2024 Summary of Advances Nominations

Table of Contents

Screening and Diagnosis ........................................................................................................................................... 2
Biology ........................................................................................................................................................................... 3
Genetic and Environmental Factors ......................................................................................................................... 8
Interventions ............................................................................................................................................................. 9
Services and Supports ........................................................................................................................................... 11
Lifespan ....................................................................................................................................................................... 13
Infrastructure and Prevalence ............................................................................................................................... 14
## Screening and Diagnosis

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<thead>
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<th>NIMH</th>
<th>Nominated article:</th>
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**Justification from IACC member who nominated article:**

Obtaining an accurate diagnosis of Autism Spectrum Disorder (ASD) is essential in order to provide families with the appropriate services and interventions their children need. However, many children are still under-diagnosed, over-diagnosed, or misdiagnosed. This present study examined 232 children diagnosed with ASD to confirm their diagnoses using extensive assessments. After dividing their sample into 2 groups: those with a confirmed autism diagnoses (ASD+) and the other with unconfirmed/inaccurate diagnoses (ASD-), the analyses showed that nearly half of the children did not meet the expert criteria for ASD. Those who truly had ASD were more likely to have had early language delays and scored higher on clinician-administered autism diagnostic tools. In contrast, children incorrectly diagnosed with ASD had higher IQ scores and more psychiatric disorders like anxiety and mood disorders. Findings from this study suggest that psychiatric issues may lead to misdiagnosis, and that expert diagnostic tools are more reliable than caregiver questionnaires for confirming ASD.


**Justification from IACC member who nominated article:**

The Sturm paper examines the psychometrics of a tool called the Ritvo Autism/Asperger’s Scale-Revised, or RAADS-R for self-diagnosis in ASD. This tool has received a lot of accolades from members of the autism community for being a diagnostic tool. This study showed that it is an effective screener, but is not a valid diagnostic instrument. They also identified some improvements that should be made before it is recommended for use diagnostic instrument, and note that those who self-diagnosed matched very closely to those who were professionally diagnosed, so it has potential.


**Justification from IACC member who nominated article:**

Children with autism and attention-deficit/hyperactivity disorder (ADHD) often experience early motor delays, but it's unclear if there are specific
signs that can tell these conditions apart. Researchers used a new method called movement curvature, measured with a wearable device, to study how infants' movements differ. They followed infants at likelihood for autism and ADHD from 12 to 36 months old. By 36 months, they categorized the children into ASD, ADHD concerns, or a comparison group. They found that infants later diagnosed with ASD had consistently lower movement curvature at 18, 24, and 36 months compared to those with ADHD concerns or typical development. Lower movement curvature also predicted ASD diagnosis, suggesting it could be an early marker for motor differences in autism as early as 18 months old.

### Biology

#### Nominated article:


**Justification from IACC member who nominated article:**

Many children diagnosed with autism commonly have language difficulties, which is also present in their non-autistic, first-degree relatives. In this study, researchers explored a potential brain mechanism behind these language issues by examining brain activity related to speech. Using a specific brain scan technique known as electroencephalography (EEG), researchers measured brain responses to speech in 125 children with autism, 121 typically developing children, and 40 non-autistic siblings of children with autism. The findings showed that children with autism had higher levels of certain brain waves (gamma power) when processing speech compared to typically developing children. Higher gamma power was linked to poorer language skills across all children. The non-autistic siblings showed brain activity and language skills that were between those of the autism and typically developing groups, suggesting that some brain characteristics of autism can also be seen in family members. This study highlights a possible brain-related mechanism responsible for language difficulties in children with autism.

#### Alycia Halladay

**Nominated article:**


**Justification from IACC member who nominated article:**

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The Chen paper utilized a novel model system, organoids, to screen for a potential drug therapy that targets the gene for Timothy Syndrome, which has autism as one of its common features. Timothy Syndrome is characterized by neurodevelopmental disorders and heart problems, and using this model, the targeted gene therapy identified through the organoid platform, was able to partially reverse the calcium signal loss and the neuron dendrite retraction characteristic of this Syndrome.

