2017 Summary of Advances Nominations: April – October 2017

Question 1 (Screening and Diagnosis)	
Joshua Gordon	Emerson RW, Adams C, Nishino T, Hazlett HC, Wolff JJ, Zwaigenbaum L, Constantino JN, Shen MD, Swanson MR, Elison JT, Kandala S, Estes AM, Botteron KN, Collins L, Dager SR, Evans AC, Gerig G, Gu H, McKinstry RC, Paterson S, Schultz RT, Styner M; IBIS Network, Schlaggar BL, Pruett JR Jr, Piven J. **Functional neuroimaging of high-risk 6-month-old infants predicts a diagnosis of autism at 24 months of age**. Sci Transl Med. 2017 Jun 7;9(393). pii: eaag2882. [PMID: 28592562]
	Funded by NIMH and NICHD; highlighted in NIMH and NIH press releases, as well as Dr. Collins' blog: • *https://www.nimh.nih.gov/news/science-news/2017/neuroimaging-technique-may-help-predict-autism-among-high-risk-infants.shtml* • *https://www.nih.gov/news-events/news-releases/neuroimaging-technique-may-help-predict-autism-among-high-risk-infants* • *https://directorsblog.nih.gov/2017/06/13/autism-spectrum-disorder-progress-toward-earlier-diagnosis/*
Geraldine Dawson	Hull L, Mandy W, Petrides KV. **Behavioural and cognitive sex/gender differences in autism spectrum condition and typically developing males and females**. Autism. 2017 Aug;21(6):706-727. [PMID: 28749232]
	This systematic review suggests that individuals with autism spectrum conditions display typical sex/gender differences in core autism spectrum condition traits, suggesting that diagnostic criteria based on these symptoms should take into account typical sex/gender differences.
Joshua Gordon	Kostopoulos P, Gerig G, Dager SR, Paterson S, Schultz RT, Styner MA, Hazlett HC, Piven J; Infant Brain Imaging Study Network. **The emergence of network inefficiencies in infants with autism spectrum disorder**. Biol Psychiatry. 2017 Aug 1;82(3):176-185. [PMID: 28460842]
	This study uses data from 260 infants at 6 and 12 months of age, including 116 infants with longitudinal data. Diffusion data was used to obtain measures of the length and strength of connections between brain regions to compute network efficiency. Group differences were assessed in efficiency within linear mixed-effects models determined by the Akaike information criterion. Inefficiencies in high-risk infants later classified with ASD were detected from 6 months onward in regions involved in low-level sensory processing. In addition, within the high-risk infants, these inefficiencies predicted 24-month symptom severity. These results suggest that infants with ASD, even before 6 months of age, have deficits in connectivity related to low-level processing, which contribute to a developmental cascade affecting brain organization and eventually higher-level cognitive processes and social behavior.
Geraldine Dawson	Mandy W, Wang A, Lee I, Skuse D. **Evaluating social (pragmatic) communication disorder**. J Child Psychol Psychiatry. 2017 Oct;58(10):1166-1175. [PMID: 28741680]
	This study pf 1,081 individuals did not find evidence that SPCD is qualitatively distinct from ASD. Rather, it appears to lie on the borderlands of the autism spectrum, describing those with autistic traits that fall just below the threshold for an ASD diagnosis. SPCD may have clinical utility for identifying

	people with autistic traits that are insufficiently severe for ASD diagnosis, but who nevertheless require support.
Question 2 (Underlying Biology)	
Joshua Gordon *Geraldine Dawson*	Constantino JN, Kennon-McGill S, Weichselbaum C, Marrus N, Haider A, Glowinski AL, Gillespie S, Klaiman C, Klin A, Jones W. **Infant viewing of social scenes is under genetic control and is atypical in autism**. Nature. 2017 Jul 12. [Epub ahead of print] [PMID: 28700580]
	In the attached paper, the authors report that variation in viewing of social scenes, including levels of preferential attention and the timing, direction and targeting of individual eye movements, is strongly influenced by genetic factors, with effects directly traceable to the active seeking of social information. In a series of eye-tracking experiments conducted with 338 toddlers, including 166 epidemiologically ascertained twins (enrolled by representative sampling from the general population), 88 non-twins with autism and 84 singleton controls, we find high monozygotic twin–twin concordance (0.91) and relatively low dizygotic concordance (0.35). Moreover, the characteristics that are the most highly heritable, preferential attention to eye and mouth regions of the face, are also those that are differentially decreased in children with autism ($\chi 2 = 64.03$, $P < 0.0001$). These results implicate social visual engagement as a neurodevelopmental endophenotype not only for autism, but also for population-wide variation in social-information seeking.
