaulted to those kids who may have

inflammation in their gut and I think that is important.

Several papers have looked at digestion errors. That was a focus of our work at Mass General. We published several papers where we saw a high frequency of lactose intolerance, a high frequency of other carbohydrate digestion issues and that's been supported by other groups. It's also been looked at and discounted by some groups. I can't tell you that there is a firm belief that this is the case for everyone.

We are now very, very focused on the next category and that is this idea of disruption of the typical microbiota in the GI tract. If you look at PubMed now and you look at the reference of gastrointestinal issues and autism, 20 years ago you wouldn't have seen a paper a month. At this point, you

are seeing multiple papers per month and half or more of them are related to the microbiota or the metabolome, which are the breakdown products or the byproducts of bacteria in the gut and how they may be affecting the gut and how they may be affecting the brain. Clearly, that's the primary focus that gastrointestinal docs have been really zeroing in on that might be accounting for some link to autism and behaviors if not causation of some of the autism issues.

There is a lot of work that is still going on looking at immune dysregulation and Paul Ashwood has done a lot of that work. Harumi Jyonouchi in New Jersey, has done a lot of that work looking at inflammation and the like. It's really exciting to be able to look at the information that has come. We have learned an awful lot in the last five

years. But really when we look back at that, a lot of the things that I am referencing weren't things I was talking about the last time I spoke here back in 2015.

We also talked a little bit earlier in the day about allergy. And certainly, environmental allergies are a topic. But food allergies and sensitivity is a hot topic. We know that our families come and they are very interested in talking about this because they are interested in whether we should try a dietary restriction. Should we stop milk? Should we look at gluten? Can we test for that? Are there other diets that might be helpful?

We know that in the general pediatric population the prevalence of food allergy is somewhere between 5 and 8 percent. There are several studies now looking at allergy in

children with autism and we find that the food allergy frequency is quite high in some of the smaller studies, not quite as high when the studies get larger populations. And the way that we test for that by doing IgE mediated skin testing or blood testing, there is a higher frequency. Almost twice as high in the children with autism compared to children who do not have autism.

Families report food sensitivity really frequently. Forty percent of families say that they see some behavioral change or some issue around food intake that makes them worried that their child has food sensitivity.

We now know as we have started to look at adults that this carries through into adulthood. And adults have this very common condition of non-celiac gluten sensitivity.

They report brain fog, but don't have an intestinal lesion. We do not have a single test that can prove or disprove that. We use clinical guidance on that. There isn't a guaranteed test that is going to tell us for sure how well people handle these foods. We really have to be thoughtful in our history and in our involvement of nutritional people to help guide that.

This is the paper that talks about the finding of a higher frequency of food allergy based on really standardized allergy testing. Even with the tests that we have, it looks like it is about twice as common as the general population.

Feeding disorders are, I think, an immense problem and they are one that we have really discounted. For me, a lot of years I discounted it because I attributed a lot of

textural sensitivity or feeding type issues to gastroesophageal reflux issues. I would try to get those things taken care of by treating reflux or the like.

But clearly now, we have an understanding of a condition called ARFID. That is avoidant restrictive food intake disorder. That has got its own DSM diagnosis. And it is common in individuals with autism. These are a variety of factors that account for why children or adults will narrow the type of foods that they take in, the texture of foods that they take in, the classes of foods that they take in. Some of that may be behaviorally based. Some of it may be physically based. But at least in the last five to ten years, there are now a variety of therapists. Speech therapists are very involved in taking care of these places.

Feeding clinics are all over the country doing evaluations for this condition and they do a wonderful job. There is a lot of progress being made in broadening out the diet of a lot of these individuals who have the feeding type issues. It is a big problem. It probably has been unrecognized for a very long time.

There has been a lot of discussion about nutritional deficiencies. And nutritional deficiencies may come from a variety of reasons. Patients who have selectivity, patients who have been put on special diets to restrict certain things may well develop some of these nutritional deficiencies. But even children who have not been placed on a diet seem to have certain things that they come back looking deficient in.

They often will have protein deficiency on a dietary calendar. They will have iron deficiency, which may affect sleep. They may have zinc deficiency, which may affect taste and sensitivity of the skin so that it is important to consider those deficiencies. They often have vitamin D deficiency. They have a fiber deficiency.

One of the best papers looking at that was a paper recently by Jim Adams and the Arizona State Group in their Fecal Transplant Study. They found that individuals with autism had an amazingly low amount of fiber intake. That may have some bearing on what is going on with the bowel environment. I think it is quite relevant. They may have other vitamin deficiencies as well.

There have been now several groups that have made suggestions about nutritional

management and what we should do to evaluate the nutritional status of our individuals. One was Rashelle Berry and Will Sharp who were at the Marcus Center for Autism down in Atlanta. They are very thorough. They are one of the most wonderful treaters of ARFID in the country. I take their advice.

This is an algorithm that you can't see, but it talks about some of the process that they go through to work up nutrition in those individuals.

We, at MGH, did a study looking at number of intestinal functions at the time that were doing endoscopy on patients. While we were doing endoscopy for gastrointestinal symptoms, we were able to look at carbohydrate digestion, intestinal permeability, and compare them to inflammatory changes in the biopsies. And

what we found was that we couldn't find a higher frequency of any particular condition in the individuals with autism that we did endoscopy. They didn't seem to have a higher frequency of esophagitis or a higher frequency of celiac. Now that has been well supported by other literature or other type of conditions, but they had bindings. They got to an evaluation at least at our institution because we're willing to evaluate those kids. I think it's important to at least not discount the symptoms that bring them there.

At this point and I will not take an enormous amount longer because I am passed my time that I am supposed to be talking is I think there are a lot of issues looking at whether gastrointestinal issues could cause autism and the idea that alterations in the

microbiome or these nutritional intake factors might be accounting for issues I think is really worth considering. And whether bodies are sensitive to inflammation anywhere might be a factor in how brain function happens.

There are a number of papers that have looked at the intestinal microbiome makeup, what the flora looks like and how that affects changes. We know that early antibiotic exposure, C section delivery, all sorts of early risk factors seem to set off the microbiome and might increase the risk factors for autism. We got to be starting to look at things even prior to the time that some of these children come out the door.

I tried to summarize some of these risk factors in a review paper that was in Clinical Therapeutics, talking about the

potential factors in these microbiome disruptions. That might be a way to talk about some of those issues.

Another paper that I think everyone in this room should read if they haven't is a paper that talks about the use of a probiotic fermented milk and the effect on brain function by functional MRI. This is work that was done by Emeran Mayer's group at UCLA. And what they showed was that they could alter the pain sensitivity in the brain, an emotional sensitivity in the brain simply by giving this probiotic mix in fermented milk. That's really has launched that group on the idea that the dietary intake and alterations in the microbiome may have bearing on irritable bowel syndrome, pain syndrome, depression, anxiety, and perhaps other neurological conditions. This paper lays out

the landscape of disruptions of the microbiome. It's a tough read, but it is extremely helpful to get your mind around these ideas.

The idea that changing the flora might alter autism behavior has been described by Sarkis Mazmanian's group and Elaine Hsiao's paper. They gave a probiotic that is not currently commercially available in the United States and altered autism behaviors in their animal model. This is getting clinical trials right now. We'll learn about this later. It's not currently available in the United States or anywhere to my knowledge to look at.

The idea of changing your microflora has really become a popular topic in general medicine right now. This is the idea of fecal transplant. This paper that I have given you

the reference to is Dr. Kang's paper, Jim Adam's group at Arizona State, looking at the idea of giving fecal transplantation and seeing the impact on autism behaviors as well as gastrointestinal symptoms. This paper is a promising preliminary study.

Currently, there are studies that are going on. This is not a commercially available product. It's not something that families can or probably should seek at this point until we get some more information. But it certainly has some promise in children who have severe intestinal disruption of the microbiome. Things are happening that I could not tell you about three years ago. It is really exciting to be hopeful about that.

It sends me back to what we said back in 2010 in our consensus paper that I think is still relevant today for families and that is

that children or individuals with autism who present with any gastrointestinal symptoms really warrant access to care. They warrant seeing a GI person and working through whether some of their symptoms might be fixable by trying to help their gastrointestinal symptoms.

One of the things that we reported in that paper in this consensus gathering and have been supported by the Autism Treatment Network work and a number of other papers since is individuals with problem behaviors have a very high frequency of gastrointestinal disturbance. The two highest frequency issues in children with problem behaviors, self-injurious behaviors and aggression is nonverbal state, your inability to express what is going on, and gastrointestinal symptoms. When we see

individuals who present with those kinds of symptoms that is a red flag for us to at least try to do a very good medical history, really tease out whether there could be underlying issues.

They are not all gastrointestinal. Some of them are headache. Some of them are dental. Some of them are coming from a whole host of other factors. It opens the door for our community to look at these individuals medically and say what is it that we may be missing. It does not keep us from treating the behaviors. In fact, I think it is really important to treat the behavior. But a benefit of responding to behavioral treatments does not keep you from seeking medical underlying issues.

This is the second paper that we wrote in 2010. It gave a list of recommendations to

gastrointestinal docs to do a work up and to pediatricians to do a work up. This is a paper that I've asked families to print and bring to their doc. If they've got concerns about doing a medical work up, copy this paper out. Write down on the paper what you think your child has and let's go talk about it with our physician. That was the intention of the paper.

My conclusions. Certainly, GI issues are common. Diet therapies may have a place. I did not go through the studies that have looked at dietary interventions because they are kind of all over the place. I think they're all over the place in part because we have not figured out who deserves what types of treatments yet.

Problem behaviors can be medically-based and behavior is a communication tool. When

kids have behaviors, we think we should talk about them as medical issues.

Here are some of the resources we talked about earlier, the places where we've got things talking about these problems that people can access.

Thank you to the people that have worked and supported me at all of my places and family and all. Thank you because I think this community has been tremendously supportive of our work and they were early believers and supporters in taking care of these medical issues.

DR. DANIELS: Thank you. Now we have some time for discussion. Louis.

DR. REICHARDT: I would say that there is certainly lots of evidence that the microbiome can feed back on the brain. In fact, all the genetics of autism points to

alterations of the nervous system. There are so many aspects of the nervous function, the enteric nervous system, sensory nervous system that impinge the GI tract. It just seems to me that it would be very interesting from a research point of view to put more effort into that.

We know that there are alterations, for example, in some mouse models of enteric nervous system function. We also know that sensory hypersensitivities and autonomic dysfunction can affect GI function. These are all abnormal in autism.

I guess one of the questions I have specifically for you is if you compare, for example, GI function to other sensory abnormalities, are there correlations? Has this been looked at? I realize there has not been nearly enough work on the enteric or

sensory innervation of the gut in autistic models.

DR. BUIE: I think functional testing has been very difficult. You well know the work that Kara Margolis is doing at Columbia is very focused on the SERT gene and serotonin regulation at the gut lining. The issue for a lot of us is how do we measure that sensitivity component. There are very few tools that we can do. We used to do a test where we would put a balloon in the rectum and stretch the rectum and see what the sensitivity was called the barostat test. That has not clinically been supported. Nobody is currently doing that as a testing tool. What we are left with is a lot of testing that looks at motility, transit type studies. These are tremendous difficult tests to do on individuals with autism. To strap

them in and do some of these tests or put tubes where they need to go to do that testing, it is a limited population that we have been able to do some of that function testing.

DR. MAZUREK: I would just add to that. In examining the ATN data, we did rely on parent report to look at symptoms of sensory sensitivity and anxiety in relation to GI problems and they were highly related in the ATN sample.

DR. REICHARDT: Oh, that's interesting. At the risk of being a record, I just ask Jim. Correlations with some of the genetically characterized cohorts.

DR. BUIE: I am not aware that there is enough information to support some of that.

DR. DAWSON: Just a couple of questions. One, following up on Louis' comment about

sensory sensitivity. There is actually pretty good literature on the relationship between sensory sensitivities and GI. We also received a Department of Defense grant to look at early research, risk factors for the development of anxiety in preschool aged children. We included Grace Baranek's sensory over responsivity. It's an actual assessment of that and found a very high correlation between GI problems and sensory sensitivity.

But what I was going to comment on is the relationship between the microbiome and neurodevelopment. I actually just last Monday went to a conference on precision medicine and saw Jeff Gordon speak. It's the second time I have heard him. I do not know if you know of his work, but it's amazing.

Basically, what he has been doing is studying children in Bangladesh who have not

received the right kind of nutrients and their microbiome is very altered. It's highly correlated with the development of neurodevelopmental disorders.

He has actually developed based on really elegant animal model studies where they have gone in and actually identified the specific proteins that are altered by the changes in the microbiota and then developed a food product that restores that and then has done randomized clinical trials in Bangladesh where he has provided this food product and showed changes in neurodevelopmental outcomes. It's stunning work, but it definitely has I think shown definitively the relationship between microbiome and neurodevelopmental conditions.

DR. KRIPKE: You were mentioning in addition to the sensory, the motor issues

that may be related. I am interested in any research on that because I suspect that might be part of the issue. I am also wondering in terms of the treatment end of things whether there are an awful lot of autistic people on chronic polyethylene glycol for constipation and what's the long-term safety of that. I know that people are starting to look at that, but I do not where the research is now.

DR. BUIE: I think that motility issues are again difficult to characterize. Certainly, there are a large number of individuals who have constipation and that can be a manifestation, a poor motility downstream although there are other things that account for that. Problems with relaxation and outlet, some behavioral factors, hydration, a number of things can affect that.

I would contend that the polyethylene glycol products are the most commonly used treatment for constipation right now, but there are many. My own experience is that if I have a sense that there is slow motility, if I see belly bloating or distention or the like, I may not tend to pick that product. I may tend to pick other products that will help with bowel contraction to really move things along.

