INTERAGENCY AUTISM COORDINATING COMMITTEE

2015

SUMMARY OF ADVANCES

in Autism Spectrum Disorder Research

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OFFICE OF AUTISM RESEARCH COORDINATION
NATIONAL INSTITUTES OF HEALTH

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ABOUT THE IACC

The Interagency Autism Coordinating Committee (IACC) is a Federal advisory committee charged with coordinating all activities concerning autism spectrum disorder (ASD) within the U.S. Department of Health and Human Services (HHS) and providing advice to the Secretary of HHS on issues related to autism. It was established by Congress under the Children's Health Act of 2000, reconstituted under the Combating Autism Act (CAA) of 2006, and renewed under the Combating Autism Reauthorization Act (CARA) of 2011 and the Autism Collaboration, Accountability, Research, Education, and Support (CARES) Act of 2014.

Membership of the Committee includes a wide array of Federal agencies involved in ASD research and services, as well as public stakeholders, including self-advocates, family members of children and adults with ASD, advocates, service providers, and researchers, who represent a variety of perspectives from within the autism community. This makeup of the IACC membership is designed to ensure that the Committee is equipped to address the wide range of issues and challenges faced by families and individuals affected by autism.

Under the CAA and subsequent authorizations, the IACC is required to (1) develop and annually update a strategic plan for ASD research, (2) develop and annually update a summary of advances in ASD research, and (3) monitor Federal activities related to ASD.

Through these and other activities, the IACC provides guidance to HHS and partners with the broader autism community to accelerate research and enhance services with the goal of profoundly improving the lives of people with ASD and their families.

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For more information about the IACC, see *http://www.iacc.hhs.gov*.

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INTRODUCTION

THE 2015 IACC SUMMARY OF ADVANCES IN AUTISM SPECTRUM DISORDER RESEARCH

Each year, the IACC releases its annual list of scientific advances that represent significant progress in the field. The 20 studies selected have given new insight into the underlying biology of autism spectrum disorder (ASD) and potential risk factors, examined the state of the science in early screening and diagnosis, and evaluated promising early intervention strategies. The advances also address health outcomes for children and adults with autism, and issues related to education, transition to adulthood, and employment. The *2015 Summary of Advances* provides short, plain language summaries of the top research breakthroughs selected by the IACC from a pool of research articles nominated by the members. Articles are grouped according to the topics represented by the questions of the *IACC Strategic Plan for ASD Research*. Citations for the articles selected for the *Summary of Advances*, as well as a complete listing of those nominated, are included at the end of the document.

ARTICLES SELECTED FOR THE 2015 SUMMARY OF ADVANCES

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- National Autism Indicators Report: Transition into Young Adulthood
- High rates of parkinsonism in adults with autism
- Longitudinal patterns of employment and postsecondary education for adults with autism and average-range IQ

QUESTION 7: WHAT OTHER INFRASTRUCTURE AND SURVEILLANCE NEEDS MUST BE MET?

- No articles were selected from Question 7. For a list of articles that were nominated in this category, see the Full Listing of Nominated Articles.

QUESTION 1

WHEN SHOULD I BE CONCERNED?

Age at autism spectrum disorder (ASD) diagnosis by race, ethnicity, and primary household language among children with special health care needs, United States, 2009–2010

Jo H, Schieve LA, Rice CE, Yeargin-Allsopp M, Tian LH, Blumberg SJ, Kogan MD, Boyle CA. *Matern Child Health J.* 2015 Aug;19(8):1687-97. [*PMID: 25701197*]

In the US age of ASD diagnosis is decreasing; however, there is limited evidence about discrepancies between race/ethnicities in age of diagnosis even though non-Hispanic-white children are still more likely than either black or Hispanic children to be diagnosed with ASD. To determine if there are differences in the timing of ASD diagnosis across different racial and ethnic groups, the researchers in this study identified 2,729 children from 3 to 17 years of age with a diagnosis of ASD using the 2009–2010 National Survey of Children with Special Health Care Needs (NS-CSHCN) (a telephone survey conducted by the National Center for Health Statistics of the Centers for Disease Control and Prevention). The 2,729 children were divided into four groups: white (and not Hispanic), black (and not Hispanic), Hispanic who speak mainly English at home, and Hispanic who speak mainly a language other than English at home. Researchers then compared ASD rates, age at diagnosis, and the percentage of children with later ASD diagnoses (defined as at 5 years of age or older) across these groups.

Although the researchers found that the average age of ASD diagnosis was similar across the racial, ethnic, and primary household language groups for children in the study who were 3 to 4 years of age at the time of the study, they did identify some differences in age at first diagnosis across these groups for children who were 5 years of age or older at the time of the study—mainly in cases of less severe, or mild or moderate, ASD. Specifically, they found that two groups of children 5 to 17 years of age with less severe ASD—white children and English-speaking Hispanic children—had a higher prevalence (15.3 and 14.1 per 1,000, respectively) of ASD and a higher proportion (50.8% and 43.5%, respectively) of later diagnoses than black children (10.4 per 1,000 and 33.5%) and Hispanic children who do not speak English (5.2 per 1,000 and 18.0%). However, these results may not be truly indicative of a higher prevalence of ASD in these groups. Rather, it may indicate that the black children and the non-English-speaking Hispanic children are under-represented in the study sample or that they are getting screened and diagnosed with ASD less often than the white and Hispanic English-speaking children. This is consistent with previous research that has found that black and Hispanic children may have reduced access to mental health care and that children of Hispanic immigrants

(measured in this study as non-English speaking households) may have additional cultural and language barriers that reduce their access to health care. This study highlights that cultural and language differences should be considered when providing care and that education about the detection and importance of early identification of ASD is needed for both parents and health care professionals.

Diagnostic stability in young children at risk for autism spectrum disorder: a baby siblings research consortium study
Ozonoff S, Young GS, Landa RJ, Brian J, Bryson S, Charman T, Chawarska K, Macari SL, Messinger D, Stone WL, Zwaigenbaum L, Iosif AM. *J Child Psychol Psychiatry*. 2015 Sep;56(9):988-98. [*PMID: 25921776*]

Although previous research has shown that a clinical diagnosis of ASD made before a child reaches 3 years of age is not likely to change over time, a critical need remains to better understand whether an early diagnosis in children who have a family risk of developing ASD also remains stable. Such an understanding is especially important because American Academy of Pediatrics (AAP) guidelines call for more intensive surveillance and screening for this high-risk group of children, which provides an opportunity for earlier intervention and treatment. This study looked at whether a diagnosis of ASD that was made at 18 and 24 months of age in infants with a family risk for ASD remained the same at 36 months of age. It also explored the differences between children who were correctly and incorrectly diagnosed at 18 and 24 months.

The study involved the analysis of data contributed by seven sites in the Baby Siblings Research Consortium (BSRC)—an international network that gathers data from individually funded research sites to study the development of infants with a family risk for ASD. BSRC contributed data for 418 infants, all of whom had older biological siblings with ASD. Each site used standard diagnosis procedures to make the diagnosis of "ASD" or "Not ASD" at 18, 24, and 36 months for each of the infants. Statistical analyses found that when a child was diagnosed as having ASD at 18 months of age, 93% of the time that diagnosis was confirmed at 24 months and 36 months of age. Also, children who were first diagnosed as having ASD at 24 months (but not at 18 months) of age were confirmed to have ASD 82% of the time at 36 months of age. These high levels of stability indicate that when ASD is identified at 18 or 24 months, the diagnosis is not likely to change—and intervention should begin as soon as possible.