Joshua Gordon	Gupta AR, Westphal A, Yang DYJ, Sullivan CAW, Eilbott J, Zaidi S, Voos A, Vander Wyk BC, Ventola P, Waqar Z, Fernandez TV, Ercan-Sencicek AG, Walker MF, Choi M, Schneider A, Hedderly T, Baird G, Friedman H, Cordeaux C, Ristow A, Shic F, Volkmar FR, Pelphrey KA. **Neurogenetic analysis of childhood disintegrative disorder.** Mol Autism. 2017 Apr 4;8:19. [PMID: 28392909]
	This study suggests that Childhood Disintegrative Disorder (CDD), a rare form of ASD characterized by late-onset, severe regression, is biologically distinct from other forms of autism. CDD candidate genes were found to be more highly expressed in non-neocortical regions than neocortical regions. This expression profile was similar to that of an independent cohort of ASD probands with regression. The non-neocortical regions overlapped with those identified by fMRI as abnormally hyperactive in response to viewing faces, such as the thalamus, cerebellum, caudate, and hippocampus. Eye-tracking analysis showed that, among individuals with ASD, subjects with CDD focused on eyes the most when shown pictures of faces. These results suggest differences between CDD and other forms of ASD on the neurobiological as well as clinical level.
Walter Koroshetz	Khundrakpam BS, Lewis JD, Kostopoulos P, Carbonell F, Evans AC. **Cortical thickness abnormalities in autism spectrum disorders through late childhood, adolescence, and adulthood: a large-scale MRI study**. Cereb Cortex. 2017 Mar 1;27(3):1721-1731. [PMID: 28334080]
	Heterogeneity in ASD, and small sample sizes in previous studies, have led to inconclusive evidence on a potential role of cortical thickness abnormalities in autism. This current study used a subset of data from the Autism Brain Imaging Data Exchange (ABIDE) data set to determine age-specific differences in cortical thickness in ASD and its relation to symptom severity. The study included 560 male subjects (266 ASD and 294 controls; age = 6-35 years) and computed

	cortical thickness measurements using the CIVET process followed by stringent multi-reviewer quality control procedures. Data were analyzed for age-related abnormalities and explored for association with symptom severity based on ADOS scores. The data showed significantly increased cortical thickness between ages 6 and 14; the effect was more pronounced in the left hemisphere. There was also a significant positive correlation between residual cortical thickness and severity scores for social affect and communication symptoms. This study used a robust data set to explore an unanswered question regarding brain structure abnormalities in autism. Longitudinal studies across the life span are needed to further explore the relationship between brain structure and development in ASD.
Joshua Gordon	Palmer N, Beam A, Agniel D, Eran A, Manrai A, Spettell C, Steinberg G, Mandl K, Fox K, Nelson SF, Kohane I. **Association of sex with recurrence of autism spectrum disorder among siblings**. JAMA Pediatr. 2017 Sep 25. [PMID: 28973142]
	Among the 3,166,542 children (1,547,266 females and 1,619,174 males; mean [SD] age, 11.2 [4.7] years) in the study, the prevalence of ASD was 1.96% (95% CI, 1.94%-1.98%) among males and 0.50% (95% CI, 0.49%-0.51%) among females. When a male was associated with risk in the family, ASD was diagnosed in 4.2% (95% CI, 3.8%-4.7%) of female siblings and 12.9% (95% CI, 12.2%-13.6%) of male siblings. When a female was associated with risk in the family, ASD was diagnosed in 7.6% (95% CI, 6.5%-8.9%) of female siblings and 16.7% (95% CI, 15.2%-18.4%) of male siblings. *These findings are in agreement with the higher rates of ASD observed among males than among females in the general population. The study provides more specific guidance for the screening and counseling of families and may help inform future investigations into the environmental and genetic factors that confer risk of ASD.*
Question 3 (Risk Factors)	
Linda Birnbaum	Arora M, Reichenberg A, Willfors C, Austin C, Gennings C, Berggren S, Lichtenstein P, Anckarsäter H, Tammimies K, Bölte S. **Fetal and postnatal metal dysregulation in autism.** Nat Commun. 2017 Jun 1;8:15493. [PMID: 28569757]
	Advance: Studies of environmental risk factors for autism are hampered by the difficulty in assessing exposures and their timing during etiologically relevant periods of early development, which occur years before diagnosis. The authors address this challenge and demonstrate the utility of tooth matrix exposure biomarkers for identifying different temporal patterns of uptake of essential and toxic metals in ASD cases and controls. *Summary: This study used teeth collected from twins that either were concordant or discordant for ASD diagnosis, and examined levels of both essential and toxic metals in precise layers of dentine from shed deciduous teeth (baby teeth) during prenatal and early postnatal periods. Levels of lead were elevated in ASD cases, particularly in the early postnatal period (5-20 weeks post-birth). Levels of the essential metals manganese and zinc also differed in ASD cases vs. controls. Manganese levels were lower in ASD cases during two time frames, one prenatally (10 weeks prior to birth) and the other during an early postnatal phase (5-20 weeks after birth). Zinc levels, meanwhile, were only*

	lower during a latter prenatal to early postnatal phase (10 weeks prior to birth until 5 weeks after). Furthermore, metal levels at three months after birth were predictive of severity of ASD later in life. This study is an important advance for identifying biomarkers of exposure to environmental risk factors during critical windows of development and supports the idea that ASD may be associated with altered regulation of essential and toxic metals.