The study that was recently published looking at toxicity or complication risk from polyethylene glycol was relatively encouraging. It was suggestive that there were not significant alterations of the microbiome when they were given a protracted course of polyethylene glycol. It had only been really approved by the FDA for two weeks' use or less so looking at it in a

longer-term use. There did not seem to be alterations in the microbiome. There weren't remarkable differences.

The one note and the conclusion of the paper was that there were no complications from long-term use. I would say that upfront.

They did find a measurable presence of polyethylene glycol in the bloodstream of those individuals. It was below the FDA guidelines for safety. This non-absorbable product that shouldn't be causing any absorption of that, there was some level of that product in the blood, which I view still as a concern for me to keep it on long term if I can find alternatives that are as safe or safer to make a difference for those individuals.

I think there are a lot of products that people do not avail to themselves. There are

aluminum-free magnesium products that are helpful. There are softeners.

One of the things that I took away from the paper recently that talked about fiber, I have really come back around to fiber. It is the first time that I have really recommended fiber for bowels in many years because the earlier pediatric studies did not suggest that fiber for constipation was helpful. But when we find that these patients are significantly depleted, I have now found that fiber has been very helpful for putting it back into the program in many of these kids. I am supplementing that a lot more often.

MS. GASSNER: I just would want to reiterate once again. I am on a Facebook group of over 500 people in the New York City area that are part of the Ehlers-Danlos community. Again, the overlap. Somebody

posted a question. How many of you have or have family members who have Ehlers-Danlos and autism. There were like 125 responses. Now, I realize that is soft science, but it's significant. We really - I cannot emphasize especially when we are looking at motility issues, the need to really rule this in or out with this population.

That being said, as a mother who just realized her son has avoidant restrictive food intake disorder.

DR. BUIE: I am so glad I came.

MS. GASSNER: Dear God. My question is - and this is something IACC might be able to help. I could ask you personally, but the entire community wants to know how we can find a provider that can help this. The IACC can put together some of these resources to help families find help. He has no sense of

taste, no sense of smell and has learned to check the dates on everything from milk to deodorant as a coping strategy for this limitation. We are pumping him full of chewable vitamins and fiber supplements because we know he cannot possibly be getting everything he needs. I am worried about the long-term implications. I am just one case.

I am asking on behalf of all the parents who have albums and albums of poop stories to share. Please dear God. How can you help us find providers to address these issues in this population? Because this is a kid who went to college and we are still having this issue.

DR. BUIE: I think that is a common problem. A lot of people will contact individuals and I know Geri has this experience at Autism Speaks. There was an

effort with the Autism Treatment Network. There have been efforts at a whole bunch of different levels to try to provide information about providers for different conditions. But the status changes so frequently that to keep an up-to-date list for these issues is really, really tough.

I am really heartened especially around the ARFID diagnosis. That's a condition that the speech and language people have been really focused on for a number of years. There are providers all over this country who are exceptionally good at this.

MS. GASSNER: SOPs.

DR. BUIE: What? Yeah. If they don't know their network is good enough that they spread the word and they can tell you who in the community or near the community may be your best resource for that or where your local

feeding teams are, that's a pretty connected, interconnected group of people.

MS. GASSNER: Thank you.

DR. TAYLOR: Greg.

DR. BARNES: Tim, I wanted to ask you. A number of the neurodevelopmental genes give an oxidative stress and possibly inflammation in the brain. Do we think the change in the microbiome leading to abnormal metabolites getting in the blood - do we think that is interacting with the immune system in some way?

DR. BUIE: I think there are people who feel that it is. One of the things that is pretty interesting to me is that we certainly have a number of individuals who have inflammatory bowel disease or remarkably biopsy-supportable inflammation. But I think there are a lot of folks who have very low-

grade inflammation and they're really sensitive to inflammation. Whether that is oxidant stress or things like that, they're often responsive to interventions that are helpful on the antioxidant level. I think people are interested in that.

Where we're going to learn a lot of that is the metabolomic studies. That's in its infancy. Our ability to evaluate those chemicals at the gut level really is within the last three to five years. You will see papers within the next two years that are going to characterize a lot of those products. And I think a lot of them are going to be related to oxidative stress and the like.

DR. BARNES: I am just really interested because I have at least one child that is very sensitive to these sorts of things who

has a significant gluten disorder. Then I've got another child actually who has intractable rolandic epilepsy who has ulcerative colitis. When the ulcerative colitis is worse, the rolandic epilepsy is worse. It's really quite fascinating.

DR. BUIE: Can I ask you a question in that regard? Can pain cause epilepsy? Can pain cause seizures?

DR. BARNES: That was the other comment. Thanks for the cue. If you treat GI problems that's one of the best anti-seizure drugs you could ever do.

UNKNOWN SPEAKER: Oh really?

DR. BARNES: Oh, yes, yes, yes. This pain, that pain that they get from - and plus you alter anti-seizure drug absorption between the two. Yeah. And really that goes for any medical condition whether you are

talking about sleep, whether you are talking about asthma or whatever. If you make the medical issues better, the seizures are better, but certainly GI specifically. Because I've sent many, many people to the GI clinic. They have come back cured of their seizures. They are suddenly not resistant to the anti-seizure drug they are on.

DR. TAYLOR: So I have Antonio, then Clarissa, then Sam.

DR. HARDAN: Very good. I am trying to think about the relationship of gastrointestinal abnormalities or the microbiome and the symptoms in autism, trying to see if it's association or causation.

I want to try to think about it in a different way. If we look at neurogenetic disorders such as Phelan-McDermid syndrome, PTEN mutation, what's there - and these are

clearly neurogenetic disorders, clear genetic abnormalities. What are the rates of gastrointestinal abnormalities or abnormalities in their microbiome? Do we have information about that?

DR. BUIE: You heard earlier of Dr. Bennett talking about a very high frequency in Phelan-McDermid. Since I have a limited number of individuals, I have to rely a little bit on that. It's not published. I could walk through a number of these genetic syndromes. We follow a number of PTEN individuals. They seem to have very refractory, gastroesophageal reflux motility type issues. Costello syndrome. A number of these genetic conditions. They are really refractory to a lot of the standard treatments that we have, maybe more so than my general autism population. I think they

have been small enough. They've been kind of orphan groups to have data on microbiome. I'm not aware of it. Maybe others have started to look at that in some of those conditions. But I don't know that.

DR. KRIPKE: In response to your questions about how do we let people know how to find clinicians who have expertise, until we solve the funding and financial issues, if you advertise, if you gain any expertise and you get a reputation, you basically get put out of business. That's why these registries go in and out so fast because the second you get on it then you get overwhelmed and you lose your job. Unless it is a very - sometimes cardiac people who do a lot of procedures like cardiac procedures can make a living by seeing complex disability back to back, but nobody else can.

DR. TAYLOR: Sam will have our last question before we move on.

MS. CRANE: It's more of a comment. But I was really struck by the consensus statement that said that people with an autism diagnosis who present with GI symptoms should get the same work up for GI symptoms that they would get if they were not autistic. I was so struck by that because you're right. People aren't giving that to us. They are saying GI symptoms are common for autism so fine and not doing work-ups.

I think this is something that I think we should really pull out as a theme from this summit that a lot of the time the barriers to health care are so easily surmountable. It really should not take a peer reviewed consensus statement to tell doctors that if we have health problems, you

should totally evaluate us for them, but that is where we are.

DR. BUIE: Those were such common-sense conclusions that even 23 specialists could come together and agree upon them. When you do a consensus gathering, that isn't so easy. And then I sat the next year and helped the consensus group on early intervention with Lonnie Zwaigenbaum's group, and man, coming to consensus in that group was really tough.

But I think our mission in writing that paper was to write the bill of rights for medical issues in autism. And I hope that is one reason that people go back to that paper and look at it. It really does stand up. I'm grateful that it gets quoted by other papers to keep the idea of it going. It had a value beyond the discussion of the gastrointestinal

issues. I probably won't ever write anything better. That is good.

DR. DANIELS: Thank you, Dr. Buie. We are going to move on now to our next session on sleep with Dr. Beth Malow.

DR. MALOW: Thank you everyone. I'm thrilled to be here. I think David Amaral might have stepped out. But 15 years-ago when I just started doing sleep in autism, I was a sleep specialist and I was pulled into autism because of my kids. I was at a MIND Institute session on sleep epilepsy- no, it was on epilepsy and autism and I spoke on sleep epilepsy and autism. Those were my kids at the time. And now these are my kids. They've grown up. They are both on the spectrum. They're doing really well.

I have to tell one funny story based on that last wonderful talk by Dr. Buie. My

older son, Austin, has ARFID, I think. He actually was on the gluten-casein diet for 15 years. All he ate was Cheerios and peanut butter and milk. When he became six feet tall, it was cured. Then he started eating everything. One cure for ARFID is as our kids get older, sometimes it resolves. Not always.

I just had a few disclosures I wanted to mention. My grant support is from Neurim and ATN. I consulted for Janssen and Vanda. We have royalties from Woodbine House. I'm going to discuss off-label uses of medications for sleep in autism because there are no approved FDA medications indicated for sleep in this population.

These are the questions I thought we would consider in the next 15 minutes. What kinds of sleep problems do individuals with autism experience? What are the causes and

contributors? What are the consequences on the individual and the family? What are the latest treatments and guidelines? What areas are most in need of future research to move the field forward?

I'd like to start with a case to give you some perspective. This is Alex. He's 10. He has autism. His bedtime is 8 p.m. He takes hours to fall asleep. His parents state that he cannot shut his brain down. He takes methylphenidate in the afternoon for his ADHD symptoms. I am from the South so he drinks sweet iced tea with dinner. He plays video games after dinner. He cannot settle down to go to sleep. He leaves his room repeatedly to find his parents. They help him fall asleep by rubbing his back. They stay with him while he goes to sleep. Once he sleeps, they leave. But then he wakes up multiple times during

the night. Sometimes he sleepwalks. Sometimes he comes to his parents' room. He falls asleep there. They are too exhausted to move him back to his own room. He also snores. He kicks his legs. In the morning, it is really hard to get him up for school. Once he gets to school, his teacher describes him as being sleep as well as hyperactive and disruptive. His parents are totally exhausted and totally overwhelmed.

There are a lot of things that we can do to unpack Alex's sleep problems. This is a very typical kid I might see in my sleep clinic on the spectrum. He's got more than one thing going on. He actually has all three of the major categories of sleep disorders. Insomnia, which is difficulty falling asleep or staying asleep. Hypersomnia, which is

daytime sleepiness. And parasomnia, with his sleepwalking.

There's multiple things going on in this kid. I think that's one of the take home lessons, is like it's not all melatonin deficiency or clock genes. I will talk about those in a moment. But there are lots of reasons kids with autism do not sleep including GI problems, including seizures, but not limited to those medical conditions. There's also snoring, leg movements. And as Tim alluded to, you can actually have low iron or ferritin levels from your GI intake, your nutritional intake and that can affect restless legs and leg movements, which can disrupt sleep. Sleep walking.

As I go through these, you'll look in the right hand corner and you will see some of the things that we might want to do for

treatment including a sleep study for the snoring, leg movements, sleep walking, eliminating the tea at dinner, taking the methylphenidate earlier, turning off the screens, teaching Alex to fall asleep on his own because we need whatever we have when we fall asleep to keep us from waking up. If we fall asleep with the TV on and we wake up in the middle of the night, which we all do. We all wake up multiple times a night, but we go right back to sleep unless the thing that we needed to fall asleep is no longer there. It may be TV for us. It may be rubbing Alex's back for Alex. If he needs his parents in the room to help him fall asleep when he wakes up, he'll need them to be there too so teaching the parents to help him fall asleep on his own is really important.

And then sometimes a later bedtime can help. Alex is now ten. He's getting into puberty. We know with puberty, everything shifts. Melatonin secretion shifts. Bedtime needs to be a little later.

Now, imagine how you might feel if you went to bed really early and you are lying awake unable to really articulate. Let's say you have limited verbal skills to tell you parents I am just not sleepy. You are going to act out. You are going to have bedtime resistance. Sometimes even pushing bedtime a little later is amazing.

I just want to go back. These are the three buckets. They are very simplistic, but I think about medical conditions, environmental behavioral conditions like the screens, and then the biological conditions. I wanted to talk about a couple of areas that

have gotten some real high interest recently. One is genes and genetics. In particular, clock genes. The Nobel Prize in medicine last year went to those who discovered clock genes. This is pretty exciting. There has been some work.

The clock genes basically work on the circadian clock, which is the suprachiasmatic nucleus in the brain. There have been a few studies looking at mutations in clock genes being more frequent in autism.

The other area is light and melatonin and circadian rhythms. The clock genes do play a role in regulating circadian rhythms, but also light is a big factor. Light enters through the retinal hypothalamic tract, the suprachiasmatic nucleus and you can see the pathways here. And it affects melatonin so endogenous melatonin, the melatonin we make

ourselves is a hormone of darkness. Light suppresses melatonin. When we have screens and when we have exogenous light, it interferes with our melatonin production.

Melatonin is very interesting because there have been multiple studies showing that melatonin can be abnormally processed in autism. The top two were older studies looking at blood levels and showing that kids with autism had lower, more blunted levels. You can see that on the screen in the slides.

And then Melke and Bourgeron recently sampled blood in the morning. They found that both melatonin levels as well as the enzyme that synthesizes melatonin, ASMT, was decreased in autism. Although their blood levels in the morning and it is hard to know what that means because melatonin is secreted at night.

Tordjman in the upper right hand looked at urinary melatonin metabolites, 6-sulfoxymelatonin, the major metabolite, and found that in prepubescent kids, there were lower levels, implying that either there is less melatonin or there is something wrong with the breakdown. These have been very tantalizing work.