These findings support the AAP guidelines for more intensive surveillance for children at high risk for ASD and provide reassurance that early screening, assessment, and referral to services for these children is needed. The study authors also suggest that the AAP guidelines may need to go even further, because the results showed that rescreening children in high-risk groups (siblings of children with ASD and children with developmental delays) at 3 years of age will identify some children whose ASD symptoms were not apparent earlier. Some implications of this finding are that screening may need to be repeated many times in the first years of life, and beyond 24 months, and that follow-up should continue for children who show early signs of social and communication difficulties, even if they are not diagnosed with ASD when they are first assessed.

Early screening of autism spectrum disorder: recommendations for practice and research

Zwaigenbaum L, Bauman ML, Fein D, Pierce K, Buie T, Davis PA, Newschaffer C, Robins DL, Wetherby A, Choueiri R, Kasari C, Stone WL, Yirmiya N, Estes A, Hansen RL, McPartland JC, Natowicz MR, Carter A, Granpeesheh D, Mailloux Z, Smith Roley S, Wagner S. *Pediatrics*. 2015 Oct;136 Suppl 1:S41-59. [*PMID: 26430169*]

Early screening of children for ASD can be helpful to both children and their families because it enables earlier diagnosis and intervention. In 2009, the American Academy of Pediatrics (AAP) issued a recommendation that pediatricians routinely screen all children for ASD at 18 and 24 months of age using an appropriate screening tool. However, in many parts of the United States, physicians are not meeting this recommendation for ASD screening. It is believed that the debate over whether there is enough evidence to support the value of early screening for ASD of all children may be contributing to the slow uptake of the AAP recommendation into clinical practice. It was within this context that an international working group of clinical practitioners and researchers with expertise in ASD and developmental disabilities met in October 2010. Their aim was to conduct an updated review of the literature that would inform the development of their recommendations for ASD screening best practices, and to discuss ways to increase the adoption of widespread early screening. The group reviewed the evidence base represented by the scientific literature over time (through 2013) and reached agreement on recommendations that addressed the following question: "How can we optimize developmental course and outcomes through ASD screening programs for children aged ≤24 months?"

The group's recommendations listed below focus on the usefulness of screening all children for ASD at 18 and 24 months of age and emphasize the importance of using the results of the screening to immediately refer children for evaluation if indicated, so that they may begin receiving intervention as soon as possible. Importantly, the findings indicate that an ASD diagnosis in children aged 24 months and older usually remains stable (unchanged) over time, and the group also identifies priorities for future research in ASD screening. The recommendations of the working group are as follows:

Statement 1: *Evidence supports the usefulness of ASD-specific screening at 18 and 24 months. ASD screening before 24 months may be associated with higher false-positive rates than screening at ≥24 months but may still be informative.*

Statement 2: *The evidence indicates that siblings of children with ASD are at elevated risk for ASD and other developmental disorders and thus should receive intensified surveillance.*

Statement 3: *Children identified through ASD-specific screening should be immediately referred for diagnostic/developmental evaluation and appropriate intervention.*

Statement 4: *The long-term stability of ASD diagnosis in children aged ≥24 months is well established. Emerging data suggest that ASD diagnoses in substantial proportions of children diagnosed before age 24 months are also stable, although further research is needed, particularly in the context of early screening.*

Statement 5: *Further attention to potential barriers to ASD-specific screening in the health care system is needed.*

Statement 6: *Methodologically rigorous research in ASD-specific screening should be a high priority.*

Statement 7: *Additional priorities for future research include studies that:*

- *Examine how broadband and ASD-specific tools can be used in a complementary fashion to maximize both sensitivity and specificity of early screening, perhaps in the context of multistage screening, in which a wide net is cast initially and false-positives are winnowed out in successive assessments;*
- *Evaluate screening strategies by using randomized experimental designs;*
- *Consider additional outcome metrics for screening: potential financial savings to society; unintended effects (e.g., family stress);*
- *Examine whether computer technology can improve screening accuracy;*
- *Examine the effectiveness of repeating screening for ASD;*
- *Evaluate how belief systems affect screening uptake and outcomes; and*
- *Examine potential screening strategies that include measurement of biomarkers.*

Early identification of autism spectrum disorder: recommendations for practice and research

Zwaigenbaum L, Bauman ML, Stone WL, Yirmiya N, Estes A, Hansen RL, McPartland JC, Natowicz MR, Choueiri R, Fein D, Kasari C, Pierce K, Buie T, Carter A, Davis PA, Granpeesheh D, Mailloux Z, Newschaffer C, Robins D, Roley SS, Wagner S, Wetherby A. *Pediatrics*. 2015 Oct;136 Suppl 1:S10-40. [*PMID: 26430168*]

Identifying children with ASD early helps to ensure that they receive treatment earlier, which leads to better long-term outcomes. It also would help reduce the average age of ASD diagnosis in the United States of 4 to 5 years, which seems to persist even though parents generally report their first concerns before their child is 18 to 24 months old. To address these concerns, an international panel of clinical practitioners and researchers met to complete an updated literature review on the advances that have been made in understanding the early development and identification of ASD in recent years. The group reached agreement on the development of recommendations based on current evidence gathered through an extensive review of the literature that addressed the following question: "What are the earliest signs and symptoms of ASD in children 24 months and younger that can be used for early identification?"

The recommendations presented below were designed to help guide clinicians and researchers in their work related to the early identification of ASD. They include a focus on the wide range of clinical characteristics seen in ASD; on the availability of evidence about behavioral risk markers, or indicators, of ASD at different ages; on the need for caution when drawing conclusions about early risk markers of ASD from certain studies; and on being cautious when generalizing findings from studies of high-risk infants. They also emphasize the importance of including diverse samples in research about these early markers and provide direction for future efforts.

The recommendations of the panel were as follows:

Statement 1: *Evidence indicates substantial heterogeneity in the presentation and natural history of clinical features associated with ASDs. This heterogeneity has ramifications for the interpretation of research literature as well as for clinical practice.*

Statement 2: *There is evidence that reduced levels of social attention and social communication, as well as increased repetitive behavior with objects, are early markers of ASD between 12 and 24 months of age. Additional potential markers include abnormal body movements and temperament dysregulation.*

Statement 3: *Reliable behavioral markers for ASD in children aged <12 months have not yet been consistently identified.*

Statement 4: *Developmental trajectories may also serve as risk indicators of ASD.*

Statement 5: *Caution should be exercised in drawing conclusions about early risk markers of ASD from studies that do not include individual-level outcome data.*

Statement 6: *Caution should be exercised in generalizing findings from studies of high-risk infants.*

Statement 7: *Research about early markers of ASD should include diverse high- and low-risk samples.*

Statement 8: *Future efforts should aim to identify: 1) early markers that can be measured in routine clinical practice, involving direct observation and parental report; 2) early biological processes measurable concurrently with, or before, overt behavioral markers; and 3) combined approaches.*

QUESTION 2

HOW CAN I UNDERSTAND WHAT IS HAPPENING?