Joshua Gordon	Geisheker MR, Heymann G, Wang T, Coe BP, Turner TN, Stessman HAF, Hoekzema K, Kvarnung M, Shaw M, Friend K, Liebelt J, Barnett C, Thompson EM, Haan E, Guo H, Anderlid BM, Nordgren A, Lindstrand A, Vandeweyer G, Alberti A, Avola E, Vinci M, Giusto S, Pramparo T, Pierce K, Nalabolu S, Michaelson JJ, Sedlacek Z, Santen GWE, Peeters H, Hakonarson H, Courchesne E, Romano C, Kooy RF, Bernier RA, Nordenskjöld M, Gecz J, Xia K, Zweifel LS, Eichler EE. **Hotspots of missense mutation identify neurodevelopmental disorder genes and functional domains**. Nat Neurosci. 2017 Aug;20(8):1043-1051. [PMID: 28628100]
	The current study sought out to deepen our understanding of genetic risk for Neurodevelopmental disorders (NDD). The research focused on identifying novel, previously less studied-missense mutations associated with NDD. Using a genome wide approach, utilizing publicly available large sample sequencing data, the research team has identified 200 genes with significant clustering of novel patient specific, protein coding missense mutations. Further analysis of the identified hotspot genes showed enrichment for synaptic signaling, and chromatin mediated regulation of transcription pathways both previously implicated in ASD and other psychiatric disorders. The current findings are a significant step forward in the complex process of identification and refinement of potential functional genetic targets that can lead to better understanding of disease etiology, course, outcome and possible personalized targeted treatment development.
Linda Birnbaum	Golding J, Ellis G, Gregory S, Birmingham K, Iles-Caven Y, Rai D, Pembrey M. **Grand-maternal smoking in pregnancy and grandchild's autistic traits and diagnosed autism.** Sci Rep. 2017 Apr 27;7:46179. [PMID: 28448061]
	Advance: This study demonstrates that environmental exposures can have effects across multiple generations. As we seek to understand autism risk and etiology, it is important to consider how we will study and measure these exposures across generations. *Summary: This study used data from the Avon Longitudinal Study of Parents and Children, a long-running population-based British study of how environment and genotype affect health outcomes. Parents of children enrolled in this study were asked about their parents' smoking habits--whether they ever smoked and if mothers smoked during pregnancy. The relationship between grandparental smoking and social and communication traits predictive of autism were studied. Granddaughters of maternal grandmothers who smoked had increased odds of adverse scores in social communication and repetitive behaviors. Smoking by maternal grandmothers was also associated with autism diagnosis, particularly in grandsons (this might be in part related to the sex bias in diagnosis; there were only 212 diagnosed cases and 4 males for every female diagnosed).*

Geraldine Dawson	Kim S, Kim H, Yim YS, Ha S, Atarashi K, Tan TG, Longman RS, Honda K, Littman DR, Choi GB, Huh JR. **Maternal gut bacteria promote neurodevelopmental abnormalities in mouse offspring**. Nature. 2017 Sep 13. [PMID: 28902840]
	Data from this study of mice suggest that defined gut commensal bacteria with a propensity to induce TH17 cells may increase the risk of neurodevelopmental disorders in the offspring of pregnant mothers undergoing immune system activation owing to infections or autoinflammatory syndromes.