I did want to say that in our work the first study was funded by NICHD. It was actually a melatonin treatment study, but we got overnight blood sampling in our kids before they got the melatonin supplements. These are kids who all responded to melatonin. But before they got treated, they had normal endogenous melatonin profiles. There is one shown here.

You can see - the blue is where the child was following asleep by actigraphy in

the week before the sampling. But they are very nice profiles in terms of what you see in the literature in typically developing kids with amplitude and timing of melatonin.

And then on the right is a study that Autism Speaks funded looking at dim light melatonin onset and saliva sampling. Again, some of these adolescents had sleep onset insomnia. They had normal endogenous melatonin profiles also.

The point of this is - and these were small. These were small numbers of kids. But I think it makes the point that not every kid with autism who cannot sleep has melatonin deficiency. There's lots of other reasons. I think there is a lot of heterogeneity going on in this population where there's lots of reasons like GI, seizures, medical,

environmental, behavioral why sleep may be affected.

I did want to make the point. We heard earlier that sleep can affect emotional regulation, behavior. Even core symptoms can be affected. Functional MRI studies have shown increased amygdala activation and decreased connectivity between the prefrontal cortex and the amygdala. The amygdala is a fear center. It regulates fear and emotion and anxiety. Our prefrontal cortex keeps those centers in check. But if you are sleep deprived, people have shown both in adults and in kids, not in autism per se, but in adults and kids that there is increased activation in the amygdala circuits and decreased connectivity. This may be why when we're sleep deprived that we are more apt to send that nasty email or send out that tweet

that we shouldn't send out. It really has been linked to a lot of problems in emotional regulation.

And then in the Simons Simplex Collection, I was happy to see someone from Simons here, Olivia Veatch, who was a postdoc with me, who is now at Penn in a faculty position, showed that in more than 2,700 children with autism, severity scores for social/communication impairment and restricted and repetitive behaviors were increased when the kids were sleeping less. Now, why is this? It could be shared genetics. It could also be you are sleep deprived. You are not going to do as well in your therapies or your parents are stressed and they are not going to be able to advocate for you as much. Sleep is really important regardless of whether it is getting at the

underlying biology or some of these other social determinants of health that affect the kids.

And then Micah Mazurek's paper. She mentioned I believe a little earlier the association with sleep and physical aggression, irritability, inattention, hypertension. And night waking seemed to be the most affected or the most important.

And then this is just mothers of children with autism stress study, showing that one of the major things that parents need is to get enough rest or sleep. It should not be surprising, but it was nice to see that this was documented.

Let's go back to Alex. What do we do? What is our goal? There haven't been a lot of practice parameter studies. We did one in the

Autism Treatment Network a few years ago. Dan Coury is on this one with me and some others.

The first thing we recommended is to hunt hard for medical co-occurring conditions that affect sleep and that includes GI, seizures, also sleep apnea, other things.

And then try to do behavioral approaches because they really do work so turning off the screens. I starred over here what those would be. Teaching Alex to fall asleep on his own. They do work. The challenge is implementing them, particularly if the family is stressed. As we get into the teenage and adult Alex that whole implementation science we talked about earlier. How do you get an adult with autism to do cognitive behavioral therapy for insomnia? Those are, I think, really exciting areas. But I will say that behavioral approaches do work. We had a paper

in JADD showing that through ATN work that we did.

And then consider medicines for overwhelmed individuals and families, but really try to do number one and number two. While you are giving them meds to help them sleep, really try to implement the behavioral strategies because it will be more effective.

I wanted to mention our Autism Treatment Network AIR-P toolkits that are all available for free on the web and walk people through visual schedules, bedtime passes, and various other things. We even have one on melatonin now.

Even kids with limited verbal skills can be taught behavioral techniques through schedule boards, through these sensory - trying to improve sensory, including music, white noise into the routine in their sleep.

And then you do not have to let a child necessarily cry it out. They can learn how to fall asleep with kinder, gentler techniques, which are more acceptable to parents with kids with autism such as having the parent in a chair in their room, but with the back to the child so the child is not fearful. But they learn how to fall asleep on their own. Or moving the mattress that the child is on next to the parent's mattress and then you gradually move the parent's mattress out of the door and reward the child in the morning.

There are many different medicine options for insomnia. I just wanted to say that they are mostly understudied. Melatonin and melatonin agonists have been the most studied. They are safe. They are well tolerated. I have some references here.

I want to point out that there are some new prolonged released preparations that improve sleep duration that can be swallowed easily. They are very tiny. And then melatonin and behavioral therapy is the most effective. You always want to think about the two combinations together whenever you can. A medicine and behavior.

And then we did some work with gagapentin, showing its efficacy.

I just want to point out here that even for things like quantity in the alpha-adrenergic agonists, there were two studies. One had 17 kids. One had 6 kids. They are very small. There are no studies on trazadone. There is one study on mitazapine.

I will say that benzodiazepines - even though they have not been studied, if you think a child has sleep walking night

terrors, you definitely want to make that diagnosis because if you start them on Clonazepam, it oftentimes works pretty effectively in that condition. I wouldn't use it just in typical night wakings though because they can get tolerance pretty quickly.

And then these other ones are just randomly tried. Over-the-counter drugs are very frequently used, but we have to worry about interactions with other drugs and safety of these drugs and possible contaminants.

Let me go through what I think are future directions for us to discuss. One is are any of the old or new medications for insomnia effective in autism and what are the side effects across the lifespan. We just don't have very good trials. There hasn't

been a great deal of interest in the pharmaceutical company in studying autism, which we could discuss.

Once we know what medicines do work, how do they compare? How would they compare to melatonin in terms of effectiveness and side effects? Can medications and behavioral treatment work synergistically? I think they can. I think we need to do that in our trials.

And then this whole implementation science. How do we get overwhelmed parents of children with autism to use behavioral strategies when they're overwhelmed?

What about teens and adults with autism? How do we motivate them? Do we show videos? Do we have coaches? What do we do to make this work?

And then finally, can genetic or biomarker studies guide our treatment plans? Would it be helpful to know that a kid is metabolizing a medication quicker or less quick? Are they having more side effects? I think that measuring some of these melatonin metabolites might also be very useful in trying to come up with a personalized treatment plan for an individual whether they be a child or a teen or an adult.

I appreciate your attention. Thank you.

DR. BUIE: Thank you so much. Question about melatonin. Earlier this year, there was a caution that came out talking about protracted use of melatonin. Can you speak to that?

DR. MALOW: Yes. There's a lot on the Internet particularly if you look at what parents are posting. There are concerns that

have been raised about puberty being blunted in kids with autism so if you think about it when they take melatonin. Melatonin in animal models basically it drops when you enter puberty. The idea is if we are giving exogenous melatonin, supplemental melatonin to our kids, could we somehow be preventing that drop? And then the idea is that they are not going to develop puberty because they are not dropping their melatonin levels.

I would say a few things there. First of all, we don't know that the melatonin drop is what is causing puberty. It's probably more complicated than that. There's a lot of other factors that are going on with releasing hormones and all in the pituitary and hypothalamus.

And then number two, I would say there are so much use of melatonin in our

population and also in the typically developing population in young kids and teens that I would be very surprised if there was a change in puberty being affected by that. I think we would hear it or see it. With that said, I think we should study it.

I have to say that it was written about very briefly, in one of the circadian papers by Neurim Pharmaceuticals that came out recently. I have actually asked them since I was part of their study if I could work with them on a more involved paper and they agreed. They basically, what we did - I was one of the sites. We had to do puberty exams. We had to do Tanner staging throughout the trial when these kids were getting melatonin. A lot of them were like prepubertal when they started and actually they had to be to be in the study. And then they followed them

through. Many of them went through and developed puberty. We actually have data showing that the rate of developing puberty was not changed by being on melatonin. But I think that those data have to be published.

And then I would love to look at large EMRs and study the relationship between melatonin ingestion and puberty. I think one of the challenges is melatonin is not your typical prescribed drug. Finding it, you have to use natural language processing in the medical record to figure out who is on melatonin.

Based on what I just said, I really feel like the benefits of melatonin outweigh risks in this population. With that said, I am a big behavioral advocate.

One thing I say to parents is let's say a 5 year-old - let's do melatonin behavioral

therapy. By the time your child is 8, maybe they can come off of the melatonin and just be on behavioral therapy. That is kind of where I go with my population.

MS. SINGER: We often hear about kids who do not sleep because they have too much sugar or the parents give them soda before bed and they have caffeine or they give them too much video games. We have to move beyond the sleep hygiene hypothesis at this point.

But we are also hearing that maybe bad sleep is because of pain from constipation or maybe the kids are having seizure disorders during the night and that is waking them up.

My question is, have we given up searching for an underlying biological cause of sleep disorder in autism? A few years ago, we were talking about acetylcholine regulation. Where did that go? What studies

are being done to see if there is a direct underlying biological cause?

DR. MALOW: It's a great question. I do not want to undermine the fact that there might be a biological cause. I just want to make sure that we don't neglect the other things. Because let's say you wanted to do a study looking for acetylcholine or something else and the kid was doing their screens. They also had reflux and seizures. You would not be able to prove it because you would get bitten by the fact that they are doing all these other things.

All I would say is number one I have seen behavioral treatments work and I have also seen medical conditions like seizures, GI problems, sleep apnea, definitely cause sleep problems. I feel like we do not want to

neglect those medical causes and we do not want to neglect the behavioral causes.

And then when we look for biological causes, I want there to be a clean slate so that we can test - if we find something that could be a culprit like clock genes or something. I don't know. Whatever it is. Or a substance that we identify. We want to design a trial carefully that we are not going to miss the result because the kid is doing screens or something else. That is all I ask.

MS. SINGER: But are we doing those studies? I feel like we have moved beyond the point where - I cannot say with 100 percent certainty, but I am pretty sure that most parents now know not to give their kids coffee before bed. Can we now move on to the studies that are looking at the underlying biological causes?

DR. MALOW: I think they know not to give coffee. I hope they do. But I still think that there is a lot of things they are not necessarily doing particularly I think the co-sleeping, the fact that they have the night wakings because they are needing their parents in the room to fall asleep. That is a huge one.

I would love to see that. I would love to see more research on sleep. I would say that as we design those studies, do make sure and do pay attention particularly to the medical co-occurring conditions and make sure. The one thing I don't want to see is I do not want to see those neglected when those could be driving.

I agree with you. I think we need more studies on sleep. We need more studies on what could be driving the sleep. I'm just

making the argument that I want to make sure they are carefully designed and look at these other factors.

DR. TAYLOR: Dena and then Kevin.

MS. GASSNER: I have been sitting here debating whether to discuss this and I am going to go for it.

DR. MALOW: Food for you.

MS. GASSNER: Yeah. I know most of the things we have done, we talked about kids today. I just wanted to share that I was misdiagnosed with bipolar disorder because I couldn't sleep for ten years. It was the implications of the co-occurring sleep disorder that was manifesting in the mood disorder. I really didn't have bipolar, clearly, because I have not been treated for it since. And the treatment for it nearly killed me because I wound up on the ten-year-

old cocktail of medications to treat the sleep disorder.

Let me just say to you too though that now I take Trazodone. I have been on it for ten years. I just added melatonin because I am in grad school and my brain does not get quiet anymore. But I lived in a dormitory setting for the last two years. And that hypervigilance, waiting for every single sound started to return. The same vigilance that I had when I had small children came back to me now at 58 years old.

I just share this story to talk again about the implications of misdiagnosis, the ensuing maltreatment, the implications of that, but also to demonstrate that it is a lifelong condition and any change in the environmental situation. We have to remember

that this goes on forever. It goes on forever,

DR. MALOW: I am really glad you brought that up. First of all, you brought us back to focusing on the lifespan, which I think is really important. I wanted to say that the impact of sleep regardless of the cause whether there is a biological cause or some of these medical conditions or whatever, the impact of not sleeping well could make you look like you have bipolar. It is so true.

And then the other flip side is that bipolar can manifest with sleep problems. It is very challenging to sort out the two.

And I feel like we are still searching for treatments for autism. We are still searching for treatments for the comorbidities and the co-occurring conditions in autism including these psychiatric

conditions. I think it is so important to recognize that sleep can mimic them or poor sleep can also drive it. It's such an easy thing to do.

And then if you are sleeping better, you are also improving your overall health and quality of life and obesity and everything else, so really paying attention to sleep. The family unit will improve. Paying attention to sleep is just so important and it is a lifespan issue.

Our young adults are struggling too. A lot of them have obesity and they could have sleep apnea. That could trigger some of these behavioral issues as well. Thank you for bringing that up.

DR. TAYLOR: Sam had her hand up for a while and I missed it. So, Sam and then Kevin.

MS. CRANE: Another thing that I think we really need to research more, and I don't know if this is something that you've seen in your overview of the research is the importance of waking up. Many of us have trouble getting to sleep and staying to sleep. But I would say that a large number of our population also have really severe, severe problems waking up. I am one of them. I have close friends and associates who are also in this situation.

One of the things that I think might need to be looked at is how cortisol over the course of the day might influence our ability to wake. Because there's quite - the typical person who wakes up gets a little surge of energy upon wake, whereas it is very common among autistic people to just never get that and to just sort of slowly melt out of bed

DR. MALOW: No, no. I think you're right.

MS. CRANE: And slowly wake up over the course of the day to the point that we're often not really functional at all until afternoon and then that in turn can make it harder to sleep because if we have this --

DR. MALOW: No, you make a great point. Can I respond? Or do you - are you finished? I don't want to -

MS. CRANE: I just want to say one more thing. I actually really want to echo what Alison was saying that a lot of us can follow sleep hygiene very well and still have really - even though sleep hygiene will help almost everyone, it doesn't get us to the place where someone else with perfect sleep like someone else who is turning off the screen at 9:30 and reliably getting eight hours in bed and reliably - everything is dark - should be

getting really good sleep whereas a lot of us even if we are doing all of that, we are getting tolerable sleep. We really need to make sure that we are going beyond that and looking at other stuff.