The idiosyncratic brain: distortion of spontaneous connectivity patterns in autism spectrum disorder
Hahamy A, Behrmann M, Malach R. *Nat Neurosci.* 2015 Feb;18(2):302-9. [*PMID: 25599222*]

Research that helps scientists understand differences in how the brain is structured and how it functions in people on the autism spectrum compared with neurotypical individuals not only increases scientific knowledge about autism but also provides a way to potentially characterize the severity of ASD symptoms and ultimately helps to provide a path for developing effective interventions. Scientists can measure areas in the brain that are associated with the processing of various tasks in thinking and reasoning (cognitive tasks) to identify abnormalities in brain activity, or connectivity, by using functional magnetic resonance imaging (fMRI). fMRI is a noninvasive imaging procedure that measures brain activity by assessing changes in blood flow in the brain that are associated with the activity of neurons. By using fMRI to measure brain function connectivity in adults at rest, scientists have developed a substantial body of research that has identified irregular patterns of brain connectivity in people with ASD. Although these findings, which include a reduction in certain brain connections, support the idea that the ASD brain is "under-connected," some more recent studies have reported results suggesting that the brain in ASD is "over-connected." To try to find an explanation for the differences between these varying reports, scientists accessed a large collection of fMRI scan data sets (the Autism Brain Imaging Data Exchange [ABIDE]).

The researchers analyzed the resting state fMRIs of 68 adults with high-functioning ASD (adults with relatively mild symptoms of ASD) and 73 control participants (participants without ASD) from the ABIDE data set. The scientists found that while the brain activity patterns in the control participants were relatively consistent, ASD participants showed significant and individually distinct (idiosyncratic) distortions of the pattern of functional connectivity. This greater variability of patterns among individuals may explain conflicting findings from previous studies, and the authors caution that brain regional connectivity differences between ASD and control groups should be examined carefully as high variability among ASD subjects may be contributing to those apparent differences. The researchers who conducted this study propose that the variations in the connectivity patterns of the ASD participants may

reveal a previously unrecognized core characteristic of high-functioning adults with ASD and could potentially be used to distinguish subtypes and severity of symptoms in ASD populations. While they did discover that there was a correlation between some measures of symptom severity and the degree of distortion from the control group, given the small sample size they were not able to distinguish any subtypes of ASD. In addition, some of the study findings indicate that the differences in the connectivity patterns among individuals, including those with ASD, may be in part a result of each person's unique interaction with his or her environment. Future studies may help explain how these distinct functional connectivity patterns arise in ASD and influence symptoms, as well as if these results can be replicated in additional populations with other disorders affecting the interaction between the brain and the environment.

Insights into autism spectrum disorder genomic architecture and biology from 71 risk loci

Sanders SJ, He X, Willsey AJ, Ercan-Sencicek AG, Samocha KE, Cicek AE, Murtha MT, Bal VH, Bishop SL, Dong S, Goldberg AP, Jinlu C, Keaney JF 3rd, Klei L, Mandell JD, Moreno-De-Luca D, Poultney CS, Robinson EB, Smith L, Solli-Nowlan T, Su MY, Teran NA, Walker MF, Werling DM, Beaudet AL, Cantor RM, Fombonne E, Geschwind DH, Grice DE, Lord C, Lowe JK, Mane SM, Martin DM, Morrow EM, Talkowski ME, Sutcliffe JS, Walsh CA, Yu TW; Autism Sequencing Consortium, Ledbetter DH, Martin CL, Cook EH, Buxbaum JD, Daly MJ, Devlin B, Roeder K, State MW. *Neuron*. 2015 Sep 23;87(6):1215-33. [*PMID: 26402605*]

Autism is known to have a strong genetic component—which is why, for example, siblings of children with autism have a higher risk of developing autism. Finding the genes and the areas of the human genome that are involved in autism can help provide a deeper understanding of how the brain works in autism and potentially lead to the development of new, more effective interventions. In this study, an international research team analyzed genomic information from 2,591 families that include at least one child with ASD. They found six large regions of the genome that contain *de novo* copy number variants (dnCNVs; widespread structural variations in the human genome that are not inherited) contributing to autism risk. In addition, the team found 65 specific genes that contribute to ASD risk, 27 of which were newly identified. Notably, 28 of the 65 identified genes are believed to be highly likely to play a role in the risk of developing ASD.

The team's analysis revealed a total of 71 locations in the genome where DNA mutation is associated with ASD (risk loci), including the six dnCNV regions and the 65 specific high-risk genes noted above. The researchers also determined that some of the ASD-associated genes are related to the development and function of synapses (the small junctures separating neurons), while others are related to chromatin (part of a cell that packages DNA and determines whether genes are "turned on" or "turned off"). Through this study, it was also found that small dnCNV regions are more likely to include a single gene with a strong effect on ASD risk, while large dnCNV regions, in contrast, are more likely to contain a number of genes each of which exert a more modest effect on autism risk. The study also considered how the sex of the individual and the type of mutation relate to non-verbal IQ (NVIQ; or thinking and problem-solving skills that do not require the use of language). It was concluded that although lower NVIQ is found in both males and females with autism, having a low NVIQ does not necessarily mean that the ASD-associated mutations are present, and having a high NVIQ does not mean that the ASD-associated mutations are missing. In other words, *de novo* mutations were found in ASD-associated genes of individuals across the entire range of intellectual levels seen in ASD, including in high-IQ individuals with ASD, suggesting these mutations confer ASD risk separately from intellectual disability. In addition, the team found data to support what is called the "female protective effect" (FPE) hypothesis as an explanation for the fact that females are far less likely than males to be diagnosed with ASD. Although the genetic mutations associated with ASD are found in the same set of genes in both sexes, more genetic mutations occur in females than in males with ASD, suggesting that in girls the number of mutations present in these genes must reach a high threshold in order to result in ASD. All of this

information can help guide researchers as they continue their work to discover which genes and genomic regions need to be studied more intensively among the hundreds that are likely to be involved in ASD—and as even more studies on these genes go forward, we can move closer to understanding the disorder and translating these basic research discoveries into treatments.

QUESTION 3

WHAT CAUSED THIS TO HAPPEN AND CAN IT BE PREVENTED?

Administration of thimerosal-containing vaccines to infant rhesus macaques does not result in autism-like behavior or neuropathology

Gadad BS, Li W, Yazdani U, Grady S, Johnson T, Hammond J, Gunn H, Curtis B, English C, Yutuc V, Ferrier C, Sackett GP, Marti CN, Young K, Hewitson L, German DC. *Proc Natl Acad Sci U S A*. 2015 Oct 6;112(40):12498-503. [*PMID: 26417083*]

This study examined whether exposure to vaccines containing ethyl mercury (found in the vaccine preservative thimerosal) or the measles, mumps, and rubella (MMR) vaccine could be demonstrated to be linked to development of autism-like symptoms in an animal model. The researchers carried out their study in infant monkeys (rhesus macaques) by exposing six groups of animals to thimerosal-containing vaccines (TCVs) and/or MMR or placebos according to one of six schedules, which included a historical and recent recommended vaccine schedule. The research team then looked for behavioral changes in the monkeys and for any unusual patterns in three brain regions corresponding to those known to exhibit changes in the postmortem brains of humans diagnosed with ASD. The six groups of animals used in the study had 12 or more monkeys per group. The control group received only saline (a salt solution), while the other groups received either a combination of vaccines from a historical (1990s) vaccine schedule, an accelerated historical vaccine schedule, a more recent (2008) vaccine schedule, or a single vaccine and saline combination. An analysis of social behavior in the juvenile monkeys showed no significant differences in "negative" social behaviors between animals (such as fear, withdrawal, or repetitive behaviors) in the control and experimental groups. In addition, when comparing postmortem tissue from animals in the control group with tissue from animals in the two groups having the highest exposure to vaccines, no neuropathological changes (e.g., changes in organ volume, cell number, or cell size) were found in three areas of the brain known to show changes in humans with ASD: the cerebellum, hippocampus, and amygdala. The researchers concluded that their study does not support the hypothesis of a role for certain vaccines in the development of autism; they state that "our data strongly support the conclusion that childhood TCVs do not produce ASD-like neuropathology or behavioral changes in the nonhuman primate."