Linda Birnbaum	Kim D, Volk H, Girirajan S, Pendergrass S, Hall MA, Verma SS, Schmidt RJ, Hansen RL, Ghosh D, Ludena-Rodriguez Y, Kim K, Ritchie MD, Hertz-Picciotto I, Selleck SB. **The joint effect of air pollution exposure and copy number variation on risk for autism.** Autism Res. 2017 Apr 27. [Epub ahead of print] [PMID: 28448694]
	Advance: While there is general agreement that both genes and environment contribute to risk of ASD, understanding their joint effects has been difficult, as it requires collection of detailed genetic and environmental data for the same group of individuals and appropriate gxe analytic approaches. The present study brought together these essential ingredients to demonstrate, for the first time, an interaction of global copy number variation (cnv) and ozone exposure in determining autism risk. The findings underscore the importance of considering how such interactions contribute to the risk architecture of ASD as well as the mechanisms by which genomics and environmental exposures may amplify the risks associated with the other. *Summary: Using a sample of 158 ASD cases and 147 typically developing controls from the NIEHS-funded Childhood Risk from Genes and Environment (CHARGE) study, this publication examines the interaction between global CNV burden and air pollution--specifically ozone. The authors report that children with high CNV burden (duplications) and high ozone exposure were at significantly greater risk for autism than those with low CNV burden and low ozone exposure, and that the risk would not have been found if these factors were studied independently. This interaction of ozone and global CNV burden was specific to autism, as there was no interaction observed with other components of air pollution (i.e., particulate matter). It is speculated that the high levels of CNVs and ozone, an oxidizing agent, may converge on oxidative and cellular stress pathways to potentiate ASD risk.*
Joshua Gordon	Lim ET, Uddin M, De Rubeis S, Chan Y, Kamumbu AS, Zhang X, D'Gama AM, Kim SN, Hill RS, Goldberg AP, Poultney C, Minshew NJ, Kushima I, Aleksic B, Ozaki N, Parellada M, Arango C, Penzol MJ, Carracedo A, Kolevzon A, Hultman CM, Weiss LA, Fromer M, Chiocchetti AG, Freitag CM; Autism Sequencing Consortium Church GM, Scherer SW, Buxbaum JD, Walsh CA. **Rates, distribution and implications of postzygotic mosaic mutations in autism spectrum disorder**. Nat Neurosci. 2017 Jul 17. [PMID: 28714951]
	About 8 percent of de novo, or non-inherited, mutations in people with autism appear in only some of the body's cells, according to an analysis of sequences from nearly 20,000 people[1]. These mutations arise after conception; the later they occur, the fewer cells they affect. Previous studies missed the vast majority of these so-called 'mosaic mutations.' The analyses also showed that the mutations in the subjects with ASD occur disproportionately in genes expressed

	in the amygdala, which plays an important role in emotional and social functioning.
David Amaral	Pardo CA, Farmer CA, Thurm A, Shebl FM, Ilieva J, Kalra S, Swedo S. **Serum and cerebrospinal fluid immune mediators in children with autistic disorder: a longitudinal study.** Mol Autism. 2017 Jan 5;8:1. [PMID: 28070266]
	This article addresses the issue of whether an ongoing inflammatory process contributes to the symptoms of ASD. The conclusion is that there is no evidence of an inflammatory process. There are also interesting data that cytokine and chemokine levels are very different in peripheral blood and CSF.
Joshua Gordon	Turner TN, Coe BP, Dickel DE, Hoekzema K, Nelson BJ, Zody MC, Kronenberg ZN, Hormozdiari F, Raja A, Pennacchio LA, Darnell RB, Eichler EE. **Genomic patterns of de novo mutation in simplex autism**. Cell. 2017 Sep 27. pii: S0092-8674(17)31006-1. [PMID: 28965761]
	To further understanding of the genetic etiology of autism, genome sequence data from 516 idiopathic autism families (2,064 individuals) was generated and analyzed. This resource includes >59 million single-nucleotide variants (SNVs) and 9,212 private copy number variants (CNVs), of which 133,992 and 88 are de novo mutations (DNMs), respectively. Comparing probands and unaffected siblings, we observe several DNM trends. Probands carry more gene-disruptive CNVs and SNVs, resulting in severe missense mutations and mapping to predicted fetal brain promoters and embryonic stem cell enhancers. These differences become more pronounced for autism genes (p = 1.8 × 10-3, OR = 2.2). Patients are more likely to carry multiple coding and noncoding DNMs in different genes, which are enriched for expression in striatal neurons (p = 3 × 10-3), suggesting a path forward for genetically characterizing more complex cases of autism.
Geraldine Dawson	Viktorin A, Uher R, Reichenberg A, Levine SZ, Sandin S. **Autism risk following antidepressant medication during pregnancy**. Psychol Med. 2017 May 22:1-10. [Epub ahead of print] [PMID: 28528584]
	Previous studies have examined if maternal antidepressant medication during pregnancy increase the risk of autism spectrum disorder (ASD) in the offspring, but the results have been conflicting. In a population-based cohort of 179 007 children born in 2006 and 2007 and followed through 2014 when aged 7 and 8, we estimated relative risks (RRs) of ASD and 95% confidence intervals (CIs) from Cox regression in children exposed to any antidepressant medication during pregnancy, and nine specific antidepressant drugs. Medication with antidepressants during pregnancy does not appear to be causally associated with an increased risk of ASD in the offspring. Instead, the results suggest that the association is explained by factors related to the underlying susceptibility to psychiatric disorders. Based on these findings, the risk of ASD in the offspring should not be a consideration to withhold treatment with commonly used antidepressant drugs from pregnant women.