DR. MALOW: I love that. I was actually thinking as you were talking about the cortisol, I was looking at Alison because I think you are right. That could be an area where there is - because people have discussed and described cortisol abnormalities in autism. The ability to have that morning cortisol peak, that waking peak, is really important. It would be great to study that. Even though people have studied cortisol in autism, I don't think they have studied specifically people who have trouble waking up in the morning with autism and whether they may have more abnormal cortisol

than those who do not have problems waking up because there is so much heterogeneity in our field. I think that's really interesting.

I will also say that there are some cases now of narcolepsy and autism and the whole auto immune link. And then there's also the idea of what is happening at night and how do we measure that. Is there something going on in your sleep at night that's disrupting your sleep so that you don't feel refresh during the morning?

And then the final point I will make is it is really interesting, and getting back to kids. As adults when we are sleepy during the day, we are sleepy. But as kids, they are not necessarily sleepy. They could be hyperactive, aggressive, and disruptive. The sleepiness can manifest itself in very interesting ways in kids.

You make some great points. I think the cortisol thing is a great example, Alison, of something that is biological that could be driving some of this.

MS. CRANE: Can I follow up because this was - I just realized what I was trying to say when the phone rang. Having trouble waking up can also drive trouble falling asleep. If you haven't been able to do anything until about 1 p.m., then, especially for teens and adults. If you have not been able to do anything until then, you are not going to want to turn your screen off at 9:30 p.m. You've still got stuff to do. But that is the point where you have the most energy and you need to use it. There is this vicious cycle that we then have to cope with.

DR. MALOW: That's so true and I think that the other piece is doing meaningful

activities during the day because when you are in school, it is built in. But when these kids leave school and they're not working and they're not, they are sleeping during the day, you are absolutely right. It is going to disrupt everything.

MS. GASSNER: And what happens to the first two weeks of on-the-job training when you get your new job? You are so out of it that you cannot even function. You do not get to keep the job.

DR. MALOW: That is so true.

MS. CRANE: Suddenly you have gone from sleeping until one to suddenly having to get somewhere at 8 a.m. and you cannot do anything. It's totally going to affect all aspects of our lives.

DR. TAYLOR: Kevin and then Scott.

DR. PELPHREY: I first wanted to point out that none of us did any self-disclosure after Timothy's talk. But now we are talking about our experiences. I have a friend who will in the middle of a good night sleep will reach out and hit his spouse that he loves very much or the headboard, and even though you are supposed to not be able to move during REM sleep. My friend thought it was just his first marriage, but it is happening in the second marriage. It is very concerning.

He also has a daughter with autism who does this quite a bit. He Googled it. It's REM --

DR. MALOW: REM Behavior Disorder.

DR. PELPHREY: My friend's initial review of that literature was very concerning because there's this higher incidence of

Parkinson's and that doesn't run in his family.

But then I was reading Joe Piven's paper and it is sort of like wow and then thinking about Alison's point about biological mechanisms. That seems like an endophenotype that from my cursory review of Google here looks like something that sometimes hits in review papers.

DR. MALOW: Yeah. REM Behavior Disorder is a harbinger for a neurodegenerative disorder including Parkinson's disease. It's an alpha synucleinopathy. I think it's fascinating to look at because the idea in the dementia world - this is not the autism world, but this is the Parkinson's, dementia, neurodegenerative. Is if you can pick up on it, you can actually maybe once we have

neuroprotective drugs to treat dementia, you can give it to that population.

But it's interesting because Ricky Robinson actually described RBD in autism many years ago. We have not found it in the kids we've done sleep studies on, but we have only done - we have not done a huge number.

It also is associated with medications like tricyclics and some of the antipsychotics. That may be the connection in some of our kids. It's fascinating.

I would be happy to talk to your friend at any point about his concerns about sleep.

UNKNOWN SPEAKER: I also noticed that he didn't offer that service when we talked about his topic.

DR. ROBERTSON: I wanted to just echo on a couple of other comments that were raised on the vicious cycles on sleep issues. I have

that where I know the feeling of going to bed too late and then waking up later and then not reaching a peak until later and then personally myself trying to work through some of the sleep things.

Also what was mentioned on employment issues too. There was actually a paper that came out recently on employment status of autistic adults in terms of under employment and unemployment. I did find much higher rates of unemployment among folks who had more extensive sleep challenges. We actually have data actually that shows that direct linkage. It is the health end and it is the employment end. Yes, it is directly affecting folks' quality of life and then their economic well-being. I am glad that you are - on the presentation.

I was taking down very copious notes seeing if maybe there were things on there to help myself including maybe going into a sleep study at some point. Maybe there might be things that might be helpful to come out of that. Because since undergrad, I've never really had - I had good sleep back then and I have not had good sleep once I went into grad school and employment. Anything in terms of creative options out there is something always that I would be interested in looking through.

DR. MALOW: I will just end with one comment on that, which is it is just so interesting because I have done a lot of advocacy for later school start times in teens, not again, not necessarily in autism, but in the general population. Because kids have to get up at 5:30 for school. It makes

no sense. Their brain is still asleep. But I realize we have to do similar advocacy for adults. While we're trying to figure out what might be causing their sleep problems, we do know that giving them the flexibility to go to bed later and wake up later would be really helpful. I think that has to be built in to what we do. Thank you for sharing that.

DR. TAYLOR: We have a few minutes left until our break. I have Jeremy and then Louis and then Connor and then Matthew and then Christina.

DR. MALOW: Oh my goodness. I thought we were done. That's fine.

DR. TAYLOR: Almost there.

DR. VEENSTRA-VANDERWEELE: Again, with the challenge of sequencing. Alison's comment made me think about the kids we have talked about - dramatic short sleepers, which is not

- these are the kids who you prescribe a medicine that puts them to sleep and then they're up the same three hours later that they are if they went to sleep at 2 a.m. There is this subset of kids. At this point, I do not think we have a genetic sample that's large enough to find something unique to them. But I would bet that the SPARK sample would give at least a peak at whether there is something unique in that subset. I think there are other examples of relatively rare things. But it's not a vanishingly rare thing. It ends up being a substantial number of kids and they end up having lots of co-occurring disorders and they end up having a lot of behavioral difficulties. These families are incredibly stressed because they can only sleep for three hours sometimes for years.

DR. MALOW: Olivia Veatch looked at that in the Simons, but I do not think she looked at bipolar. I think she just looked at social communication repetitive, but we had those kids less than seven hours. I can go back and look and see if we looked at anything else in that sample.

DR. TAYLOR: Louis.

DR. REICHARDT: Actually, I first wanted to just point out that for all these compelling clinical trials, I hope you consider the SPARKS group because there are more than 30,000 individuals. More than half of them have come in through clinical centers. It seems like it is one of the easier, more amenable kinds of trials to test some of these hypotheses.

The second thing, which is not immediately helpful to patients. I would just

say that our knowledge of the brain pathways that are involved in sleep control has really exploded in the last few years. There is huge space at the moment for looking at the impact of these pathways of the various genetic models of autism. This would be something that for organizations that have post-doc fellowships and stuff might just make sure you advertise to these and so on. It is a huge area of opportunity at least.

DR. TAYLOR: Connor.

DR. KERNS: I was just thinking that everybody's presentations are so compelling. We keep saying sleep and anxiety and attention and gastrointestinal. They are all related. I am just wondering if we are actually talking in that way in our models and looking at what could actually be

underlying all of these things as a starting point.

I think behaviorally, we understand how these things unravel and start to influence each other. I think there is great potential for us to make changes for people by hitting the different - it is not even a triangle. It is probably a square or something larger, but once it is there. I want to make sure too. I do not know the answer to this question. Are we looking at - could there be something at the top of this related to what Alison was saying that is really leading to some kind of general problems in arousal that are also leading to mood problems and things like that?

I also wonder if in our clinical trials we should really be looking at all these outcomes together. I think sometimes we fall

into patterns where here is the sleep trial, here is the anxiety trial, and here is the gastrointestinal trial. I wonder if we could improve on that.

DR. MALOW: First of all, I am glad I left this slide up because I think Micah Mazurek's group has done wonderful work with over arousal and linking - I think there is a hyper arousal that is driving GI anxiety sleep. I really do. Not in every kid, but in some.

I think looking at cortisol is great. We talked about the electrodermal activity and Affectiva, different measures that could get at hyper arousal. Heart rate variability is a simple one.

I would just advocate - when we are doing a trial on anxiety, let's throw in some measures and let's look and see what happens

because I think that there is a lot of low lying fruit - low hanging fruit to do that in some of these trials. Thank you for that.

DR. TAYLOR: Matthew and then Christina.

DR. SIEGEL: Just following Alison's comment and then Louis'. I do think while it is very important to work on sleep hygiene and trials of medications and things for treatment, I think there is still a vast amount we do not know about sleep and particularly sleep physiology in autism particularly over developmental phases. Circadian clock genes are very important. Do we understand how the circadian rhythm is similar or different from neurotypical populations as they age? Is the - because we see this behavioral and possibly adaptive skilled deterioration that occurs kind of

peri to after puberty. Is that related in some way?

I think, so there's - in terms of the IACC and our research agenda, I think we again do not want to skip over looking at a call for a better understanding of what is driving sleep and sleep changes in autism.

DR. MALOW: That is an excellent point. One question I have is the delayed sleep phase that we see in typically developing kids is about 10 to 20 percent. Is it higher in kids with autism and in teens with autism? I think you make a really good point.

DR. DANIELS: Thank you very much, Beth. Is there someone on the phone that wants to comment?

MR. JOYCE: Yes. If it's my turn.

DR. DANIELS: Yes, who is this?

MR. JOYCE: This is Joe Joyce.

DR. DANIELS: Oh, hi Joe.

MR. JOYCE: Just a very brief comment. In regards to Trazodone, my son who is now 19, almost 20, has been using Trazodone for ten years and has had very successful results. That may be something that could be studied further. I would recommend Trazodone.

And then, secondly, just I think another side issue related to sleep issues is from the behavioral standpoint. Our son, David, has very severe self-injurious behavior. So it's very important that he does sleep throughout the night because sometimes even though he does typically sleep throughout the night occasionally he will wake up out of a cold sleep and just begin engaging in very severe fist to face self-injurious behaviors just without any advanced warning. We literally need to have someone in the room

with him all night long just to prevent that from happening should he happen to wake up. That just adds to the cost of supporting a person with self-injurious behaviors. That may be an interesting thing to study from a sleep perspective also. Thank you.

DR. DANIELS: Thank you. Thank you, Beth. And now we are going to be moving into our break. We are starting again at ten after.

(Whereupon, The Working Group members took a brief break starting at 3:06 p.m. and reconvened at 3:24 p.m.)

DR. DANIELS: We are going to get started on the next portion of the meeting. Dena Gassner suggested, or she requested, that we show a short video that is relevant to the next section of the meeting that's on patient-provider interactions. We squeezed

that in. That video is here now and is going to be played.

Dena, do you want to say anything about it before you start?

MS. GASSNER: The young lady in this video is Chloe Rothschild. She is one of the individuals that has a lot of co-occurring medical issues. You can see that she is carrying a lot of her stuff with her, her equipment that keeps her regulated.

It is ironic. One of the first contacts I had with her, the IEP team was trying to force her to not use assistive technology. She advocated for herself saying when she's stressed, she communicates better with it even though she has speech.

In this video with the University of Michigan, what they are basically saying is person-centered care for autistic individuals

in terms of those wrap-around supports, the soft skills, the patient services, doesn't disappear because a person magically turns 21. I think it is a really well-done video.

DR. DANIELS: Great. So go ahead.

MS. GASSNER: Thank you for letting us do this.

(Video Shown)

MS. GASSNER: I want to say she asked to participate and to create this. This was initiated by her. That's what we were talking about, about autistic people being part of the conversation from the front end. I think she is pretty darn good at it too. Thank you for indulging me.

DR. DANIELS: Thank you for sharing that, Dena. Great. We're ready to launch into the next session so introducing Dr. Micah Mazurek.

DR. MAZUREK: Thanks so much for the opportunity to talk with you today. Thanks Dena for that video. That was really awesome. That is hard to follow.

Today I am going to be talking with you about health care experiences of children with Autism Spectrum Disorder with an eye towards some opportunities for improvement of the health care experience. I just want to preface this talk by saying that this is actually going to be just a reiteration of the things we have already talked about today. It's been such a great discussion. I think some of these themes will be very familiar.

As we know and have been talking about all day today, Autism Spectrum Disorder is much more than what is typically considered the core diagnostic features of social

communication and interaction difficulties and repetitive behaviors.

In fact, we know that people with autism are at very high risk for a number of co-occurring conditions including the ones we have spent a lot of time on today and in addition to a lot of psychiatric and behavioral difficulties, cognitive problems and lots of other disorders we have not even touched on today.

And the other thing that we have discussed is the fact that not only are these conditions very common in our population, many children and probably most children on the spectrum have multiple conditions that are happening at the same time, which adds to the complexity for clinicians. Many of those symptoms and conditions are interrelated and a lot of the symptoms overlap with one

another and may exacerbate core symptoms of autism or mask them. It makes it difficult when we are thinking about diagnostic assessment for either the co-occurring condition or for autism and for treatment planning.

This slide really goes without saying. We actually know that co-occurring conditions can have a larger impact on day-to-day life and functioning for families and people with autism a lot of times over and above the core symptoms of autism.

