2019 Summary of Advances Nominations: January – April 2019

Question 1 (Screening and Diagnosis)	
There were no nominations covering Question 1 topics from January - April 2019.	
Question 2 (Underlying Biology)	
Joshua Gordon	Ingiosi A, Schoch H, Wintler TP, Singletary KG, Righelli D, Roser L, Medina E, Risso D, Frank MG, Peixoto L. **Shank3 Modulates Sleep and Expression of Circadian Transcription Factors.** Elife. 2019 Apr 11;8. pii: e42819. doi: 10.7554/eLife.42819. [Epub ahead of print] [PMID: 30973326]
	The authors investigated the role of Shank3, a high confidence ASD gene candidate, in sleep architecture and regulation. They showed that mice with defective Shank3 have problems falling asleep even when sleepy. The Shank3 mutants also have altered expression of several transcription factors that regulate circadian rhythms. Overall, our study shows that Shank3 is an important modulator of sleep and clock gene expression.
Alison Singer, Walter Koroshetz	Schafer ST, Paquola ACM, Stern S, Gosselin D, Ku M, Pena M, Kuret TJM, Liyanage M, Mansour AA, Jaeger BN, Marchetto MC, Glass CK, Mertens J, Gage FH. **Pathological priming causes developmental gene network heterochronicity in autistic subject-derived neurons.** Nat Neurosci. 2019 Feb;22(2):243-255. [PMID: 30617258]
	This study showed that neurons derived from the skin cells of people with and without autism spectrum disorder exhibit different patterns of growth and development.
	This study looked at gene expression and gene network regulation throughout the course of neuron maturation, using induced pluripotent stem cells from individuals with and without ASD. By analyzing snapshots at different timepoints, the authors found that some ASD-associated phenotypes are set in motion very early in development at the neural stem cell stage and are associated with altered chromatin dynamics affecting gene expression. Targeted over-expression of certain network factors in control cells could trigger ASD-associated changes, and conversely, these changes could be blocked in ASD-derived cells by experimentally skipping over the neural stem cell stage.
Question 3 (Risk Factors)	
David Amaral	Al-Haddad BJS, Jacobsson B, Chabra S, Modzelewska D, Olson EM, Bernier R, Enquobahrie DA, Hagberg H, Östling S, Rajagopal L, Adams Waldorf KM, Sengpiel V. **Long-term Risk of Neuropsychiatric Disease After Exposure to Infection In Utero.** JAMA Psychiatry. 2019 Mar 6. [PMID: 30840048]
	A large-scale epidemiological study indicating a link between maternal infection and psychiatric disorders (including autism) in offspring.