Autism occurrence by MMR vaccine status among US children with older siblings with and without autism

Jain A, Marshall J, Buikema A, Bancroft T, Kelly JP, Newschaffer CJ. *JAMA*. 2015 Apr 21;313(15):1534-40. [*PMID: 25898051*]

Although numerous research studies over the past 15 years have suggested that vaccines, and in particular, the MMR (measles, mumps, and rubella) vaccine is not associated with development of ASD, this issue continues to be a concern among some members of the autism community as well as the general public. The goal of this study was to compare autism rates in MMR-vaccinated and MMR-non-vaccinated siblings of children with autism (a high-risk population) to determine whether vaccination increases autism risk in this population. This study examined the occurrence of ASD by vaccine status in a sample of 95,727 children in the United States between birth and 5 years of age and who have an older sibling with or without ASD. This study used a large administrative commercial health plan claims database (the Optum Research Database) to identify the study participants. Children were determined to have received the MMR vaccine if they received a medical code indicating that they received each component (zero, one, or two doses) after 1 year of age. Children and their older siblings were determined to have ASD through a review of insurance claims, with the requirement that two or more claims had been made on separate dates with the appropriate medical codes for autistic disorder, other specified pervasive development disorder (PDD), including Asperger syndrome, or an unspecified PDD.

The study found that receiving the MMR vaccine was not associated with an increased risk of ASD at any age. Specifically, the study found that for children, age 2, with an older sibling with ASD the relative risk of ASD for one dose of MMR vaccine compared to no vaccine was 0.76, and for children age 5, the relative risk of ASD for two doses compared to no vaccine was 0.56. For children, age 2, who did not have an older sibling with ASD, the relative risk of ASD for one dose of MMR vaccine compared to no vaccine was 0.91, and at age 5, the risk of ASD for two doses was 1.09. The finding that no link was observed between MMR vaccination (either one or two doses) and increased ASD risk among children with older siblings that have ASD is consistent with studies done in other groups, and supports the conclusion that MMR vaccination is not associated with ASD. These findings indicate that there is no harmful association between receiving the MMR vaccine and ASD, even among children already at a higher risk for ASD.

Association of maternal diabetes with autism in offspring

Xiang AH, Wang X, Martinez MP, Walthall JC, Curry ES, Page K, Buchanan TA, Coleman KJ, Getahun D. *JAMA*. 2015 Apr 14;313(14):1425-34. [*PMID: 25871668*]

There is some evidence children who are exposed to maternal diabetes (a mother's diabetes diagnosed prior to pregnancy) are at increased risk for ASD although there is less evidence about prenatal exposure to gestational diabetes mellitus (GDM, diabetes diagnosed during pregnancy). Importantly, no studies have collected data on the importance of timing of exposure to hyperglycemia (high blood sugar, or too much glucose in the bloodstream) through maternal diabetes or GDM on the risk of ASD. To help fill this knowledge gap, this study analyzed already existing data from a single health care system to try to determine if there is a connection between maternal diabetes and the risk of ASD in children. The study also investigated using the timing of the GDM diagnosis as a surrogate, or substitute, for the timing of fetal exposure to hyperglycemia.

The study included a group of 322,323 children from diverse backgrounds who were born at 28 to 44 weeks of pregnancy in Kaiser Permanente Southern California (KPSC) hospitals between January 1, 1995 and December 31, 2009. The children were followed for an average of 5.5 years after their birth, and during this time, 3,388 children (2,963 unexposed to either type 2 diabetes or GDM, 115 exposed to type 2 diabetes, and 310 exposed to GDM) were diagnosed with ASD. The main study finding was that in these 3,388 children, having a mother who had GDM diagnosed by 26 weeks of pregnancy was associated with the risk of ASD, but children whose mothers had diabetes before they became pregnant did not have this increased risk. The authors speculate that this difference may be due to the fact that mothers who are known to have type 2 diabetes may already be receiving treatment to control hyperglycemia, which could reduce the exposure of the fetus to high blood sugar and thus maternal diabetes may have less of an impact on fetal brain development than GDM diagnosed early in pregnancy. Although this kind of study cannot determine whether the mother having GDM caused autism in the child, the results do suggest that the children of women with GDM who are diagnosed by 26 weeks of pregnancy are at higher risk, and therefore should receive early screening for ASD. In addition, until further research is conducted on GDM and autism risk, it is important to screen pregnant women for GDM and control maternal blood sugar levels to potentially reduce the risk of autism for the child.

QUESTION 4

WHICH TREATMENTS AND INTERVENTIONS WILL HELP?

Long-term outcomes of early intervention in 6-year-old children with autism spectrum disorder

Estes A, Munson J, Rogers SJ, Greenson J, Winter J, Dawson G. *J Am Acad Child Adolesc Psychiatry*. 2015 Jul;54(7):580-7. [*PMID: 26088663*]

While most studies of early behavioral interventions for children with ASD have looked only at immediate outcomes at the end of early interventions, this long-term study is the first to search for evidence of sustained effects of early interventions. In this study, the researchers conducted a follow-up analysis on the results from a previous randomized clinical trial, which compared groups of children with ASD aged 18 to 30 months receiving either the Early Start Denver Model (ESDM) intervention or the more usual "Community treatment" approach in the greater Seattle area over a 2-year period. ESDM includes integrating applied behavioral analysis methods with developmental approaches and parent coaching to promote learning, social reciprocity (the back-and-forth flow of social interaction), and affective (emotional) engagement. Results reported in a previous study showed that at the end of the treatment period, ESDM had an overall positive impact compared with treatment as usual, including significant improvement in intellectual ability (particularly in how the children spoke and what they understood when others were talking) and daily living skills, and a less severe autism diagnosis than at the start of the trial. There were also significant differences in social behavior between the two groups, although there were no significant differences in autism symptom levels.

The current study examined whether long-lasting outcomes could be observed 2 years after the interventions in the first study ended. To accomplish this, the 39 children remaining available from the original study of 48, now age 6, were again assessed. The researchers found that while the two groups were not significantly different in terms of the observed improvements in intellectual functioning, the adaptive behavioral improvements seen in the ESDM group were maintained even though these children had received fewer services than the "Community treatment" group after the end of the original intervention trial. The ESDM group also showed a trend toward improved peer relations, a measure which had not been previously measured. Surprisingly, the ESDM group had less severe overall ASD symptoms than the "Community" group, which was unexpected given that this had not

been observed immediately following the intervention. This is the first study to examine the longer-term effects of early ESDM behavioral intervention on the course of ASD. It suggests that early intensive interventions can not only produce immediate improvements in intellectual ability, language, and social behavior, but that these improvements can be sustained over time and be generalized to core ASD symptoms.

Parent-mediated intervention versus no intervention for infants at high risk of autism: a parallel, single-blind, randomised trial
Green J, Charman T, Pickles A, Wan MW, Elsabbagh M, Slonims V, Taylor C, McNally J, Booth R, Gliga T, Jones EJ, Harrop C, Bedford R, Johnson MH; BASIS team. *Lancet Psychiatry*. 2015 Feb;2(2):133-40.
[*PMID: 26359749*]

Research has suggested that when children receive interventions during the prodromal phase of ASD—which occurs during the first year of life when very early signs and symptoms might indicate the start of ASD, but before more specific symptoms are observed and before the disorder is diagnosed—the severity of the ASD may be reduced. This study tested the effect of a very early intervention during this prodromal period. This study used an adapted Video Interaction to Promote Positive Parenting (iBASIS-VIPP), in which parents are guided by therapists to improve social interaction in their infants, as it has been shown to improve parental interaction with their infants in other developmental contexts. Families were randomly assigned either to receive the intervention (28 families) or no intervention (control, 26 families). The members of the study team who assessed the level of attentiveness displayed by the infants were blinded, that is they did not participate in the intervention and were not aware of which infants were assigned to which group.