They interfere with functioning just across the day. So from learning environments to family engagement, engagement in the community, and they lead to a lot of stress and burden for both the person affected and their families.

We also know that children with autism who have a number of co-occurring problems have greater health care expenses and worse health care experiences and families experience a lot of financial strain as a result of that.

This tells us that we're dealing with a very medically complex condition here that requires a lot of support that really requires coordination and comprehensive care and that's what we think would be best for children with autism. But despite that need for care, we have done a lot of research on this topic and what we are finding is that children with autism receive worse health care experiences than other children, even other children with special health care needs. They have much higher unmet health care needs. They have worse access to medical

home and they have less coordinated and family-centered care.

We know that the medical home model is very helpful for children with special health care needs and autism. And kind of embedding, coordination, comprehensive care across the lifespan, helping families connect the dots and doing that in a culturally competent family-centered way. We know that that model works, but children with autism are not typically receiving that care. Those who have a lot of comorbid conditions have even worse access to medical home and family-centered care.

What is going wrong? What are we missing here and why are we gathered here today to talk about how to address these barriers? I am going to talk about a few different types of barriers that I think we can target as a

group today. One of them is access to care. We have talked a lot today about just lack of capacity of specialists. There are few providers with autism expertise. As the prevalence of autism increases, the numbers of providers have not really matched that. We have shortages of autism specialists and subspecialists of all types in most communities. That means that if you do not live near an academic medical center, you are probably unlikely to live near a specialist who can help you.

That also means that for families who do live near an autism center or a specialist they need access to, there's a long wait list that can be months or years, which is really not acceptable.

And then when we think about our families who live in rural areas or remote

areas, they may not be able to access care at all. That requires traveling long distances to bring your child to a specialist. If you have to come for multiple appointments, sometimes that is just impossible because you either don't have the money to do that, you may not have transportation, or your child's behavior may be so significantly impaired that traveling is not safe. There's a lot of barriers there when we think about people who do not have community access.

And then on top of that, health care is expensive. And the more specialists that you need access to, the more expensive that becomes in terms of both health care costs, but also families needing to take off work to take their child to multiple appointments. That just kind of balloons out from there.

Finally, I just want to mention that we also know that there are disparities in health care within the autism population that have to do with cultural and linguistic barriers. We need to think about all these kinds of access issues when we are thinking about how to solve the problem of improving health care experiences.

Actually, the video that we saw I think was a really good example of the clinic environment and some barriers within our own settings that can present for children and families. Clinics and hospital settings are really noisy. They're unpredictable. They are oftentimes uncomfortable for most people. If you have autism, it is even more uncomfortable. A lot of children may have discomfort with unfamiliar people. With lots

of folks coming in and trying to touch you that can be very overwhelming.

And then as we also saw in the video, communication can pose a big barrier when you are coming in for a clinic appointment. If you are having trouble communicating your own experiences that's going to get in the way.

Also, if you cannot really understand the verbal cues that the physician or the clinician is trying to use with you that can make it more unpredictable and anxiety provoking.

And then sensory issues can get in the way from the waiting room all the way through procedures, making them much more uncomfortable for this population.

Another type of barrier that we have touched on just a little bit, but I think is worth mentioning is that we have a limitation

in our ability to assess symptoms across the health care conditions and mental health conditions that we have talked about because of some of the problems that we have already discussed. Difficulties with communicating can pose a barrier.

If we have atypical symptom presentation, it is sometimes difficult to differentiate between one type of symptom or another. If children are displaying pain in behavioral ways and if you are not attuned to that, you might miss that diagnosis or you might miss the condition.

I think a lack of validated tools for our population is a barrier. Over-reliance on parent report of symptoms is also a barrier especially for internally experienced symptoms like pain, anxiety, or depression.

One final group of barriers that I want to talk about probably for more of my time today is this barrier of provider knowledge. We've hit on this topic multiple times today. But I think it's a really important one.

Because we have such a limited number of specialists in the autism field, I think primary care and physicians who are going to be able to work with their patients across the lifespan in a coordinated way or could provide a medical home are the ideal types of providers when we are thinking about improving the overall health care experience. But those folks are reporting to us that they don't feel ready and they don't feel competent and they don't feel that they have the knowledge they need to be able to serve children with autism.

There have been a number of studies looking at provider self-efficacy and beliefs about their own knowledge. They consistently are reporting that they feel like they don't have enough knowledge. They don't understand the needs of the population. They don't know how to identify symptoms of autism.

And when you ask parents of children with autism, they agree with that. They feel dissatisfied with their experiences in the health care system and they also lack confidence in their provider's understanding of their child. This is an area where we can come together and think about ways to improve this.

The other thing that I'll add is that across the studies that I am reporting here and our knowledge of colleagues in the field, I don't think the problem is a lack of

desire. I think the problem is not having the tools to be able to meet the needs that are presenting. Providers are feeling overwhelmed. I think it is up to us to help them, help support them, and mentor them in this area.

This is just some consolidated data across a couple of studies that we have done recently with primary care providers. We asked them to tell us what are the barriers that you see in providing care for children with autism. Sadly, some of my labels have gotten cut off here. The number one barrier was lack of time. That has come up multiple times today. That if you want to provide good accommodated care for someone with autism, you need more than ten minutes with them. That's a common concern among primary care physicians.

The second most common was lack of access to autism specialists for consultation. Again, I think providers want to help. They want to know what to do. They want to know what best practice is. But if they do not have anyone to ask, it's going to make them feel inadequate in being able to support their patients. Self-efficacy was another big one.

And then some folks wrote in comments about some things that they identified. The wait time at autism centers was one, a lack of knowledge about autism resources, and a lack of tools that can help with assessment.

I think these barriers set us up to think as a group about opportunities for improvement. How can we equip families, communities, and providers with the knowledge they need to be able to do a better job?

Some of that work has been done by people in this room already in thinking about empowering families and providers with resources through toolkits and guidelines, for example. These are just a couple of examples that have come out of the work of the ATN and AIRP that put tools in the hands of people who need them around these health care issues. I think that's a good example of a way to address this problem.

I think we can also do a much better job of helping to inform redesign of clinic spaces to be more autism friendly, thinking about how to change clinic flow in a way that is more accessible for people with autism.

Another opportunity I see is the development of additional tools and guidelines for assessment and treatment of these common comorbid conditions. Here are

some examples of practice pathways that have been published in recent years as well as some work in this work again around developing psychometrically sound tools for assessment. This work needs to continue and we need to think about how to get those guidelines and algorithms into the hands of the frontline providers. I think technology may be one way to do that.

For the rest of my time today, I am going to share an example of some work that we have been doing to try to train physicians in rural and underserved areas by giving them information about best practices for autism. The model that we are using has been brought up a couple of times this morning actually and it is based on the Project ECHO model that was developed at the University of New Mexico for hepatitis C treatment.

It's a really interesting model because the whole purpose is to extend capacity for treating complex patients in their own communities by taking knowledge out of the silos of academic centers and spreading it into rural and remote areas to improve access to care.

The way it works is that the model uses multi-point video conferencing technology. It uses a zoom platform to connect a team of experts at an academic center to providers that could be located anywhere in the world and they join together and form a learning community.

What happens is instead of a one-to-one consultation or a call to the specialist that is just between the primary care provider and that one specialist, everybody is learning together and then it exponentially impacts

the entire patient populations of the communities that are represented. I think it's a really interesting model for autism.

The other thing about ECHO is that it includes both didactics and resources like the tool kits and guidelines I talked about. But it also is a case-based learning model so that providers are presenting their own cases for discussion. They receive recommendations. They go try it in their practice. They can come back and share with the group what happened. The community begins to learn from one another.

We thought this was a great model for autism. We completed a six-month pilot study with colleagues at the University of Missouri: Kristin Sohl, Rachel Brown, and Alicia Curran. Our team included a pediatrician, a clinical psychologist, a

psychiatrist, a parent of a child with autism, a dietitian, and a social worker. That was our interdisciplinary hub team. We reached out to providers in rural areas and underserved areas across Missouri.

The way it worked in our model was we typically had two cases presented each clinic, which happened every other week. And then we gave a brief didactic on a topic focused on comorbid conditions or screening for autism.

We did this model for six months, every other week. In this pilot, we had 14 participants, again specifically focusing on screening and management.

We found - I apologize for the graph here - we found significant improvements in self-efficacy across domains. I know you cannot see the domains, but they include

screening, management of medical comorbidities, management of psychiatric comorbidities, and access and understanding of autism resources. Providers across the board improved in their confidence in their abilities to manage these conditions.

They also improved their abilities to do autism screenings at regular well-child checks. We were pleased with those results. I guess what we learned from that initial pilot was the model is not only feasible, but it was really well-received by the providers. They felt extremely satisfied and wanted to continue on beyond the pilot.

They also developed a community. A lot of these providers were working in isolation in their rural communities. Every other week they had a team of colleagues to come together and bounce ideas off of.

As a result of that pilot, we decided that it might be a good idea to try it in a larger sample with better measures. We are currently working with the ATN and AIRP and ten collaborating sites through the ATN to replicate that pilot.

Through this project, we are reaching out to 150 primary care providers in the regions that are shown in the map there. Each site that is shown by a star has formed their ECHO hub team of specialists and each site is reaching out to 15 providers in their regions. They are doing the same curriculum that we tried in our pilot. We are doing assessments at four time points that also include knowledge assessments and chart reviews so that we can actually look at change and practice, not just self-reported change.

The study design is a cluster-randomized, sequential, staggered roll out. Each site was randomized to when they were going to start. As you can see, we are now wrapping up the final data collection of the final time points. We are really excited to see the results of that study.

But I think this gives you an idea of a type of model that can embed some of this knowledge that we have generated as a field and put it into the hands of people who need it in a way that is a little bit more rich and relevant to them than sitting and watching a webinar, for example.

We are actively testing and developing new applications of the ECHO model for other participant groups. One example is that we recently published a paper in JADD on an early diagnostic model focused on primary

care physicians called ECHO Autism STAT. We are getting ready to launch a transition-focused ECHO. If anybody knows any physicians who are interested in that, contact us about that. And we are planning an adult health care ECHO as well. And then these are some other examples of some working groups who are focused on different topic areas.

I think this model is one of many types of models that can leverage technology and that relationship with providers to try to improve knowledge and expertise in autism. I am looking forward to hearing everyone's thoughts and comments. I am going to turn it over to Christina to talk about adult health care experiences.

DR. DANIELS: Thank you, Micah. We will have Christina Nicolaidis and Dora Raymaker is going to be joining us by phone.

DR. DORA RAYMAKER: Hello, can you hear me?

DR. NICOLAIDIS: I can hear you, Dora.

DR. RAYMAKER: Hooray!

DR. NICOLAIDIS: Thank you for having us and thank you for hanging through this very long day. Last talk. Dora and I will be presenting a lot of work that we have done collaboratively as part of the Academic Autism Spectrum Partnership in Research and Education or AASPIRE. Dora and I cofounded AASPIRE back in 2006.

AASPIRE is made of quite a number of autistic adults, academic researchers, family members, disability services and health care providers. We use a community-based participatory approach for all of our projects. That means that autistic adults, family members, and other community members

serve as equal partners throughout all phases of our research and pretty much anything Dora and I are seeing here is a collaborative effort from our many partners over the years. Dora.

DR. RAYMAKER: We will be using identity-first language in keeping with our community-based participatory research practices because the autistic community prefers identity-first language and this is much for the same reason why the deaf community prefers it because we see autism not as something that should be shamed and put aside as something that is apart from us, but an important part of our identities and our culture.

DR. NICOLAIDIS: We have already touched upon a lot of health care disparities so I am going to rush through these fairly quickly.

Our first AASPIRE study actually was to even show there was a problem. I don't think anybody in the room would be surprised to think that health care disparities exist, but we certainly had to demonstrate those before we could get funding to do anything about them.

We did an online survey comparing autistic adults to non-autistic adults and unsurprisingly we found that the autistic adults had greater unmet health care needs including physical health care needs, mental health needs, prescription medication needs, and greater use of the emergency department, which to me is a failure of our primary care system.

We also found that we had lower use of Pap smears for those where Pap smears were indicated and overall lower satisfaction with

patient-provider communication and health care self-efficacy.

Since then a few other studies have found similar disparities including the study that came out recently out of the Kaiser Permanente system, which compared a very large number of thousands of autistic adults to adults with ASD and typically developing adults. And the autistic adults had increased primary care visits, increased outpatient mental health visits, increased hospitalizations for ambulatory care sensitive diagnoses, decreased gynecologic visits including cervical cancer screening. All the differences that they found comparing the autistic adults to adults with ADHD were even more pronounced when comparing to the general population.

Again, we also have already touched upon quite a lot about the problems with provider knowledge and self-efficacy. Back before we started our work, we had done a brief online survey of internal medicine and family medicine providers who care for adults. And 73 percent felt uncomfortable in their ability to provide quality care for adults on the spectrum.

The disheartening part was that 84 percent of them however had no plans to seek additional training in ASD. I say this as a primary care provider who 15 years ago would've had the same exact response. This is not because they are bad people. It is not because they do not care for their patients. We have so many priorities. When you have one or two autistic adults on your panel that you might see a few times a year, this doesn't

raise to the level that it does for a pediatrician whose panel might actually be - whose day might be quite different in terms of how much they are seeking. They are seeing patients on the spectrum.

Interestingly, 88 percent would accept an autistic adult into their practice, but even with a new autistic patient, less than half would attend CME. What they would do, which is why we have structured a lot of our work around this is they said they would search for information on the Internet and they'd read customized reports and information, things that had to do with their particular patient.

Since then, again, other studies have shown similar things. This is, again, from Kaiser, Lisa Croen's group, where providers, medicine, OB-GYN, mental health, almost all

of them were showing similarly low rates of self-rated knowledge.