Geraldine Dawson Alison Singer	Weiner DJ, Wigdor EM, Ripke S, Walters RK, Kosmicki JA, Grove J, Samocha KE, Goldstein JI, Okbay A, Bybjerg-Grauholm J, Werge T, Hougaard DM, Taylor J; iPSYCH-Broad Autism Group; Psychiatric Genomics Consortium Autism Group, Skuse D, Devlin B, Anney R, Sanders SJ, Bishop S, Mortensen PB, Børglum AD, Smith GD, Daly MJ, Robinson EB. **Polygenic transmission disequilibrium**

	confirms that common and rare variation act additively to create risk for autism spectrum disorders. Nat Genet. 2017 May 15. [Epub ahead of print] [PMID: 28504703]
	Using a novel approach called the polygenic transmission disequilibrium test and data from 6,454 families with a child with ASD, this study shows that polygenic risk for ASD, schizophrenia, and greater educational attainment is over-transmitted to children with ASD. These findings hold independent of proband IQ. It is found that polygenic variation contributes additively to risk in ASD cases who carry a strongly acting de novo variant. Lastly, the study shows that elements of polygenic risk are independent and differ in their relationship with phenotype. These results confirm that the genetic influences on ASD are additive and suggest that they create risk through at least partially distinct etiologic pathways.
	First, common polygenic risk -- the tiny little effects of common genetic variation spread throughout the genome -- appear relevant, and almost equally so, to all groups examined. Regardless of whether the cases had intellectual disability or not, were male or female, or carried a large impact de novo mutation, common polygenic risk was a significant contributor. Second, evidence was presented showing that genetic risk for ASD comes in many different flavors. The very large impact de novo variants that create risk for ASD, for example, are strongly associated with intellectual disability, epilepsy, and motor delays. The common variant risk factors are comparatively neurologically gentle. They don't show those associations. In fact, common polygenic risk for ASD is associated with higher IQ in general population samples.
Question 4 (Treatments and Interventions)	
Alison Singer	Brian JA, Smith IM, Zwaigenbaum L, Bryson SE. **Cross-site randomized control trial of the Social ABCs caregiver-mediated intervention for toddlers with autism spectrum disorder**. Autism Res. 2017 Jun 2. [Epub ahead of print] [PMID: 28574669]
	Another randomized clinical trial – multisite no less – shows the effectiveness of targeting very early behaviors for the treatment of autism.
Larry Wexler	Commons ML, Adhikari D, Giri S, Weinberg M, Baran JJ, Malik E. **Measuring developmental outcomes in autism spectrum disorder (ASD).** Behav Dev Bull. 2017 Apr;22(1):197-208.
	Commons and colleagues created a behavior-developmental scale to predict performance in students with Autism Spectrum Disorder (ASD). Forty-two children were given the Autism Developmental Task Sequence (ADTS). Using the Rasch Analysis, researchers ascertained the order of hierarchical complexity (MHC) of various tasks, including the behavioral developmental difficulty of task items. The scale derived from the Rasch Analysis will help create interventions and provide diagnostic data. Furthermore, this tool could improve progress monitoring strategies for children with ASD. In turn, such improvements could strengthen the design of behavioral and educational materials.
Larry Wexler	Corbett BA, Blain SD, Ioannou S, Balser M. **Changes in anxiety following a randomized control trial of a theatre-based intervention for youth with autism spectrum disorder.** Autism. 2017 Apr;21(3):333-343. [PMID: 27154909]

	Corbett and colleagues examined the impact of peer-mediated, theatre-based intervention on reducing anxiety and stress. Thirty youth with autism spectrum disorder (ASD) (ages 8-14) participated in the study. Seventeen youth were randomized into the experimental (EXP) group. Sixteen participants were randomized into the waitlist (WLC) control group. The EXP group received interventions during a 10-week period. The WLC group received interventions during a 10-week summer session after the EXP group had completed their trial. Results indicated a reduction in trait-anxiety and an overall increase in social competence for the EXP group. Recommendations include continued studies in this area with the incorporation of physiological and self-report metrics of stress or anxiety and the use of other anxiety reduction techniques. Students with ASD often exhibit greater anxiety in comparison to typically developing peers. This study provides an innovative approach to identify strategies that support children with ASD in reducing anxiety.