There is some evidence that following intervention, infants showed improvements across multiple outcomes and risk-markers for developing ASD, including behavior, social interaction, and brain function. The primary outcome measured in this study was the infants' attentiveness to their parents, and there was a positive improvement in this measure following intervention, although given the degree of statistical uncertainty there is the possibility that there was no effect or a negative effect of the intervention. The secondary outcomes overall provide more evidence for a positive treatment effect, primarily due to the strong impact that intervention had on parent directiveness, or the degree to which parents control or direct the interaction with their child during play. Parent non-directiveness encourages children to engage and interact with their caregivers, and may be reduced in parents with children with neurodevelopmental abnormalities. This intervention acted directly on improving parent non-directiveness, so it is important that there was a strong effect in improving this measure. Although the results need to be confirmed in a larger study before more definite conclusions can be made, the trial did show that it is possible to deliver and test a very early intervention of this kind, in particular because all of the families who began the intervention completed it successfully.

Children with autism spectrum disorder and social skills groups at school: a randomized trial comparing intervention approach and peer composition

Kasari C, Dean M, Kretzmann M, Shih W, Orlich F, Whitney R, Landa R, Lord C, King B. *J Child Psychol Psychiatry*. 2016 Feb;57(2):171-9. [*PMID: 26391889*]

Establishing positive peer relationships can be challenging for children with ASD. This study looked at children with ASD, in kindergarten through fifth grade, in their regular school settings rather than in clinical settings to compare two social skills interventions. One group consisted of a mix of children with ASD who were from different grade levels and classrooms, and the other group had a mix of typical children and children with ASD from the same grade level/classroom. The teaching approach was also varied—comparing direct instruction on social skills (didactic SKILLS that make information logical and accessible) to shared, activity-based teaching of social skills in a natural setting (activity-based ENGAGE groups). The purpose of the study was to assess improvement of social network connections (such as increase in social interactions and mutual feelings of friendship) for children with ASD, and this was measured using a confidential survey administered to both the children with ASD and neurotypical peers who agreed to participate. The survey assessed peer engagement in the playgroup, the number of peers nominated as friends by the child with ASD, and the number of peers who nominated the child with ASD as a friend. Based on a previous study, the researchers expected the ENGAGE groups (the inclusive groups with both neurotypical children and children with ASD) to establish better relationships with other children.

The 137 study participants were school-aged children with ASD located at four different school sites across the U.S. and observed over the course of 2 years. The children's interactions were assessed using the peer surveys prior to the start of the experimental interventions, immediately after the 8 weeks of intervention (two times per week), and again 8 weeks later. The SKILLS intervention included lessons that described social interactions, body language, teasing, and friendship tips. The ENGAGE intervention, which included not only children with ASD but their school peers (in a ratio of about 1:3), had the children meet in social groups targeting peer engagement and acceptance, and shared interests of each group were used to generate a list of possible activities—such as conversational exercises, structured games, free play, improved storytelling, and music. A Friendship Survey evaluated the friendships children made and their networks of peer relationships. In addition, observers who did not know which children had ASD conducted behavioral observations at time-points before, during, and after interventions that assessed a child's engagement with his/her peers.

After the intervention, the study authors found there was no significant change in social network connections over time based on intervention group, but there were other modest effects of improvement. Overall, the results unexpectedly showed more benefits from a SKILLS-based, social skills group consisting of all ASD children than for a mixed/inclusive (typical plus ASD children) group. Children in the SKILLS group had more peer engagement and less isolation during recess. Another observation concerned the quality of the child-teacher relationship; children

with low teacher-child closeness or high conflict improved more in their social connections through the SKILLS intervention while children with higher teacher-child closeness improved more through the ENGAGE intervention. This study shows the importance of inclusion and social participation for students with ASD and suggests that the quality of teacher-student relationship may be an important factor in choosing a social intervention approach; however, research is still needed to understand how we can best support opportunities for these interactions inside and outside the classroom.

The effect of oxytocin nasal spray on social interaction deficits observed in young children with autism: a randomized clinical crossover trial

Yatawara CJ, Einfeld SL, Hickie IB, Davenport TA, Guastella AJ. *Mol Psychiarty*. 2015 Oct 27. [*PMID: 26503762*]

There is a critical need for more effective treatments to address the core symptoms of ASD, including impairment in social interaction and communication, during early childhood. Some psychotropic drugs (drugs that change chemical levels in the brain, affecting mood and behavior) seem to be effective for behavior problems, but they can have unwanted and sometimes harmful side effects and do not sufficiently address the core social impairments of ASD. Behavioral interventions, on the other hand, can significantly improve social impairments, but they are often time-consuming and costly. The hormone oxytocin has been identified as playing an important role in social thinking and behavior, and it has been hypothesized by researchers that it could be used to treat psychiatric disorders and conditions that are characterized by social difficulties. Initial studies with oxytocin in adults with autism and in youths with autism (ages 12 to 19) have showed some promise, but research has also shown that earlier interventions for autism offer the best chance for improvement over the long term. This study is the first to test the use of the synthetic hormone oxytocin as an early intervention for young children with autism to improve their ability to interact socially.

This clinical trial, conducted by researchers at the Brain and Mind Centre at the University of Sydney (Australia) between October 2010 and October 2012, assessed whether oxytocin nasal spray improved the social interaction of 31 children with ASD ages 3 to 8, as observed by caregivers, and found that among these children, a 5-week course of oxytocin nasal spray significantly improved their social responsiveness, as reported by caregivers, compared with no treatment, or placebo. In addition, the study showed that after oxytocin administration, there was no evidence of decline on any of the social interaction or behavioral scales that were used, and the treatment was well tolerated, with no significant differences in reports of adverse events between oxytocin and placebo. Thirst, urination, and constipation were the most common, relatively mild side effects. If these findings can be confirmed in studies with larger numbers of children, it is possible that oxytocin could be the first medical treatment developed for the core symptom of impaired social interaction in childhood autism.

Early intervention for children with autism spectrum disorder under 3 years of age: recommendations for practice and research

Zwaigenbaum L, Bauman ML, Choueiri R, Kasari C, Carter A, Granpeesheh D, Mailloux Z, Smith Roley S, Wagner S, Fein D, Pierce K, Buie T, Davis PA, Newschaffer C, Robins D, Wetherby A, Stone WL, Yirmiya N, Estes A, Hansen RL, McPartland JC, Natowicz MR. *Pediatrics*. 2015 Oct;136 Suppl 1:S60-81. [*PMID: 26430170*]

The second year of life can be a particularly critical developmental period for children with ASD: there is dynamic brain growth overall, as well as changes specifically in the nerves and their connections in the brain. Interventions during this period may therefore be able to alter the abnormal developmental trajectories associated with autism and prevent some ASD impairments. However, interventions that have been developed for older children may not be appropriate for infants or toddlers, as younger children interact and learn differently from older children. It is within this context that a multidisciplinary working group of experts met to perform a review of the literature evaluating early interventions (designed for children <2 to 3 years of age) and to develop recommendations for policy makers and clinical practitioners. The recommendations listed below represent a mix of guidelines for clinical practice as well as directions for future research. The statements focused on clinical practice emphasize that intervention should start as early as possible and use multiple approaches to target a broad range of ASD symptoms. The recommendations for both clinical practice and future research include sociocultural context as a moderating factor that should be considered and incorporated into studies and practice. The authors recommend that future research should focus on improving the rigor and consistency within and across studies, to improve applicability and utility for developing personalized intervention strategies. Lastly they recommend that researchers and clinicians consider medical comorbidities (co-existing medical conditions) that may affect the response to intervention. The recommendations of the panel were as follows:

Statement 1: *Current best practices for interventions for children aged <3 years with suspected or confirmed ASD should include a combination of developmental and behavioral approaches and begin as early as possible.*

Statement 2: *Current best practices for children aged <3 years with suspected or confirmed ASD should have active involvement of families and/or caregivers as part of the intervention.*

Statement 3: *Interventions should enhance developmental progress and improve functioning related to both the core and associated features of ASD, including social communication, emotional/behavioral regulation, and adaptive behaviors.*

Statement 4: *Intervention services should consider the sociocultural beliefs of the family and family dynamics and supports, as well as economic capability, in terms of both the delivery and assessment of factors that moderate outcomes.*

Statement 5: *Intervention research should include socially and culturally diverse populations of participants and evaluate familial factors that may affect participation, acceptability, and outcomes of therapeutic approaches as well as willingness to participate in investigative studies.*

QUESTION 4: WHICH TREATMENTS AND INTERVENTIONS WILL HELP?

Statement 6: *Future research should prioritize well-defined sampling strategies, rigorous investigative design, fidelity of implementation, and meaningful outcome measurements.*

Statement 7: *Research is needed to determine the specific active components of effective interventions, including but not limited to the type of treatment provided, the agent implementing the intervention(s) (parent, therapist, teacher, or combination), consistency of service provision across environments and between providers, and duration of treatment and hours per week.*

Statement 8: *Adopting a common set of research-validated core measures of ASD symptoms (including but not limited to cognitive function, communication, and adaptive behavior) that can be used across multiple sites will facilitate comparisons across studies of children with ASD aged <3 years.*

Statement 9: *Future research should examine biological and behavioral heterogeneity as moderators of individual responses to interventions.*

Statement 10: *Intervention providers should consider medical disorders that may affect a child's clinical presentation (especially behavior) and response to an intervention and should refer to appropriate health care providers as indicated.*

QUESTION 5

WHERE CAN I TURN FOR SERVICES?

Effect of parent training vs parent education on behavioral problems in children with autism spectrum disorder: a randomized clinical trial

Bearss K, Johnson C, Smith T, Lecavalier L, Swiezy N, Aman M, McAdam DB, Butter E, Stillitano C, Minshawi N, Sukhodolsky DG, Mruzek DW, Turner K, Neal T, Hallett V, Mulick JA, Green B, Handen B, Deng Y, Dziura J, Scahill L. *JAMA*. 2015 Apr 21;313(15):1524-33. [*PMID: 25898050*]

Children with autism often exhibit disruptive behavior (e.g. tantrums, aggression, self-injury), which can interfere with the children's daily functioning, while also posing a challenge for parents and caregivers. Although parent training is an intervention that shows promise for treating these behaviors, a large-scale clinical trial approach had not previously been undertaken to evaluate parent training for the treatment of children with ASD. In this study, the researchers designed the first large-scale randomized trial to assess the efficacy of parent training compared with a parent education-based intervention to address disruptive behavioral problems in children with ASD. Parent training intervention provides parents with specific strategies for managing disruptive behavior, while parent education provides parents with information about autism, but does not include behavior management strategies. Six research centers participated in the study; 180 children aged 3 to 7 years with ASD and disruptive behaviors were selected in a screening process and randomly assigned to the parental training versus parental education intervention groups.

Parental training (done individually) and education were carried out over 24 weeks through center and home visits, as well as through telephone conferences for parent training. At various times during the 24 weeks and for another 24 weeks afterwards, parents rated their child's disruptive behavior and noncompliance using specific scales and questionnaires. In addition, clinicians unaware of the group category of each child also rated the children's behaviors to assess the outcomes. While both treatments led to improvements in disruptive behavior as measured by both parent-reported outcomes and blinded clinician ratings, the analyses showed that parent training produced better outcomes than parent education. The difference in improvements between the two groups did not meet the level of clinical significance that the research team had anticipated, but the authors still consider the difference noteworthy. Prior to conducting the study, the researchers had expected parent training to be much

more effective than parent education; they suggest that the smaller-than-expected difference observed in this study may be due to a higher-than-predicted level of improvement produced by parent education. Future analyses are required to examine and identify which child and family characteristics may predict success with either the parent training or the parent education approaches. Another factor that may be useful to investigate in the future is the cost effectiveness of each type of intervention. In addition, because the researchers involved in this study were well trained and because there was a low dropout rate among study participants, the authors propose that further study is also needed to evaluate results of these interventions in settings with less-skilled clinicians and/or lower levels of parental cooperation.

QUESTION 6

WHAT DOES THE FUTURE HOLD, PARTICULARLY FOR ADULTS?

The health status of adults on the autism spectrum

Croen LA, Zerbo O, Qian Y, Massolo ML, Rich S, Sidney S, Kripke C. *Autism*. 2015 Oct;19(7):814-23. [*PMID: 25911091*]

Recognizing that children with ASD have higher rates of co-occurring medical and psychiatric illnesses compared to the general pediatric population, the authors decided to explore whether this is also the case in adults with ASD, compared with the general population. The authors point out that a better understanding of health status in the growing population of adults diagnosed with ASD might help lead to the identification of specific interventions that would improve the delivery of effective health care to this population. Participants in this study included 1,507 adults with ASD who were members of Kaiser Permanente Northern California (KPNC) and a sampling (15,070) of other adult members of KPNC who did not have ASD ("the control group"). The researchers found that more than half of the adults with ASD in this study were diagnosed with a psychiatric condition, and the risk of having various psychiatric conditions (e.g., depression, schizophrenia) was consistently higher for adults with ASD than for controls. In addition, women with ASD were diagnosed more often (than were men with ASD) with anxiety, bipolar disorder, dementia, depression, schizophrenic disorders, and suicide attempts, but less often with obsessive compulsive disorder, attention deficit disorder, alcohol or drug abuse, and drug dependence. The findings of a high prevalence of psychiatric disorders among adults with ASD are consistent with those of previous, smaller studies. The conditions that were diagnosed less often among adults with ASD than among the control population included alcohol abuse dependency, infections, and genitourinary disorders. The medical conditions diagnosed more often among adults with ASD included immune conditions, gastrointestinal and sleep disorders, seizures, obesity, abnormal amounts of fats in the blood, high blood pressure, and diabetes—as well as some rarer conditions, such as stroke and sleep disorders. The authors conclude that further research is needed to understand the social, health care-related, and biological factors underlying the observations reported in their research paper. For example, some of the social and communication impairments (e.g., isolation, discrimination, sensory sensitivities) accompanying ASD may prevent individuals from accessing preventive health care or accurately reporting pain or other symptoms.

The costs and benefits of employing an adult with autism spectrum disorder: a systematic review
Jacob A, Scott M, Falkmer M, Falkmer T. *PLoS One*. 2015 Oct 7;10(10):e0139896. [*PMID: 26445345*]

Current estimates are that 50 to 75% of adults with ASD are unemployed, despite a desire by adults with ASD to find employment. Recognizing that few studies have looked at the cost-benefit ratio of employing adults with ASD—and even fewer have looked at this issue from the viewpoint of employers—the researchers leading this study undertook a review of existing studies. Their aim was to examine the costs, benefits, and cost-benefit ratio of employing adults with ASD from (1) a societal perspective and (2) the perspective of employers.