This is from our latest study that is happening right now where we're working with providers in multiple different clinics and three health systems. Here we have gone a little bit more granular as to what their self-efficacy needs are. If you'll notice that overall providers did not feel very confident in any of these skills when it comes to taking care of adults on the autism spectrum. However, the things that really stood out were communication, identifying accommodations, and making accommodations. Those were where we had the lowest scores, not that the other ones are great.

Now let's turn to what we have learned from autistic adults about their experiences with health care. Dora?

DR. RAYMAKER: As part of that same online survey Christina talked about, looking at disparities, we also looked at barriers to health care and we compared autistic people, people who identified as having a disability, but not being on the autism spectrum and people identified as neither. We found that the autistic group - the people without disabilities experience far fewer barriers to health care than anyone else, which you would imagine.

The autistic group reported both more barriers to health care than people with other disabilities, plus they were very different things that they had endorsed. The top barriers. Some of these are a little bit of an echo of what we saw with the previous talk. Fear and anxiety kept a lot of people from seeking care. A lot of people said that

their biggest barrier was that they could not process information fast enough in real time in order to participate actively in what was going on. There was concern about cost. There was facilities causing sensory issues and there was difficulty communicating with providers, which is probably not a surprise to anyone.

DR. NICOLAIDIS: We moved from there to doing some qualitative work trying to understand what the health care experiences actually were. We found lots of stories of people having bad experiences. We found some stories of people having good experiences. But ultimately what made sense was that whether or not a health care interaction was successful had to do with this interplay between patient-level factors and provider-level factors. The patient-level factors

aren't surprising to anyone who knows anything about autism because they kind of read through like a DSM diagnosis.

What we were hearing was that on the patient level, people's verbal communication skills or sensory sensitivities, their challenges with body awareness, their slow processing speed, the atypical non-verbal communication and challenges with organization were all getting in the way.

But really what ultimately made it work or not work was how that interacted with the provider-level factors. This is from the patients and the supporters. The provider-level factors that were identified was knowledge about autism in adults, a lot of incorrect assumptions, providers willingness or unfortunately sometimes unwillingness to allow written communication, use of

accessible language, openness in providing other accommodations, and skills in incorporating supporters. All of this of course is in the larger context. I think Clarissa has done a good job of reminding us of this larger context multiple times today. But this is where we don't work in a vacuum. And certainly the availability of formal and informal supports just how hard and complex and difficult our health care system is, accessibility of health care facilities and then societal stigma about autism and other social determinants of health were always factoring in there. Dora.

DR. RAYMAKER: These are some of the things that people told us in those interviews about these key points. The first one is about sensory sensitivities, which everybody has, but not everybody is going to

become unable to get health care because of them. This person said, "The lights in the office are very bright and that is exacerbated by the white walls. Sometimes the waiting rooms are crowded and I cannot filter out the background of people talking or shuffling magazines. I feel disoriented by being led down long hallways to different rooms. I am not able to bring up my concerns because it is all I can manage to figure out what the doctor is saying so I can respond to his questions. But he refills my usual meds and I go on my way."

The sensory things extend of course to one's experience of one's own body as well as the outside world. These are some quotes from participants around challenges with body awareness. "Like when they ask if the pain is

shooting or stabbing or burning, it is like I do not know. It just feels funny."

Another person said, "The problem is it is difficult for me to isolate specific sources of pain and identify duration and intensity. It is sort of the equivalent to white noise."

Then there were a lot of providers' incorrect assumptions on both ends, sometimes thinking people were more capable than they were, sometimes thinking they were less capable than they were. This one person said, "I have used my Alphasmart, which is a portable communication device, when my speech is too slow or difficult to understand for medical appointments. Some of the doctors have been really great, but others have acted really condescending when I used it and also immediately assuming that I could not be

alone, had to have parents there too. I tried to go without, even when my speech is in poorer shape."

Another person talked about the other direction. "Usually when I demonstrate a large vocabulary or some fundamentals, my needs especially around communication are then ignored. My choice is then to pretend to be less intelligent and accept their infantilism, or to be confused, frustrated, and stressed out."

Openness to accommodations helped with some of this stuff, but people talked a lot of resistance from providers to get the accommodations they needed or not even understanding what that was in the first place. This person related, "I prefer and find it easier to communicate in text. But with every doctor I speak to, they wave away

the note card and look at me to ask the same question I have just answered and interpret my confusion as my being non-compliant with the medicine. I wish health care providers would read the notes I make for them."

And then this is a quote from a supporter. "But they talk to him in the same words that they would use if they were talking to me. If they are going to talk to him, they need to say it how he can understand it."

All of these things will lead then to decrease patient autonomy and ability to participate in the process of health care. This person said, "Just because I might need more information to understand things, it does not mean they can or should just talk to me like a child and leave me with my own

health. My body is my body and my experiences and wishes about my body are mine to make.”

DR. NICOLAIDIS: In this study, we also asked people for their recommendations of what would make things better. We got an amazing list of literally hundreds of codes of recommendations. They are all great recommendations. But one thing that we have to remember is when you have met one autistic person, you have met one autistic person. With adult providers, I don't get six months of working with them to train them about autism. If I get an hour, that's a lot, if that. It is very hard in an hour to explain every accommodation and every different thing that every different person on the spectrum might need because they're different. And what Dora might need may be very different than what somebody else on the spectrum may

need and they are both equally as valid and important. That's why we moved on to thinking about making really individualized tools.

We will start off by showing you a bit about our AASPIRE health care tool kit. Again, as a reminder, this is the work of our entire collaborative and every piece of this has been really painstakingly worked through with all of our autistic partners and our family members and our health care providers.

DR. RAYMAKER: This is the first page and you can see there are a patient side and a provider side. I am going to run through this fairly quickly. But you can go and look at it yourself. It is free. It is online. It is available to the world at autismandhealth.org.

Next slide. Looking at the provider side, this is information for health care

providers and it has a number of topic areas of how autism can affect health care, legal and ethical considerations, general information about autism, some resources and such. It's also got some tips for successful office visits where we go through and we actually address things in a very practical sense that health care providers can do in order to better accommodate autistic patients in the main areas that are important.

Next slide. This is the side for patients and supporters. It is not pictured here, but there is actually also a number of topics including staying healthy, which is information about nutrition, exercise, recreation and preventive care. There's a section about rights in health care and self-advocacy. There is information about autism

and adult diagnosis, getting access to the Internet and some medical information.

Over here on the health care side, the health care topic, we kind of step people through all of the phases of receiving care from finding providers to making appointments, preparing for a visit, getting through the visit, and then after the visit.

Next slide. We also provide forms and worksheets to help with those steps. There is making an appointment worksheet that includes scripts for people to say. There is a checklist for what to bring. There is a symptom worksheet that helps people work out how to communicate what is going on with them in a way that the doctor may be receptive to, and after the visit worksheet for follow up care. And then there is the Autism Healthcare

Accommodations Tool, which is a customized report.

Next slide. The idea behind that is that the patient with or without the help of a supporter or supporter on behalf of the patient would fill out a survey about the things that help accommodate them in health care. And then we have a program that translates it into a format that hopefully health care providers will be receptive to.

Next slide. This is an example of one of the AHAT items. You can see that on the left side of all of the different areas are a part of obtaining health care and then it's got the section with what can help you do one of those things that you need to do. This is about making good decisions so people will check what would help them, for example, give

me extra time to make a decision even if that means I need to come back later.

Next slide. And then this is what the report looks like on the other side. It is formatted differently. We spent a lot of time working with health care providers and talking to health care providers and trying to get something that was easy for them to process and did not just look like a whole bunch of more work. That is what the report looks like.

DR. NICOLAIDIS: Okay. Those provider reports took us many, many versions, but we do have a version that primary care providers seem receptive to at this point.

Our initial testing of the toolkit was with mixed-methods, single arm, one-month pre-post intervention study where we recruited 170 autistic participants and had

them use the toolkit and then we sent the reports to the providers if they gave us permission to and if we could find the providers.

We were actually relatively pleased. These are just preliminary results, but almost everybody said they found it easy to understand and felt that it was important or useful. We were able to find statistically significant and clinically significant changes between the pre and the post-test in the number of barriers to health care. Patients report of their health care self-efficacy and patients' provider with patient provider communication.

We also had some open-ended questions. Interestingly - we were very focused on the report. I do think the report is the center piece and a key part of it. But we also find

that the patients gave us a lot of examples of how it was helpful in other ways. A lot of them said that even just going through the process was a mean to clarify and communicate their needs that there was validation of their experience and a lot of empowerment around self-advocacy, improved self-efficacy, and especially being able to better prepare for visits made the interactions go more smoothly. And then thankfully, we also got quite a few examples of concrete changes that patients reported their providers were making.

Thanks to a second grant from NIMH, we're now working to integrate the toolkit into three health care systems including Kaiser Permanente with Lisa Croen's group and then two health systems in Oregon.

The first study we did - we were just getting people out in the Ether and we found that that of itself may have been helpful to them, but it does not actually help with the system. This time we are very concertedly working with health care systems and with clinics to try to figure out how to best integrate it into their practices. We've finished working with seven clinics to find processes that work and now we are doing a six-month comparison between our intervention clinics and our control clinics.

We have many steps coming up for this. The biggest thing is dissemination. A large part of this morning we were talking about needing tools and I am sitting there going there but we have tools, but most people do not know about them. A large part of what we need and we haven't been very good at is

getting information out there so that people can actually use them.

As Jeremy already mentioned, we are working with Jeremy who is going to be trying to adapt a toolkit and build onto other things for use in the National Health System in the UK. Dr. Urbanowicz is a Fulbright Scholar, who is working with us this year to adapt the toolkit for inpatient settings. Hint. Hint. I am looking for collaborators who can help us use the toolkit in a multi-site randomized controlled trial. If you have a health system with many clinics, let me know. And then of course with appropriate resources, we also feel that there's a lot of places where it can go.

Now, the toolkit is just one tiny piece of a much larger need for bigger solutions. We have already talked a lot about training.

I understand and I appreciate. It was kind of interesting to see how many common things were from the child report, but we're a few steps back. We do not have residency requirements. It's not even on our radar in adult medicine. To be honest, I don't know if we are going to get it on there. We have very crowded curricula. I've been doing this work for 12 years now. The residency program director is one of my closest friends. I still do not have an hour in the residency program curriculum. This is hard to do.

There are some potentials and I think it would be nice to collaborate with some of the accreditation councils. That has come up earlier today about trying to get some accreditation requirements in there. I think that would go a long way.

And then there are a few model programs including Clarissa's and some in Indiana especially in Med-Peds programs or in adult developmental medicine where they are having training and having actual rotations.

Again, it is also important to do continuing medical education, continuing training for practicing providers, but again many competing priorities. And as I mentioned earlier, in an adult provider's day, the autistic patients may be very few and far between because so much of our day gets taken up by taking care of patients with chronic illness. Even if the prevalence is the same in adults and children my day will never look like a pediatrician's day. Really interested in looking for collaborative and creative ways to get people involved. And of course decision support tools, referral resources,

et cetera. Scott already mentioned, but I want to just reiterate.

None of this can be done without the involvement of autistic adults. If we were doing cultural sensitivity trainings and we had never included anyone who was a person of color that would just be horrid, if we were doing LGBTQ trainings and we were doing this without anybody who - this would be unthinkable; yet, we have so many trainings that we do that have not incorporated autistic adults. That's just not acceptable.

And then we have already I guess in the discussion been talking a fair amount about health care workforce and systems. Already in the discussions talks have come up about consult services and specialized clinics with challenges for access to large parts of the population.

We've mentioned already that developmental medicine is a new field or Med-Peds that are focusing on developmental medicine. There is some interest in this.

As we said, I think it has to be a combination. We need to have specialists. We need to have people who are going to be there for that high-level care. At the same time, every single provider has to also know how to take care - we are not going to have specialty clinics for our African American patients, but I would expect every provider should know to have some cultural sensitivity about working with an African American patient. I think we have to have that same expectation that any provider needs to have some basic level of understanding and then we may have specialists on top of that.

Jeremy already talked about the annual health check and then peer navigators and others.

And then part of health care is providers and part of health care is patients. I think we have to be just as focused on increasing patient activation and self-advocacy, self-management. Some of our tools do that, but there is so much more that can be done especially in terms of mHealth tools and other such things.

We recently reviewed a number of common mHealth tools for things like managing your diabetes and things like that. On the one hand, they were completely inaccessible. On the other hand, if they were made accessible then potentially they could actually capitalize on some of the stereotypically characteristics and autistic strengths that

might actually make using such tools be quite effective.

And then of course thinking about patient advocacy training for supporters because that is a really big part of all of this is making sure that supporters can appropriately support, especially as people are growing older where it gets even trickier as to what the role of a supporter is.

Again, we've talked about a lot of this all day long. It's no surprise to anybody here that autistic adults currently experience significant health care disparities. We know that the adult health care system is currently not really equipped to manage autistic adults' needs.

As we have said, we've been working our AASPIRE toolkit as a first step in improving care, but there are many, many more solutions

that are needed at the patient level, the provider level and the systems level. And I really hope that this group can help us move forward both in getting the stuff that exists, actually used and then building more things that are desperately needed.

Dora - I am going to make a real quick plug because we have been talking all day about things that are so important to us. We have many editorial board members in the room. Shameless self-promotion. I am just going to make a plug. We have a new journal of Autism in Adulthood. Health issues and health care are a very, very high priority. Anything around this is very much of interest to our new journal. This is a participatory journal with a lot of input from autistic individuals.

Thank you to our funders including NIMH and to all of our collaborators. We'll take questions. Please also contact us outside of here if you want.