Geraldine Dawson	Sathe N, Andrews JC, McPheeters ML, Warren ZE. **Nutritional and dietary interventions for autism spectrum disorder: a systematic review**. Pediatrics. 2017 May 26. [Epub ahead of print] [PMID: 28562286]
	A systematic review of nutritional and dietary interventions for autism. It was concluded that there is little evidence to support the use of nutritional supplements or dietary therapies for children with ASD. Note that there is an accompany editorial, which I am not nominating as an advance but might be of interest to the committee: https://www.ncbi.nlm.nih.gov/pubmed/28562291
Larry Wexler	Shire SY, Chang YC, Shih W, Bracaglia S, Kodjoe M, Kasari C. **Hybrid implementation model of community-partnered early intervention for toddlers with autism: a randomized trial.** J Child Psychol Psychiatry. 2017 May;58(5):612-622. [PMID: 27966784]
	Using an effectiveness-implementation hybrid design in tandem with the Joint Attention, Symbolic Play, Engagement, and Regulation model (JASPER), Shire and colleagues tested 113 children enrolled in local public early intervention classrooms in low SES settings. Shire and colleagues addressed the practicability of supervised teacher assistant (TA)-implemented JASPER within an early intervention program and the influence of intervention on children's core developmental challenges concerning JASPER related skills. Results indicated fidelity of implementation by paraprofessionals and notable increases in engagement between children and paraprofessionals. Students receiving JASPER interventions demonstrated gains in joint engagement, joint attention, and play skills. Recommendations include formal evaluation of supervisor's TA coaching, adding additional measures to more fully understand clinical significance of staff questionnaire scores, and extension of intervention analysis. This study is consequential because paraprofessionals are often assigned to work with children with ASD. This study shows how to support paraprofessionals in implementing an intervention with fidelity.
Larry Wexler	Strain PS. **Four-year follow-up of children in the LEAP Randomized Trial: some planned and accidental findings.** Top Early Childhood Sp Educ. 2017 Jun 23;1-6. [http://journals.sagepub.com/doi/pdf/10.1177/0271121417711531]
	Strain described a 4-year follow-up study from the Learning Experiences and Alternative Program for Preschoolers and their Parents (LEAP) randomized trial.

	In the previous randomized study trial, moderate to large effect size differences were evident for students receiving the complete LEAP inclusion model. Due to such promising outcomes, Strain and colleagues received funding for the 4-year follow-up study. In this study, Strain outlined four a-priori questions: What is the stability of classroom placement across 4 years (K-3)? What is driving initial kindergarten placement decisions? How did classroom quality vary across settings? What do children in the LEAP Randomized Control Trial (RCT) look like 4 years away from intervention? Initial decisions about placement seemed to be made according to preestablished district perceptions of students with autism, not based on individual student need. Statistically significant differences were observed, with students in inclusive settings performing better than those in segregated settings. Recommendations include program replication and further longitudinal studies. This article is noteworthy because it shows that a decision about a child's placement (which appeared to be based more on district policy then a child's individualized need) can significantly impact their developmental trajectory and their academic success.
Geraldine Dawson	Weitlauf AS, Sathe N, McPheeters ML, Warren ZE. **Interventions targeting sensory challenges in autism spectrum disorder: a systematic review**. Pediatrics. 2017 May 26. [Epub ahead of print] [PMID: 28562287]
	A systematic review of interventions targeting sensory challenges in autism. It was concluded that some interventions may yield modest short-term (<6 months) improvements in sensory- and ASD symptom severity-related outcomes; the evidence base is small, and the durability of the effects is unclear. Although some therapies may hold promise, substantial needs exist for continuing improvements in methodologic rigor.
Question 5 (Services)	
David Mandell	Barry CL, Epstein AJ, Marcus SC, Kennedy-Hendricks A, Candon MK, Xie M, Mandell DS. **Effects of state insurance mandates on health care use and spending for autism spectrum disorder**. Health Affairs (Millwood). 2017 Oct 1; 36(10), 1754-1761. [PMID: 28971920]
	This study comprises the most rigorous study to date of the effects of states' autism insurance mandates on service use and spending among children with autism. The study finds that mandates result in substantial increases in spending on autism-specific services, although the effect is not apparent until two years after the mandates are passed. A notable finding is that the effect is concentrated among younger children and dissipates among adolescents, suggesting the need for additional strategies to improve service access and use among older children with autism.
Larry Wexler	Caron V, Bérubé A, Paquet A. **Implementation evaluation of early intensive behavioral intervention programs for children with autism spectrum disorders: A systematic review of studies in the last decade.** Eval Program Plann. 2017 Jun;62:1-8. [PMID: 28189054]
	Caron and colleagues reviewed studies, within a ten-year period, related to Early Intensive Behavior Interventions (EIBI). These interventions were provided to children with autism spectrum disorders (ASD). Researchers catalogued program implementation components evidenced in the studies. Twenty-eight studies met the selection criteria. Implementation components included dosage,

	adherence, differentiation, quality, and participation. Variables related to dosage and adherence were well described throughout selected studies, while the majority of studies did not report on participation, differentiation, or quality. Recommendations include examining the fidelity of EIBI interventions, a more comprehensive definition of EIBI programs, and enhanced evaluations of implementation in practice. This study is significant because it provides an expansive overview of EIBI interventions through the examination of current research.