Nominated article:

**Justification from IACC member who nominated article:**
Adolescence is a critical period for the onset of psychiatric conditions like depression, which can be particularly prevalent for youth with autism. While both autistic and typically developing (TD) youth experience worsening depression during adolescence, it’s unclear if their experiences are similar. This study followed autistic and neurotypical youth over four years, using linear and logistic mixed effects models to track depressive symptoms. The study involved 244 youths aged 10 to 13. Researchers found that autistic youth had higher depression scores than their TD peers, and females had higher scores than males in both groups. Significant interactions were found between diagnosis and age, and diagnosis and pubertal stage. In the autism group, depression scores were high in early adolescence but decreased during middle adolescence and puberty, whereas the TD group showed increasing depression symptoms as they aged. The findings suggest that while autistic youth initially have higher rates of depressive symptoms, these decrease over time, whereas TD youth see an increase, leading to similar levels of depression by late adolescence.

Nominated article:

**Justification from IACC member who nominated article:**
This study explores the biological underpinnings of the variability in social and communication traits in toddlers with autism, distinguishing between those with improving abilities and those with higher support needs who require lifelong care. Researchers measured size and growth in brain cortical organoids (BCOs) derived from autistic and non-autistic toddlers, finding significantly larger BCOs in autistic toddlers. The study revealed two ASD subtypes: one with markedly enlarged BCOs, accelerated neurogenesis, severe social traits, and reduced cognitive and language abilities, and another with milder BCO enlargement. Larger
embryonic BCO size correlated with more severe social traits and reduced cognitive abilities. The study highlights dysregulated cell proliferation and neurogenesis as key factors in the biological basis of ASD subtypes from embryogenesis, suggesting the need for larger samples to identify additional subtypes.

| 8 | NIDCD, NIMH | **Nominated article:**

**Justification from IACC member who nominated article:**
**NIDCD:** Language and social symptoms improve with age in some autistic toddlers, but not in others, and such outcome differences are not clearly predictable from clinical scores alone. This study demonstrates that autistic toddlers show differentially larger or thicker temporal and fusiform regions; smaller or thinner inferior frontal lobe and midline structures; larger callosal subregion volume; and smaller cerebellum. These brain alterations improve accuracy for predicting language outcome at 6-month follow-up beyond intake clinical and demographic variables. Among autistic toddlers, brain alterations in social, language and face processing areas enhance the prediction of the child’s future language ability. This article highlights important predictors of future language ability as well as important underpinnings for language growth.

**NIMH:** Differences in the improvement of language and social skills cannot be reliably predicted by clinical scores alone. The investigators in this study sought to identify early brain changes in autism that can predict future language abilities. By analyzing MRI scans from 166 autistic and 109 typical toddlers, researchers found that toddlers diagnosed with ASD have unique brain differences in regions related to language and social processing. These identified brain changes help predict language outcomes more accurately than clinical scores alone. Continued study of these brain alterations can help identify which autistic children might need more support with language development.

| 9 | NIMH | **Nominated article:**

**Justification from IACC member who nominated article:**
Research remains unclear whether nonspeaking autistic individuals can acquire spelling skills. Researchers conducted a study to investigate this possibility, involving 31 autistic teenagers and adults who speak minimally or not at all. They engaged in an iPad game where they tapped flashing letters, and researchers observed how quickly they responded. The participants demonstrated three key spelling behaviors. They tapped letters faster when they formed coherent sentences compared to random sequences, showed quicker responses to commonly paired
letters, indicating an understanding of spelling conventions, and paused before tapping the first letter of a new word, demonstrating awareness of word boundaries. These findings suggest that many nonspeaking autistic individuals may be capable of learning to spell.