DR. DANIELS: Thank you so much, Christina and Dora and Micah for all of your presentations. Now, we have some time for discussion.

Sarah Gardner is on the phone and she has been wanting to make a comment. Sarah, are you there? Would you like to make your comment?

MS. GARDNER: Hi. I am. Thank you. First, as a parent of a person on the spectrum, I want to say thank you to all of you participating who is so passionately dedicated to either helping people on the spectrum in a variety of different ways or looking for answers to research. The

descriptions of symptoms, medications, family stress, absolutely perfectly described the last 26 years in the life of the Garner family.

Just to give you a little bit of background. My son is 26 years old and is severely impacted with autism. He, from a very young age, has had severe sleep issues, gastrointestinal issues, injurious behaviors, seizures, the list goes on. We left no stone unturned looking for help in all of these issues, which was almost as challenging as trying to help our son day in and day out.

Today, he is on a long list of medications, but lives in his own home. He has to have 24/7 support. He is non-verbal. He has trouble sleeping still, struggles to communicate, needs a lot of assistance

navigating his everyday life. He has more patience than anybody I know.

A few years ago, he started having issues with his legs. Chas was just falling over. His legs were almost becoming rubbery. We were not sure if it was a side effect of a medication or something else. His neurologist ordered every test imaginable, even a long list of genetic tests. Now, that was another challenge.

Long story short, Chas was diagnosed with GAS1. It is a very rare genetic anomaly that presents with among other things autism. This is a very similar story to the one that we heard much earlier today about the family whose child was diagnosed with Phelan-McDermid syndrome. Even though we've had this diagnosis for a few years now and I have reached out to researchers all over the world

for what little information is available on the disorder, we still do not have any type of doctor or clinician who can address his specific issues, tell us if he is on the right meds or if there are new tests or meds that might be more effective for him.

Now, while I've learned so much in listening to all of you talk today about the latest information and help that is out there, I feel like this puzzle that was just beginning to come together over the last few years now has a lot more pieces and they are scattered all over the room. Now, there are more pieces because of your work. There is so much more information available to us now. Except for a family trying to pull those pieces together, it's challenging. It is really difficult.

Long story short here with what I am trying to say is that when we talk about addressing the health and life needs of people on the spectrum, I think that it is important to help families, for instance, pursue genetic testing. Because at least then maybe there is an answer to some of these underlying issues, maybe specific treatments even or maybe specific things we shouldn't be doing, and then provide a roadmap for families to maybe appropriate research studies to health care professions for personalized medical plans. We heard somebody talk about that issue just today. Help in navigating insurance, which can be just mind blowing what it takes to navigate insurance whether it is for an individual or a family with a young child and then hopefully to treatments to improve the quality of their

lives because that is really why we're all here.

DR. DANIELS: Thank you. Anyone want to comment on that or are there more comments? Donna?

DR. MURRAY: I think this sort of builds on that and something I have been thinking about, which is the more we learn, the more we do not know. But I also think - I think, Micah, you made this point earlier about thinking about these co-occurring conditions of those clusters guiding us along with some genetic testing and phenotypic subtypes because my question in the front lines, working in medical centers, is how do we ask the right questions in our review of systems knowing these common co-occurring conditions without leading families to overburden and with testing or cost. It seems like we need

to be able to make good decisions about how - it is not just what we ask, but we know with this population and communication issues, it's also about how we ask it and making sure we get the information we need to make really good choices about what co-occurring conditions to pursue in depth.

I would say that part of the work of this group might be just a beginning. We don't know everything yet, but taking what we do know and having that help us make some decisions about these subtypes and then maybe what testing we should be pursuing based on that. Just some thoughts there.

DR. TAYLOR: Dena, did you still want to say something?

MS. GASSNER: I just want this to be my last comment. I want to go back to the theme of poverty. When a child has a seizure

disorder, somebody stops going to work. When someone has severe autism, somebody stops going to work. When a parent has a child that is even academically capable in a district that doesn't want to choose to support them, somebody doesn't go to the work. When a child has a behavioral issue, somebody does not go to work. And the work I do to get people \$700 a month from Social Security lands them \$18,000 a year below the federal poverty line. \$18,000. Every environment that an autistic individual has to enter to get that measly \$1,800 below the poverty line, the food stamps office, the Section 8 office, they could report exactly what was on that slide about the lighting, the environment, no accommodations, no supports.

I had to go into a governmental office and there was a lot of noise from children

that were acting out. That did not bother me. What bothered me were the parents assaulting their children in front of me. I simply could not wait there anymore. I am very coherent. I am very articulate. I got very upset. I had a little mini meltdown, but I contained it long enough to ask for a separate place to wait and they looked at me like I had five heads.

When we talk about accessing services whether it is health care or this tiny amount of money by which the money is not why we go, we go for health care. When we are talking about accessing these services, all those environments need to be made accessible for us because the one permeating trauma that every family will endure is the implications of poverty. Whether it is the poverty of therapies because they have spent their entire retirement trying to facilitate for

the person they love most in the world or whether it is an adult whose family is not here to support them anymore again living far below the poverty line. We can change that through policy. We can definitely change that.

I just urge the IACC to - I've talked about this again in giving testimony at IACC about the lack of accessibility for these government offices that we have to endure. Thank you and thanks for putting up with me today. I had a lot to say. Sorry

DR. DANIELS: That is why we are here in discussion. Thanks.

DR. ROBERTSON: Just a couple of comments and then a question on the last presentation. One comment was it seems like - if I did not acknowledge - labor, the workforce issues are coming a lot, workforce in terms of training

and things like that. I will see if there are ways to work that into conversations with folks about the workforce system as this could fit into systems level changes. I have been leading the charge in terms of what we can do about educating other folks at Department of Labor about autism and about broader divergence. This is something I am keeping in mind in terms of as things are coming up related to employment and workforce.

And then the intersectionality. I am wondering as far as the tool you have with the existing toolkit and I am guessing, hopefully that's launching off a series of awesome tools that we have over the next five or ten years because while I love the toolkit, I am thinking we need toolkits of toolkits. We need lots of awesome different

things that even work. Some things are going to work better for some folks than the others. In some of the cases, we might need specialization like you mentioned on a diabetes tool or whatever as long as it is made accessible to folks. I'm wondering what your plans are both like on that end and the intersectionality issue and terms of that was mentioned as far as socioeconomic and rural and then we have to cover all these crossovers because I don't think we do it purposefully, but sometimes on research we end up - sometimes more ending up with folks who may not be reaching diversity as much and maybe almost sometimes reaching middle class. And sometimes - I don't want to belabor the point on that, but I do think the socioeconomic issues are pretty major and then some folks are experiencing more

disparities if they have that socioeconomic disparity to begin with on the health care end.

So I'm just wondering in terms of your focus is on beyond the current work you are doing on the system, all the changes. Is it a plan also on research to be looking on sectionality with the toolkit and other tools out there?

DR. NICOLAIDIS: Dora, if you want to answer any of these questions, please speak up. But I'll take a first stab. There is a lot to unpack in there. I do not know if I will get to all of it.

Again, both Dena and Scott bring up the issues of poverty and socioeconomic status, any other form of marginalization too. I think it's huge. And it is really unfortunate when we are sitting here talking about this

one little aspect, which oftentimes there is a lot of intersectionality. I'll let Dora speak because she is the PI on a separate study on employment where I know there's been quite a bit of a focus on intersectionality between autism and --

DR. ROBERTSON: Which is NIMH funded too.

DR. NICOLAIDIS: I'll let Dora speak to the intersectionality issue. And there, I can say in the health care system, we've known for decades that social determinants of health matter more than anything else. Like we know - how many studies do they need out there to tell us that that is actually a much bigger driver to health outcomes than biology or the health care system or anything else is social determinants? I do think that there are a lot of issues.

I'll take off my provider and my researcher hat and I will put my parent hat on. There are many times where I am at my wit's end. How could somebody do this who didn't have every bit of power and privilege that I have? If this stressing me to the edge, then what if I didn't have a good job and an education and a lot of respect and a loving husband and plenty of money and white privilege and everything else that goes along with it. I don't know how people can do it with any less privilege than I have because I know how hard it can be just with that.

That being said, I do think it's incredibly important that we think about ways of not just getting the most privilege. And some of that is as we do these programs, thinking about ways that we could really be spreading it around. I love the concierge

ideas, but those are the types of things that sometimes end up potentially increasing disparities and marginalization. I think that's really important for us to be remembering all the ways through.

I don't know, Dora, if you want to mention anything about the intersectionality findings you have been getting from your employment study.

DR. RAYMAKER: Sure. This is about health but as has been noted, there is a lot of intersection between health and employment. I just completed a pretty large amount of qualitative interviews. The intersectionality is huge. And it's something that is not addressed very explicitly in employment programs. Employment programs are like this is an employment program that's related to disability and it doesn't look at multiple

marginalizations for when you have a disability, but you are also trans or you have a disability and you are also trans, queer and black. That further marginalizes and pushes people out of the workforce and jeopardizes them and makes them less able to manage either their disability in an autism sense or their - any other health things that they have going on. These things all compound. I don't - I'm still in an early exploratory phase of that.

But I would like to see more work being done to look at multiple marginalizations in the programs that we develop because it's different. The experience that you have of the world and how people are going to be treating you is different.

DR. NICOLAIDIS: Scott, if I can get back to - you also mentioned toolkits of toolkits

and everything else. I struggle with this. On the one hand, I am absolutely convinced that this is one drop in the bucket and that we need a heck of a lot more. On the other hand, we sometimes are working in environments where you are drowning in a sea of plenty and there is a lot of stuff out there. Putting back a provider hat, as a provider, I don't need yet more toolkits or yet more videos or yet more things. I need something that I can act upon that's quality. That is actually why we focus a fair amount of the interaction with the providers is through these reports. Because maybe the pediatricians have more hope, but again as an adult provider, there's just so much that I can do. I want to take care of my patient and I will do everything I possibly can to do good care for my patient, but autism as a topic isn't there.

And that's kind of why - there are the toolkits of toolkits of toolkits. We have actually taken the approach of being really, really minor. And going you can have this toolkit. You may or may not look at it. You can do these trainings. You may not do it, but these are the ten things that your patient needs to take care of them. That's about as much as I think we can handle given 15-minute visits and panels of 2,000 patients.

DR. MURRAY: I agree with you. I think that is the point I was trying to make earlier, which is I think we need to be thinking about scalability. There is this sort of expert level that we have to get this information back out to the community. What are those one-pagers?

What are those - I think Dan Coury was saying this earlier about the guidelines that are written for perhaps even Down's syndrome. What do you look for? What questions do you ask? It is sort of like a decision-making tree. Then what's the next step? I agree with you. There is a lot out there, but I am not sure it is utilized in a way that is incredibly useful and particular for those primary care physicians and those adult physicians. We want to inform, but not overwhelm.

DR. KRIPKE: Thank you. You've said a lot of the things that I wanted to say. In terms of ideas, the Office of Developmental Primary Care has a decade work now on how do we train people, how do we get to them, how do we build this workforce - and there are some lessons learned that we can share.

Number one, literature shows CME doesn't work. I don't think that should be our emphasis.

Number two, there is going to be a lot of pushback about any sort of requirements and there will be a lot of pushback about the idea of specialization, although the issue of funding and access to expertise is a separate issue, but creating an actual specialization will get a lot of pushback. We can go into why later if somebody wants to.

But in terms of training, there is a distinction between exposure and experience. We need to think in terms of how do we get, for example, all medical students some exposure, but that is not really going to get them experience like a three-year fellowship would or the kinds of things that a developmental pediatrician would or even a

two-week rotation. I can do a lot with a medical student in a two-week rotation. They are profoundly different in how they approach people with disabilities after a two-week rotation, but that takes resources. In terms of things that do work.

In terms of concierge care, that has a name. I have a specialty practice that's all home care based and you can do things very efficiently. When you go to people's homes, you don't need to build the bricks and mortars so you can get things up very quickly. You can scale it very quickly. You can be very flexible and the model is very simple. It's a very small patient panel with a cell phone and a laptop, somebody who is very flexible and available to a small panel of patients. And for people who really - a clinic-based model is not going to work. I

think we need to look for that and people have very significant behaviors or are very medically fragile where it's very difficult to get them into a clinic and that model is just not going to work. Then we should think about that. It's not all autistic people or even most, but for the small subset of people who that is not going to work, we should look at those kinds of models. You can fund them.

Sending information with the patient like the AASPIRE toolkit, but you can send - the Office of Developmental Primary Care has a bunch of one to two-pagers. We have a series called What I Wish My Doctor Knew. They are all written by self-advocates. It has things like how to interact with a nontraditional communicator or what you need to know about my sensory sensitivities or things like people - that that are designed

for patients to bring to the appointment because that is when doctors are most receptive when the patient is right in front of them. But it has to be something that they can absorb in the context of a 50-minute appointment or a half an hour appointment. We have those kinds of tools on our website so that the patient could be a mechanism to get information to their doctors.

And then other point of care resources that can be incorporated into electronic medical records. You bring up your SmartPhrase. It kind of guides you through the questions or guides you through what to do or guides you through the resources, integrating that stuff so at the point of care, you can draw it up really quickly. We also provide phone and email contacts. We do need toolkits of toolkits because two pages

are not enough to tell you everything you need to know.

But what you were saying about we are not going to spend that much time learning about this topic. The trick is how do you get the right two-page to the right doctor at the right time. That can be done. We have warm lines so people pick up the phone and whatever issue they have, we've seen it before and we have a two-pager for you and we will get it to you right now. We can do that really quickly. When you have those toolkits then when somebody calls, you can very quickly get them exactly what they are looking for.