Larry Wexler	Chou Y, Wehmeyer ML, Palmer SB, Lee J. **Comparisons of self-determination among students with autism, intellectual disability, and learning disabilities: a multivariate analysis.** Foc on Autism and Other Dev Disabil. 2017 Jun 1;32(2):124-132. [http://journals.sagepub.com/doi/pdf/10.1177/1088357615625059]
	Chou and colleagues considered the differences in self-determination between students with autism spectrum disorders (ASD), students with intellectual disability (ID), and students with learning disabilities (LD). Researchers selected 222 participants, with equal numbers in disability categories. Using a multivariate analysis of covariance (MANCOVA), Chou and colleagues examined four dependent variables: autonomy, self-regulation, psychological empowerment, and self-realization. Students with ASD scored lower in the categories of autonomy and psychological empowerment than students with ID or LD. However, students with ASD did not demonstrate significant variance from students with ID or LD in self-regulation. Implications for educators include, but are not limited to, selection of domain interventions based upon profile distinctions and increasing educational opportunities for students with ASD to develop self-determination skills and participate in inclusive settings. This study should be considered because students with disabilities typically do not demonstrate self-determination practices to the degree of their general education peers. Therefore, engaging in studies that examine such behaviors may lead to increased strategies for self-determination practices among students with disabilities.
Geraldine Dawson	Cidav Z, Munson J, Estes A, Dawson G, Rogers S, Mandell D. **Cost offset associated with Early Start Denver Model for children with autism**. J Am Acad Child Adolesc Psychiatry. 2017 Sep;56(9):777-783. [PMID: 28838582]
	This study determined the effect of early intensive behavioral treatment of young children with autism on health care service use and costs. In the postintervention period, compared with children who had earlier received treatment as usual in community settings, children in the early intervention group used less ABA/EIBI, occupational/physical therapy, and speech therapy services, resulting in significant cost savings in the amount of about $19,000 per year per child. Costs associated with ESDM treatment were fully offset within a few years after the intervention because of reductions in other service use and associated costs.
David Mandell	Jamison JM, Fourie E, Siper PM, Trelles MP, George-Jones J, Buxbaum Grice A, Krata J, Holl E, Shaoul J, Hernandez B, Mitchell L, McKay MM, Buxbaum JD, Kolevzon A. **Examining the efficacy of a family peer advocate model for black**

	and hispanic caregivers of children with autism spectrum disorder. J Autism Dev Disord. 2017 May;47(5):1314-1322. [PMID: 28168677]
	This study comprises a randomized trial of a relatively inexpensive intervention to improve outcomes for poor and ethnic minority caregivers of children with autism. The study found that the intervention increased parent knowledge of autism and reduced parent stress, but had no effect on service use, suggesting that interventions like these may be necessary but not sufficient for improving overall parent and child outcomes.
David Mandell	Leslie DL, Iskandarani K, Velott DL, Stein BD, Mandell DS, Agbese E, Dick AW. **Medicaid waivers targeting children with autism spectrum disorder reduce the need for parents to stop working**. Health Aff (Millwood). 2017 Feb 1;36(2):282-288. [PMID: 28167717]
	This paper is emblematic of a body of work coming from this group that merges Medicaid claims data with national survey data and uses ecological associations to examine the effects of different state Medicaid policies on child and family outcomes. This particular study examines the effect of the generosity of Medicaid waivers on parents' workforce participation. Prior research has demonstrated that mothers of children with autism are much more likely than parents of other children to drop out of the workforce. The present study finds that parents of children with autism who live in states with more generous Medicaid waivers are more likely to stay in the workforce, suggesting that these state policies have important economic implications beyond the immediate care for which they pay.
Geraldine Dawson	Zuckerman KE, Lindly OJ, Reyes NM, Chavez AE, Macias K, Smith KN, Reynolds A. **Disparities in diagnosis and treatment of autism in Latino and non-Latino white families**. Pediatrics. 2017 May;139(5). pii: e20163010. [PMID: 28557734]
	Study compared barriers to autism spectrum disorder (ASD) diagnosis and current ASD-related service use among non-Latino white (NLW) families and Latino families with English proficiency (L-EP) or limited English proficiency (L-LEP). English proficiency was an important marker for barriers to ASD diagnosis and treatment in Latinos. Increasing ASD-related knowledge and provider trust may decrease disparities in the diagnosis and treatment of ASD among US Latinos.
Question 6 (Lifespan Issues)	
Julie Lounds Taylor	Ditchman NM, Miller JL, Easton AB. **Vocational rehabilitation service patterns: an application of social network analysis to examine employment outcomes of transition-age individuals with autism**. Rehabil Counseling Bull. 2017 May 31. [http://journals.sagepub.com/doi/abs/10.1177/0034355217709455]
	There have been a handful of studies that have used vocational rehabilitation databases to determine which individual services are associated with employment outcomes at case closure. This study also uses the voc rehab database (i.e., the Rehabilitative Service Databases), but instead of looking at individual contribution of services, they used social network analysis to examine patterns/combinations of services that might facilitate employment outcomes for adults with ASD in the VR system. Using this method, they were able to identify six "core services" (assessment, job placement assistance, counseling, job search assistance, on-the-job support, transportation) – for every one

	increase in core services, the odds of successful employment were 1.54 times greater. This study is interesting because it takes an innovative approach to understanding service effectiveness.