10 NIMH  

Nominated article:

Justification from IACC member who nominated article:  
Researchers aimed to see if the myelin content in the brain's cortex differed between middle-aged and older adults with autism and those without autism. They analyzed data from 30 people with autism and 36 non-autistic participants aged 40-70 years. Using both group and individual analyses, they found no significant differences in the average myelin content or age-related changes in myelin content between the groups. However, they did find that myelin content increased with age across the cortex in both groups. Individual analyses showed that some autistic participants had unusually high myelin content in certain brain areas, and these individuals had lower cognitive abilities, including overall intelligence, processing speed, and executive function. This study highlights the importance of examining individual differences, providing initial insights into the relationship between brain structure and cognitive abilities in older adults with autism. These findings suggest that unusual myelin content might be linked to poorer cognitive outcomes in some older autistic adults, reflecting their diverse neurodevelopmental histories and aging processes.

11 NIMH  

Nominated article:

Justification from IACC member who nominated article:  
The amygdala, a part of the brain, grows rapidly in the first year of life, resulting in an enlarged size by 12 months in infants who are later diagnosed with autism. This overgrowth may affect brain function during infancy. Researchers investigated whether the amygdala's connectivity with other brain regions differs in 12-month-olds at high likelihood (HL) for autism (those with an older sibling with autism) compared to those at low likelihood (LL). They focused on the connectivity between the left and right amygdalae and other brain areas, particularly the visual cortex, as previous studies suggested that visual brain regions develop differently in children with a genetic risk for autism. The study found that HL infants had weaker connections between the right amygdala and
the left visual cortex, and between the left amygdala and the right anterior cingulate. These differences were seen in specific subgroups of the HL infants. Additionally, the strength of amygdala connectivity with the visual cortex was linked to motor and communication skills in HL infants. These findings suggest that atypical connections between the amygdala and visual areas are present in infants with a genetic likelihood for autism and may influence early adaptive behaviors.


**Justification from IACC member who nominated article:** This study utilized Diffusion MRI to develop mathematical models of brain microstructures that have helped identify structural differences in the brains of those with autism and those without. The results are a first-of-its-kind approach to calculating the conductivity of neural axons and their capacity to carry information through the brain. The team found slower electrical conductivity in autistic brains due to variations in axon diameter. These differences have been directly linked to participants’ scores on the Social Communication Questionnaire, a common clinical tool for diagnosing autism. The research is part of the NIH’s Autism Center of Excellence initiative.


**Justification from IACC member who nominated article:** Many autistic individuals face significant mental health issues such as anxiety, depression, inattention, and aggression, posing challenges for effective interventions. Executive function difficulties, common among autistic individuals, may contribute to these mental health problems or complicate treatment efforts. While some respond well to therapies or medications, others do not. This study aimed to identify distinct subgroups of autistic youth based on their patterns of executive function, including abilities like flexibility, planning, self-monitoring, and emotion regulation. Researchers then examined whether these executive function subgroups were associated with specific mental health issues. The study identified three distinct executive function subgroups among autistic youth, each showing unique patterns of mental health challenges. These findings offer insights into tailoring personalized supports, services, and treatment strategies to address the specific executive function strengths and challenges of individuals with autism and their associated mental health conditions.

| 14 | NIMH | **Nominated article:** }
Vakilzadeh G, Maseko BC, Bartely TD, McLennan YA, Martínez-Cerdeño V. Increased number of excitatory synapsis and decreased number of inhibitory synapsis in the prefrontal cortex in autism. *Cereb Cortex*. 2024 May 2;34(13):121-128. [Read Abstract Here]

**Justification from IACC member who nominated article:**
Previous studies have shown an increase in excitatory pyramidal cells and a decrease in inhibitory parvalbumin+ chandelier interneurons in the prefrontal cortex of postmortem brains. However, how these changes affect the overall abundance of excitatory and inhibitory synapses in the cortex remains unclear. To address this, researchers quantified the number of excitatory and inhibitory synapses in the prefrontal cortex of 10 postmortem autistic brains and 10 non-autistic brains. Their findings revealed an increase in excitatory synapses in the upper cortical layers and a decrease in inhibitory synapses across all cortical layers in autistic brains compared to controls. These alterations in synapse numbers could lead to neuronal dysfunction and disturbed network connectivity in the prefrontal cortex in ASD. This study provides insights into the cellular and synaptic changes in the brains of autistic individuals.