Joshua Gordon	Hviid A, Hansen JV, Frisch M, Melbye M. **Measles, Mumps, Rubella Vaccination and Autism: A Nationwide Cohort Study.** Ann Intern Med. 2019 Mar 5. [PMID: 30831578]
	This nationwide cohort study strongly supports that MMR vaccination does not increase the risk for autism, does not trigger autism in susceptible children, and is not associated with clustering of autism cases after vaccination. It adds to previous studies through significant additional statistical power and by addressing hypotheses of susceptible subgroups and clustering of cases.
Linda Birnbaum	Schmidt RJ, Iosif AM, Guerrero Angel E, Ozonoff S. **Association of Maternal Prenatal Vitamin Use With Risk for Autism Spectrum Disorder Recurrence in Young Siblings.** JAMA Psychiatry. 2019 Feb 27. [PMID: 30810722]
	While prenatal vitamins have previously been associated with reduced risk of autism, this study is the first to identify prenatal vitamins during the first month of pregnancy as a potential protective factor in a population at higher risk of autism diagnosis. It is also one of the first to associate prenatal vitamins during the first month with lower scores of autism symptom severity as well as higher cognitive function using standardized measurements.
Geraldine Dawson	Septier M, Peyre H, Amsellem F, Beggiato A, Maruani A, Poumeyreau M, Amestoy A, Scheid I, Gaman A, Bolognani F, Honey G, Bouquet C, Ly-Le Moal M, Bouvard M, Leboyer M, Bourgeron T, Delorme R. **Increased risk of ADHD in families with ASD.** Eur Child Adolesc Psychiatry. 2019 Feb;28(2):281-288. [PMID: 30267210]
	Study provides a representative estimate of the family distribution of ADHD in relatives of ASD probands but supports the modest effect of shared genetic and environmental factors between both disorders.
Question 4 (Treatments and Interventions)	
Geraldine Dawson	Rogers SJ, Estes A, Lord C, Munson J, Rocha M, Winter J, Greenson J, Colombi C, Dawson G, Vismara LA, Sugar CA, Hellemann G, Whelan F, Talbott M. **A Multisite Randomized Controlled Two-Phase Trial of the Early Start Denver Model Compared to Treatment as Usual.** J Am Acad Child Adolesc Psychiatry. 2019 Jan 24. pii:S0890-8567(19)30044-9. [PMID: 30768394]
	This single-blind, randomized, multi-site, intent-to-treat study was designed to replicate and extend Dawson et al.'s (2010) randomized controlled trial (RCT) testing effects of the Early Start Denver Model (ESDM), an intensive play-and routines-based intervention delivered in natural settings. In the planned two-way analysis that pooled the data across all three sites, there was a significant advantage for language outcomes found for the ESDM group.
Question 5 (Services)	

Joshua Gordon	Monz BU, Houghton R, Law K, Loss G. **Treatment patterns in children with autism in the United States.** Autism Res. 2019 Mar;12(3):517-526. [PMID: 30629336]
	The authors sought to understand what types of treatment children (aged 3-17 years) with ASD receive in the United States, how and where the treatments take place and for how long. While overall non-drug treatment rates for children with ASD were high in the United States in our study, differences existed depending on where the family lives; not only regarding the type of therapy, but also where it takes place. Almost half the caregivers reported at least one barrier to treatment, such as "waiting list" and "no coverage."
Question 6 (Lifespan Issues)	
Joshua Gordon	Kirby AV, Bakian AV, Zhang Y, Bilder DA, Keeshin BR, Coon H. **A 20-year study of suicide death in a statewide autism population.** Autism Res. 2019 Apr;12(4):658-666. [PMID: 30663277]
	This study examined suicide risk among individuals with autism spectrum disorder (ASD) in Utah over a 20-year period. Risk of suicide death in individuals with ASD was found to have increased over time and to be greater than in individuals without ASD between 2013 and 2017. Females with ASD were over three times as likely to die from suicide as females without ASD. Young people with ASD were at over twice the risk of suicide than young people without ASD. Individuals with ASD were less likely than others to die from firearm-related suicides.
David Mandell	Rast JE, Roux AM, Shattuck PT. **Use of Vocational Rehabilitation Supports for Postsecondary Education Among Transition-Age Youth on the Autism Spectrum.** J Autism Dev Disord. 2019 Mar 8. [PMID: 30848406]
	This paper uses a good dataset to demonstrate low use of VR services among adolescents and young adults with ASD, but excellent outcomes among those who do use those services.
Jennifer Johnson	Wehman P, Schall C, McDonough J, Sima A, Brooke A, Ham W, Whittenburg H, Brooke V, Avellone L, Riehle E. **Competitive Employment for Transition-Aged Youth with Significant Impact from Autism: A Multi-site Randomized Clinical Trial.** J Autism Dev Disord. 2019 Mar 1. [PMID: 30825082]
	This study reports the results of a multi-site, parallel block randomized clinical trial to expand the previous findings regarding the implementation of Project SEARCH plus ASD Supports (PS + ASD) on employment outcomes upon graduation from high school.
Question 7 (Infrastructure and Surveillance)	
There were no nominations covering Question 7 topics from January - April 2019.	