Julie Lounds Taylor	Taylor JL, DaWalt LS. **Brief report: postsecondary work and educational disruptions for youth on the autism spectrum**. J Autism Dev Disord. 2017 Sep 9. [PMID: 28889215]
	Nearly all studies of employment outcomes use data collected at one point in time, and thus cannot speak to issues around maintaining vocational positions once obtained. This study, using detailed longitudinal data collected from a small sample (n = 36), examined the proportion of youth with ASD who experienced instability in vocational/education in the first 2-3 after high school exit, as well as whether behavioral and family factors measured in high school distinguished those who did versus did not experienced instability. Although most youth transitioned into some sort of post-secondary activity, 50% experienced instability in those activities. Maternal and family functioning – and not the characteristics of the youth with ASD – distinguished those who did versus did not experience instability. This study suggests that the factors that predict whether youth with ASD get a job or go to college might be different from the factors that predict maintaining those activities.
Julie Lounds Taylor	Van Schalkwyk GI, Marin CE, Ortiz M, Rolison M, Qayyum Z, McPartland JC, Lebowitz ER, Volkmar FR, Silverman WK. **Social media use, friendship quality, and the moderating role of anxiety in adolescents with autism spectrum disorder**. J Autism Dev Disord. 2017 Jun 14. [PMID: 2861685]
	This study examined social media use, anxiety, and friendship quality in 44 adolescents with ASD and 56 clinical comparison controls. More time on social media and greater social media utility was associated with higher friendship quality as rated by both parents and adolescent with ASD – particularly for those with lower parent-rated anxiety. There were no relationships between friendship quality and social media use for control group adolescents. This study suggests that adolescents with ASD may be a unique subgroup in terms of their capacity to benefit from social media.
Question 7 (Infrastructure and Surveillance)	
Joshua Gordon	Durkin MS, Maenner MJ, Baio J, Christensen D, Daniels J, Fitzgerald R, Imm P, Lee LC, Schieve LA, Van Naarden Braun K, Wingate MS, Yeargin-Allsopp M. **Autism spectrum disorder among US children (2002-2010): socioeconomic, racial, and ethnic disparities**. Am J Public Health. 2017 Nov;107(11):1818-1826. [PMID: 28933930]
	ASD prevalence and 95% confidence intervals (CIs) were computed from population-based surveillance, census, and survey data. SES categories were defined using area-level education, income, and poverty indicators. ASD was ascertained in 13,396 of 1,308,641 8-year-old children under surveillance. The prevalence of ASD increased with increasing SES during each surveillance year among White, Black, and Hispanic children. The prevalence difference between high- and low-SES groups was relatively constant over time (3.9/1000 [95% CI = 3.3, 4.5] in 2002 and 4.1/1000 [95% CI = 3.6, 4.6] in the period 2006-2010). Significant racial/ethnic differences in ASD prevalence remained after stratification by SES. A positive SES gradient in ASD prevalence according to US

	surveillance data prevailed between 2002 and 2010, and racial and ethnic disparities in prevalence persisted during this time among low-SES children.
Geraldine Dawson	Hoffman K, Weisskopf MG, Roberts AL, Raz R, Hart JE, Lyall K, Hoffman EM, Laden F, Vieira VM. **Geographic patterns of autism spectrum disorder among children of Nurses' Health Study II women**. Am J Epidemiol. 2017 May 19. [Epub ahead of print] [PMID: 28525627]
	Analyses included 13,507 children born from 1989-1999 (486 with ASD). The study explored relationships between ASD and residential location at both birth and age 6 years (i.e. closer to average diagnosis age). Using the residential address at age 6 produced similar results; however, areas of significantly decreased ASD odds were observed in the Southeast, where children were half as likely to have ASD. These results may indicate that diagnostic factors are driving spatial patterns; however, it is possible that other environmental factors are influencing distributions.
Geraldine Dawson	Loomes R, Hull L, Mandy WPL. **What is the male-to-female ratio in autism spectrum disorder? A systematic review and meta-analysis**. J Am Acad Child Adolesc Psychiatry. 2017 Jun;56(6):466-474. [PMID: 28545751]
	The purpose of this study was to derive the first systematically calculated estimate of the relative proportion of boys and girls with autism spectrum disorder (ASD) through a meta-analysis of prevalence studies conducted since the introduction of the DSM-IV and the International Classification of Diseases, Tenth Revision. Of children meeting criteria for ASD, the true male-to-female ratio is not 4:1, as is often assumed; rather, it is closer to 3:1. There appears to be a diagnostic gender bias, meaning that girls who meet criteria for ASD are at disproportionate risk of not receiving a clinical diagnosis.