The authors identified 11 articles describing scientific studies that focused on competitive employment of adults with ASD, including casual employment (usually temporary with no regular hours or benefits); these studies included a total of 67,251 participants. Four of the studies were cohort studies (following a group of people over time), three were case-control studies (comparing adults with ASD with neurotypical adults), three were descriptive, and one was a correlational study (studying whether two factors can be related to each other). In addition, four of the studies described the costs to governments when employing adults with ASD, four explored the costs to society when employing adults with ASD, and three explored the cost-benefits to the employer of adults with ASD. Reviewing the studies that looked at government costs showed that employing individuals with ASD, even with government support for their employment, actually saves government costs by reducing the number of benefits that people with ASD need when they are unemployed. Other studies showed that when assessing the costs of vocational rehabilitation services per wages earned by individuals with ASD, ASD is more costly than other conditions (such as traumatic brain injury, mental illness, and learning disabilities). However, adults with ASD who receive these supportive services have a high likelihood of subsequently gaining employment, and the costs to society (including adult care) are more than paid back when adults with ASD become employed. One benefit to employers described in three studies is that adults with ASD can maintain consistent hours worked per week for significant periods of time, demonstrating reliability. However, the authors also conclude that further studies are warranted to more thoroughly explore the benefits, costs, and cost-benefit ratio of employing an adult with ASD from the perspective of employers.

National Autism Indicators Report: Transition into Young Adulthood

Roux AM, Shattuck PT, Rast JE, Rava JA, Anderson KA. Philadelphia, PA: Life Course Outcomes Research Program, A.J. Drexel Autism Institute, Drexel University, 2015. [*Available at: http://drexel.edu/autisminstitute/research-projects/research/ResearchPrograminLifeCourseOutcomes/IndicatorsReport*]

Young adults with autism have a difficult time transitioning to adulthood after high school, when many of their supports and services required through the Federal law in high school are dropped. It can be difficult for a young adult with ASD after high school to find steady employment, continue school, live independently, socialize and participate in the community, or stay healthy and safe. This report describes a collection of national indicators detailing the transition from adolescence to young adulthood for those with ASD. Data used for this study was from the U.S. Department of Education's National Longitudinal Transition Study-2, which collected youth and parent responses to survey questions every 2 years from 2000–2009. This study reports on outcomes of young adults in the areas of transition planning, services, health and mental health, postsecondary education, employment, living arrangements, social and community participation, and safety and risk. A major finding for transition planning was that only 58% of youth with ASD had a transition plan in place by the federally required age. For young adults' part of the services cliff, nearly 26% of young adults with ASD received no services that could help them become employed, go on to post-secondary education, or live independently. Among those with ASD, 60% had at least two health or mental health conditions as well as ASD. After high school, only 36% of young adults with ASD ever attended postsecondary education—including 2-year or 4-year colleges or vocational education. For employment, only 58% of young adults with ASD worked for pay outside the home after high school and into their early 20s, which is much lower than young adults with other disabilities. After high school, most young adults move out of their parent or guardian's home. For young adults with ASD, only one in five ever lived independently between high school and their early 20s. Among the outcomes young adults hope to achieve after high school, is participating and socializing within their community. However, one in four young adults with ASD is socially isolated, meaning they never saw or talked with friends or were never invited to social activities within the last year. Lastly, the safety and well-being of young adults with ASD is a crucial part of them having successful outcomes. However, nearly 27% of youth engaged in wandering behavior—putting them at risk of harm or becoming lost. Although the report does not explain why and how these are the outcomes for transition-age youth with ASD, it addresses the gaps in outcomes for these youth and gives guidance for future research to address the needs of young adults transitioning out of high school.

High rates of parkinsonism in adults with autism

Starkstein S, Gellar S, Parlier M, Payne L, Piven J. *J Neurodev Disord*. 2015;7(1):29. [*PMID: 26322138*]

Although autism is a disorder that impacts an individual throughout his or her lifetime, few studies have looked at older adults with ASD and the additional conditions they may develop, including parkinsonism and Parkinson's disease (PD)—a progressive disorder of the nervous system that affects movement, often causing tremors. The current study grew out of a broadly descriptive study the same researchers began years ago of adults 50 years of age and older with ASD. As this descriptive study progressed, the current study researchers observed what seemed to be high rates of parkinsonism signs among a small number of their ASD adult subjects (Study I). They therefore went on to assess signs of parkinsonism in a second sample of ASD adult subjects who were 40 years of age or older (Study II). The final study sample included 56 individuals with ASD 40 years or older (19 from Study I and 37 from Study II).

All study subjects were assessed for cognitive level and motor symptoms of PD; a diagnosis of PD requires that a patient display bradykinesia (a slowness of movement characteristic of parkinsonism) as well as rigidity, resting tremor, or postural instability. This study found elevated rates of parkinsonism in both samples, with three of 19 (Study I, 16%) and 12 of 37 (Study II, 32%) subjects having met the diagnostic criteria for PD. However, seven subjects in Study I and 29 subjects in Study II were taking antipsychotic medications that can cause Parkinson-like symptoms. The two studies were therefore combined due to low numbers. Of the 20 subjects who were not taking neuroleptic medications, four (20%) met the diagnostic criteria for parkinsonism, a diagnosis that was confirmed by independent community-based neurologists. The rate of parkinsonism in the general population is below 1%, considerably lower than the 20% found in this sample, which suggests that there is a higher rate of parkinsonism among adults 40 or older with ASD than in the general population. In addition, if current study findings are confirmed, medical science can begin to examine and understand the underlying biological connections, if any, between ASD and parkinsonism.

Longitudinal patterns of employment and postsecondary education for adults with autism and average-range IQ
Taylor JL, Henninger NA, Mailick MR. *Autism*. 2015 Oct;19(7):785-93. [*PMID: 26019306*]

In this study, researchers focused on one particular set of adults with ASD—those with average-range IQs (intelligence quotients) and no diagnosed intellectual disabilities. The aim was to determine the long-term success of these ASD adults in postsecondary education participation and competitive employment. The 73 adults who were followed over 12 years were from families that were part of a larger longitudinal study. Although two-thirds of the adults with ASD participated in competitive employment/postsecondary education during the study, fewer than 25% were found to have maintained these activities consistently over the study period. It was also uncommon for those who had received postsecondary education to have found work in their field of study, many had low rates of employment even after receiving their degree, and those who found employment were often in entry-level jobs. These results suggest the need for more services and supports to help adults successfully make the transition between postsecondary education and employment.

The study also looked at factors that could potentially correlate with different patterns of employment and postsecondary education participation by adults with ASD over time; these included whether the individual with ASD was male or female, maternal and paternal levels of education, activities of daily living, maladaptive behaviors, autism symptoms, level of family support, and maternal mood (depressive symptoms, anxiety, or pessimism). Individuals with ASD who were consistently or sometimes engaged in postsecondary education/competitive employment had lower levels of some negative behavioral characteristics, including maladaptive behaviors and autism symptoms, relative to those who were never engaged. However, there were no differences in behavioral characteristics between those who were consistently engaged and those who were only sometimes engaged. Consistent with previous findings, this study found differences between men and women with ASD in the consistency of their engagement in postsecondary education/competitive employment. None of the 15 women with ASD in this study were found to be consistently engaged throughout the study period, while nearly one-third of the men with ASD were, yet there were few behavioral differences between the men and women. Familial context could also influence the stability of an individual's engagement in postsecondary education/competitive employment. For example, a higher paternal education level indicated a greater likelihood of the adult child with ASD being competitively employed. The researchers also recommend that future studies expand their scope to examine the potential effects of both social factors and individual characteristics on outcomes for adults with ASD.