And then having consultation and mobile consultation. The Office of Developmental Primary Care had a mobile consult team that was multidisciplinary. We would go all over

Northern California sometimes traveling eight hours and do a very comprehensive consult in someone's home three hours, looking at their records from forever. We would be taking on the cases that merited that intensive work where people who were at very high risk of housing loss and being institutionalized and where they tried one of everything and were at their wit's end. And then our team would come in and really do that deep dive. A lot of times people just weren't asking the right questions. They really didn't even understand - they didn't have a framework for understanding what was going on. Sometimes you had to do the deep dive to figure it out, but sometimes the solutions were not that expensive or complicated. Sometimes it was just reframing how people were thinking about what they were seeing or sometimes it was -

anyhow, that was a very successful model and having that kind of expertise that can go to people.

It can go to communities and at the same time, we were able to do trainings. Let me see your patients with you to the local primary care doctors. There is one person in town. They are going to see everybody. Let's develop a relationship. We have a face relationship. When you call me, we have a very different kind of relationship when you call me about your patient next time. I've met your patient. I've been to your community. We know each other. We can be of use to you.

Having regional resources to support those primary care doctors so that when they have their one or two patients, they can call and they can get the help that they need.

DR. SPENCE: Clarissa, just a point of clarification. Who paid for an eight-hour drive and a three-hour visit for a team?

DR. KRIPKE: Regional centers, which are the state system.

DR. SPENCE: Yeah, I trained at UCLA so I know what they are.

DR. KRIPKE: Yes, state systems.

DR. SPENCE: So the state paid?

DR. KRIPKE: Indirectly Medicaid waiver money basically.

DR. SPENCE: And how did you set that up?

DR. KRIPKE: It fell apart so I shouldn't spend too much time on that. Ten years of work, ten years of work to build the relationship and to get that interdisciplinary work and partnering.

DR. TAYLOR: Beth and then Jeremy Parr.

DR. MALOW: First of all, great lectures. They were really helpful. Sorry, it's late and I'm forgetting my mic. Really great lectures. I think the emphasis on implementation science is so important. I had one example I wanted to give at Vanderbilt with the opioid crisis. What our CME office did, which was really cool - it is called Quiz Time. We got like this little case every day. It took like a minute to read it and then we answered one question. I am not saying that is the end all. But the idea of really thinking creatively about ways because I agree. We have so many toolkits and I have learned about so many today. And I want to give you one of ours. It's amazing what is out there, but we have to use them. And figuring out little kernels because we are

all so busy. I just wanted to give that example.

We might want to look at what other fields are doing like the opioid crisis, the idea of addiction medicine and how are they educating their providers. I know that there's differences in complexities. But I really think that's the answer. We have the materials, but we have to figure out how to get them out.

DR. NICOLAIDIS: I think as you say there are important lessons to be learned from all these other fields and then at the same time we have to be careful about over generalizing.

I've had a few different phases in my career. I started doing intimate partner violence research, which was my main topic for the first ten years. It was one of these

things where it was really hard to get providers to care about intimate partner violence.

And then I switched over to chronic pain and substance use. I went from speaking to empty rooms to people literally fighting to get into the room because there weren't enough seats. And then I went to autism and I'm back to speaking to empty rooms again. I do not think I was actually a better lecturer when it came to chronic pain and opioid use than when I was for intimate partner violence or autism.

Some of this is how much of this is driving the provider's pain. With chronic pain and issues around opioid use that drives a lot of our pain. That drives a lot of - the challenge of our day is taking care - which then means that there is a lot of desire for

that. I think potentially maybe in some practices especially around pediatrics that might be happening where again this has become enough of an issue where it's driving me to seek extra resources in education and knowledge.

The problem is with adult autism, very much like intimate partner violence. That oftentimes what's happening is we are actually having unmet health care needs. People aren't coming in for care. They are not actually presenting for things that they should have presented with. On a population level, we can say this is a huge problem.

But in my, my little viewpoint of what made my day difficult and what is going to make it go better tomorrow, that is probably not going to be what I am seeking care for. And I think we have to be realistic about

that as we think of solutions because it doesn't mean that it is any less important for us to do all these things, but it means we can't rely on providers coming and knocking on our doors because it is oftentimes the folks that aren't coming in that are really ending up having the biggest troubles.

DR. TAYLOR: Jeremy and then Micah.

DR. PARR: I just wanted to make a few reflections on what I have heard. One of that relates to the huge amount of agreement between various presentations during the day. It is really interesting. Lots of people approached presentations without speaking to one another and yet people have presented from different data sets about different studies from different countries from different health settings, and yet in terms

of the prevalence of co-existing conditions, in terms of the adjustments that you talked about, I talked about and that you talked about, they are all the same across the life course internationally across different health settings.

I wanted to make the case, I suppose, that while there is some increased evidence needed in terms of characterization probably GI, epilepsy. I agree with that, I agree with the comment about sleep. We can continue going with the science in relationship to characterization for some of those elements. In a way having characterized a bit of the problem, it's sort of time to move on simultaneously to starting to think about how we create change within services.

And of course we can do an intervention in relationship to GI problems or anxiety or

whatever, but actually people have multiple co-existing conditions and therefore we also need to move beyond single interventions to multiple interventions simultaneously. Because if we don't do multiple interventions simultaneously, we are not addressing the whole problem, if you like.

And as I said in my presentation, I think if we think about the effects of having a poor diet because you do not eat anything other than white food when you are age 4 and you are anxious at age 5 and you have epilepsy and so on and so on. The negative impact on health builds through the life course.

I suppose I just wanted to put that there. Because part of the challenge I suppose for research is people are always looking for things to research. But actually,

there comes a time where you have to say there is enough evidence on this. Like cerebral palsy and thinking about the amount of evidence around characterizing the co-existing conditions that go along there. People have moved on. I think we should move on from some of the things that have been talked about and start moving to the next stage. Thanks.

DR. MAZUREK: I was just going to reflect on I think a theme that has come up in this discussion is the idea of the need to get tools into people's hands when they need, when there is a patient in front of them that needs help. That's part of what was so successful with our pediatric ECHO because the providers are so motivated and they want to take better care of their patients. For us, that was a great way to get the toolkits

that we had worked on through the ATN into the hands of the providers for the cases they are presenting. I think that was successful.

I really like the idea of using the EMR to try to give just in time tools to people in the clinic when they are seeing a patient. I would love to hear more about how that's working.

DR. TAYLOR: We have Nina and then the other Jeremy and then Scott. And Denise did you want? Okay. Nina. You're up.

DR. SCHOR: Very good. There's a couple of things that I haven't heard about that I might have expected to hear about in this discussion. And probably the most prominent of them is the role of the handoff from the pediatrician to the adult provider. If you're saying that these pediatricians are seeing a gazillion of these patients in their practice

and they certainly get trained, although I must say my pet peeve is that they are not required to do a rotation on child neurology, but they are required to do developmental and behavioral pediatrics. They see and they do hands-on care of autistic children.

The American Academy of Pediatrics has in fact the one-page handout protocol for doing the hand off. It's very easily adaptable to people with chronic conditions. In fact, it's almost best for that population. What is the role for the pediatrician to shepherd that patient to the adult care?

And then the other thing, which I suspect I know the answer to, but I'm just going to put it out there, is what is the role for the dreaded MOC in maintenance of certification in educating people or at least

indicating that leaders in the field think this is important.

DR. NICOLAIDIS: I'll take a stab at both of them. Like many other things, I think transition is important and we have entire field of work around transition. I don't mean to underplay the importance of transition. And at the same time, I find it very interesting. It's sort of a theory of mind issue when it comes to pediatricians. Because I now am involved with all sorts of pediatric things because I do autism. I'm often the only internist in the room. From a pediatrician's standpoint, it's all about transition. For us, transition is like nothing. We have 60 years with them after that.

Population-wise if you take general populations, the age of transition is the age

where people seek the least health care. That age period, if you take autism away, is --

DR. SCHOR: (inaudible comment) see it as an opportunity for education.

DR. NICOLAIDIS: Absolutely.

DR. SCHOR: If you don't have a proper transition you may never see that patient in those (inaudible comment) years.

DR. NICOLAIDIS: Absolutely. It's an "and". Absolutely and many of our patients - the patients that are having very high needs, the issue is finding an adult provider who is willing to care for them. I get probably a - I get a few emails a month asking who can see this patient. The very high needs, the ones that are actually taking a lot of provider time, the biggest issue is finding a provider who's willing to do that and who has the skills to do that. We also have family

practice where they do not need to transition. I don't mean to ignore that.

For many of the other patients though, which is I think a larger portion of the population, the transition even if you have that hand off, you're going to have that hand off with a provider who, again just normally may not see - we do not see people in their 20s. If I see somebody who is 40 or 50, I think they're young. In my life - I can count the number of 20-year-olds I have taken care of on probably a few hands. It's just not a common time for people to be coming in.

Yes, it is important, and we have to remember that we can't fix everything by transitions because really when we are seeing folks is the 60-year-old who has the multiple medical problems and their pediatrician is long gone. Et cetera. Again, I do not mean to

downplay importance of transition. I know there is wonderful, wonderful work being done on transition.

The other issue is MOC. If you can find or if this group can find a way to have MOC in some way care about having something about autism and especially about adult autism, I will be thrilled. And I think that, just having studied for my 20-year recertification, you study what's on there. And I think that having that be something that's actually even considered.

I went into my 20-year recertification, which is a ten-hour test, saying at least I'll get the one question on autism. There was not one question on autism. Luckily, I passed. There was not one.

DR. TAYLOR: Jeremy V.

DR. VEENSTRA-VANDERWEELE: At first off, let me say that this has been just a wonderful discussion. I wanted to highlight one thing that was sort of a thread at the beginning, the tension between needing to better understand, discover, some of the roots of the co-occurring medical problems in autism spectrum disorder, how things go together, versus do better with what we currently know. We have really shifted to talking about how to do better with what we know, but I think it is important that we acknowledge that we need both things. Since this is the IACC, I think we need research on both things.

The other thing is I am struck by hearing this that really what we are talking about is difficulty motivating and engaging as being the primary barrier. That's actually

a different thing than what we sometimes imagine. To do my MOC, I had to relearn some things about geriatric psychiatry that I now don't know. I passed. I think I got those questions right even. But I don't know them now.

I think really where people learn in such a way that they are going to be helpful to the people we're all caring about is when they have somebody in front of them that they need to help. It feels to me like we may be needing studies of how best to engage autistic people and their families and then help them seek care from people who are willing to provide that care. That's a complicated thing to study.

And then we also have to study how to help those people who are willing to care for them to learn to care for them appropriately.

And it feels like those are two different things. And it feels like we are doing the second one. It's hard to figure out. You guys are doing the first one too. I know that. But it is sort of hard to figure out how to do the first one. They are really separate pieces and we need to figure it out. Unless we motivate and engage people to seek the care in a way that can yield good care, we're not going to provide the training for the providers because they are never going to be motivated. I think somehow we have to address that.

DR. TAYLOR: Scott, do you have a comment?

DR. ROBERTSON: I just wanted to say that it has been a great discussion all day. I think we have covered a lot of ground. I think there is always a lot more to cover in

this space. It's a really large complex set of topics. As I say, it weaves other things like employment, et cetera.

I mentioned sort of briefly, but just to touch upon it maybe a little, since pain came up, is that I am collaborating with one of my colleagues. I collaborate a lot on occupational therapy research. We are looking at pain experience of autistic adults right now qualitatively. Probably be able to share findings out with that probably in the next several months or year. We're finding crossover with some of these things already. We're just looking at the data right now, but obviously things like sensory and things like that come up when you are looking at pain experience and a lot of literature on challenges with interacting in terms of describing pain and things like that for

autistic adults. It hasn't been really studied that much yet because most of the literature on pain cross connected when you are looking on autism has mostly been focused only on kids. There is not as much out there on adults. Hopefully, we'll have more on shaping the change in terms of growing some more research out there on the barriers.

I relayed a lot to some of the qualitative that you actually had up there of like describing pain. I can't do that. I have no body kind of awareness in terms of from a cognitive kind of physio - there's nothing like changes or makes that better other than having understanding I think from the service provider that they may have to think a little creatively on how I could better self-describe my pain or other challenges. But that's one of the things that always gives me

intense anxiety with the health care system. It's so dependent on self-report. I know that people do that more now even maybe than years before. Like a lot of the imaging and things like that are expensive and people don't want to do the cost so self-report. Like talking doesn't costs extra money.

At the other end of the thing, it just means it's a bigger barrier for us because communication already being an issue when you have cross intersection. I always feel trepidations when it's mental health or physical health, going into this setting.

I feel a little bit more energized after today that I think we are moving forward based on the discussions. I think we had really productive conversations. Kudos to everyone on the presentations today. Kudos to Dr. Taylor for shepherding all the complex

questions and discussions because we had a lot of active energy and engagement. I think you did an awesome job with triaging all the queries that folks have. I'm really excited after what we have discussed today. This has been awesome. Thanks.

DR. TAYLOR: Let's end on that note. I like that a lot. Jeremy?

DR. DANIELS: Great. We are right on time ending. We didn't have time for general discussion, but just briefly to summarize it. It was a really great day of discussion. I think this will really help the working group and members of the committee who've been here today.

After the call, David and Julie and I will be getting together to try to put together something to reflect what happened here and then we'll be convening another

phone call of the Working Group, probably not until after the October 17th IACC meeting that is coming up, an all-day meeting. It will be here in this room, and everyone is also welcome to join us for that.

Thank you so much for those of you who traveled here to be here with us today and those who stood by on the phone all day. That was quite a feat and for our public listening audience. We really appreciate your joining us. Safe travels everyone and good night.

(Whereupon, at 5:00 p.m. the meeting adjourned.)