QUESTION 7

WHAT OTHER INFRASTRUCTURE AND SURVEILLANCE NEEDS MUST BE MET?

While no articles directly related to *Question 7: What Other Infrastructure and Surveillance Needs Must Be Met?* were selected by the Committee for inclusion in the final *2015 IACC Summary of Advances in Autism Spectrum Disorder Research*, three articles were nominated in this category, and they are listed in the Full Listing of Nominated Articles.

ARTICLES SELECTED FOR THE 2015 SUMMARY OF ADVANCES

QUESTION 1: WHEN SHOULD I BE CONCERNED?

Jo H, Schieve LA, Rice CE, Yeargin-Allsopp M, Tian LH, Blumberg SJ, Kogan MD, Boyle CA. Age at autism spectrum disorder (ASD) diagnosis by race, ethnicity, and primary household language among children with special health care needs, United States, 2009–2010. *Matern Child Health J.* 2015 Aug;19(8):1687-97. [*PMID: 25701197*]

Ozonoff S, Young GS, Landa RJ, Brian J, Bryson S, Charman T, Chawarska K, Macari SL, Messinger D, Stone WL, Zwaigenbaum L, Iosif AM. Diagnostic stability in young children at risk for autism spectrum disorder: a baby siblings research consortium study. *J Child Psychol Psychiatry.* 2015 Sep;56(9):988-98. [*PMID: 25921776*]

Zwaigenbaum L, Bauman ML, Fein D, Pierce K, Buie T, Davis PA, Newschaffer C, Robins DL, Wetherby A, Choueiri R, Kasari C, Stone WL, Yirmiya N, Estes A, Hansen RL, McPartland JC, Natowicz MR, Carter A, Granpeesheh D, Mailloux Z, Smith Roley S, Wagner S. Early screening of autism spectrum disorder: recommendations for practice and research. *Pediatrics.* 2015 Oct;136 Suppl 1:S41-59. [*PMID: 26430169*]

Zwaigenbaum L, Bauman ML, Stone WL, Yirmiya N, Estes A, Hansen RL, McPartland JC, Natowicz MR, Choueiri R, Fein D, Kasari C, Pierce K, Buie T, Carter A, Davis PA, Granpeesheh D, Mailloux Z, Newschaffer C, Robins D, Roley SS, Wagner S, Wetherby A. Early identification of autism spectrum disorder: recommendations for practice and research. *Pediatrics.* 2015 Oct;136 Suppl 1:S10-40. [*PMID: 26430168]*

QUESTION 2: HOW CAN I UNDERSTAND WHAT IS HAPPENING?

Hahamy A, Behrmann M, Malach R. The idiosyncratic brain: distortion of spontaneous connectivity patterns in autism spectrum disorder. *Nat Neurosci.* 2015 Feb;18(2):302-9. [*PMID: 25599222*]

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QUESTION 3: WHAT CAUSED THIS TO HAPPEN AND CAN IT BE PREVENTED?

Gadad BS, Li W, Yazdani U, Grady S, Johnson T, Hammond J, Gunn H, Curtis B, English C, Yutuc V, Ferrier C, Sackett GP, Marti CN, Young K, Hewitson L, German DC. Administration of thimerosal-containing vaccines to infant rhesus macaques does not result in autism-like behavior or neuropathology. *Proc Natl Acad Sci U S A*. 2015 Oct 6;112(40):12498-503. [*PMID: 26417083*]

Jain A, Marshall J, Buikema A, Bancroft T, Kelly JP, Newschaffer CJ. Autism occurrence by MMR vaccine status among US children with older siblings with and without autism. *JAMA*. 2015 Apr 21;313(15):1534-40. [*PMID: 25898051*]

Xiang AH, Wang X, Martinez MP, Walthall JC, Curry ES, Page K, Buchanan TA, Coleman KJ, Getahun D. Association of maternal diabetes with autism in offspring. *JAMA*. 2015 Apr 14;313(14):1425-34. [*PMID: 25871668*]

QUESTION 4: WHICH TREATMENTS AND INTERVENTIONS WILL HELP?

Estes A, Munson J, Rogers SJ, Greenson J, Winter J, Dawson G. Long-term outcomes of early intervention in 6-year-old children with autism spectrum disorder. *J Am Acad Child Adolesc Psychiatry*. 2015 Jul;54(7):580-7. [*PMID: 26088663*]

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Kasari C, Dean M, Kretzmann M, Shih W, Orlich F, Whitney R, Landa R, Lord C, King B. Children with autism spectrum disorder and social skills groups at school: a randomized trial comparing intervention approach and peer composition. *J Child Psychol Psychiatry*. 2016 Feb;57(2):171-9. [*PMID: 26391889*]

Yatawara CJ, Einfeld SL, Hickie IB, Davenport TA, Guastella AJ. The effect of oxytocin nasal spray on social interaction deficits observed in young children with autism: a randomized clinical crossover trial. *Mol Psychiarty*. 2015 Oct 27. [*PMID: 26503762*]

Zwaigenbaum L, Bauman ML, Choueiri R, Kasari C, Carter A, Granpeesheh D, Mailloux Z, Smith Roley S, Wagner S, Fein D, Pierce K, Buie T, Davis PA, Newschaffer C, Robins D, Wetherby A, Stone WL, Yirmiya N, Estes A, Hansen RL, McPartland JC, Natowicz MR. Early intervention for children with autism spectrum disorder under 3 years of age: recommendations for practice and research. *Pediatrics*. 2015 Oct;136 Suppl 1:S60-81. [*PMID: 26430170*]

QUESTION 5: WHERE CAN I TURN FOR SERVICES?

Bearss K, Johnson C, Smith T, Lecavalier L, Swiezy N, Aman M, McAdam DB, Butter E, Stillitano C, Minshawi N, Sukhodolsky DG, Mruzek DW, Turner K, Neal T, Hallett V, Mulick JA, Green B, Handen B, Deng Y, Dziura J, Scahill L. Effect of parent training vs parent education on behavioral problems in children with autism spectrum disorder: a randomized clinical trial. *JAMA*. 2015 Apr 21;313(15):1524-33. [*PMID: 25898050*]

QUESTION 6: WHAT DOES THE FUTURE HOLD, PARTICULARLY FOR ADULTS?

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QUESTION 7: WHAT OTHER INFRASTRUCTURE AND SURVEILLANCE NEEDS MUST BE MET?

No articles were selected from Question 7. For a list of articles that were nominated in this category, see the Full Listing of Nominated Articles.

FULL LISTING OF NOMINATED ARTICLES
(SELECTED ARTICLES APPEAR *RED)

QUESTION 1: WHEN SHOULD I BE CONCERNED?

*Jo H, Schieve LA, Rice CE, Yeargin-Allsopp M, Tian LH, Blumberg SJ, Kogan MD, Boyle CA. Age at autism spectrum disorder (ASD) diagnosis by race, ethnicity, and primary household language among children with special health care needs, United States, 2009–2010. *Matern Child Health J*. 2015 Aug;19(8):1687-97. [*PMID: 25701197*]

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QUESTION 2: HOW CAN I UNDERSTAND WHAT IS HAPPENING?

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QUESTION 4: WHICH TREATMENTS AND INTERVENTIONS WILL HELP?

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