### Genetic and Environmental Factors

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<th>15</th>
<th>NIMH</th>
<th><strong>Nominated article:</strong> Sandin S, Yip BHK, Yin W, Weiss LA, Dougherty JD, Fass S, Constantino JN, Hailin Z, Turner TN, Marrus N, Gutmann DH, Sanders SJ, Christoffersson B. Examining Sex Differences in Autism Heritability. <em>JAMA Psychiatry</em>. 2024 Apr 17:e240525. [Read Abstract Here] [Free Full Text Article]</th>
<th><strong>Justification from IACC member who nominated article:</strong> The etiology of Autism Spectrum Disorders (ASD) is rooted primarily in genetic factors, but the reasons for its higher occurrence in males are not well understood. This research investigation examined the genetic basis of ASD and its differing prevalence between males and females. Using data from Swedish national health registers, the study analyzed non-twin siblings and cousins born between 1985 and 1998, totaling over a million individuals (1,047,649 individuals in 456,832 families (538,283 males [51.38%]; 509,366 females [48.62%]). The researchers estimated that genetic factors contribute to 87% of ASD cases in males and 76% in females. The results found no evidence that shared environmental factors play a role in ASD occurrence and suggest that the observed sex differences in ASD are largely due to genetic differences. As a single study future additional studies will further enhance our understanding on the interplay between genetics and environment in ASD.</th>
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<td>16</td>
<td>SAMHSA</td>
<td><strong>Nominated article:</strong> Tadesse AW, Ayano G, Dachew BA, Betts K, Alati R. Exposure to maternal cannabis use disorder and risk of autism spectrum disorder in offspring: A data linkage cohort study. <em>Psychiatry Res</em>. 2024 Jul;337:115971. [Read Abstract Here] [Free Full Text Article]</td>
<td><strong>Justification from IACC member who nominated article:</strong></td>
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This was a retrospective cohort study led by Australian and Ethiopian academic authors “based on population-based, linked administrative data that included a sample of 259,150 mothers-offspring pairs, including all live births from 01 January 2003 to 31 December 2005 in New South Wales (NSW), Australia.” The authors examined exposure to cannabis use disorder in the pre-pregnancy, prenatal and perinatal periods using cross-linked data from the Admitted Patients Data Collection (APDC) and outpatients visit (Mental Health Ambulatory data collection) (MH-AMB-DC) with maternal health diagnoses with the Australian Prenatal Data Collection (PDC) registry. The authors reported a three-fold increased risk of autism spectrum disorder in infants whose mothers were diagnosed with cannabis use disorder compared to non-exposed offspring. The authors examined and adjusted for potential confounders such as socioeconomic status and smoking. The authors note that male infants faced increased risk compared to female infants and note the need for additional research, including examination of the impacts of paternal behavioral health factors.

| 17 | NIMH | **Nominated article:** Yin W, Pulakka A, Reichenberg A, Kolevzon A, Ludvigsson JF, Risnes K, Lahti-Pulkkinen M, Persson M, Silverman ME, Åden U, Kajantie E, Sandin S. Association between parental psychiatric disorders and risk of offspring autism spectrum disorder: a Swedish and Finnish population-based cohort study. *Lancet Reg Health Eur*. 2024 Apr 23;40:100902. [Read Abstract Here] [Free Full Text Article] | **Justification from IACC member who nominated article:** This study analyzed all children born in Sweden and Finland from 1997 to 2016, with diagnoses confirmed through national registers up to 2017. Researchers calculated adjusted hazard ratios (aHRs) and 95% confidence intervals (CIs) for ASD in children of parents with psychiatric disorders. Out of 2,505,842 children, 33,612 were diagnosed with ASD, with 20% having a parent with psychiatric disorders. The likelihood of autism was higher for children with fathers or mothers with psychiatric disorders, and even higher when both parents had psychiatric disorders. The likelihood further increased with the number of different psychiatric disorders in parents. This study underscores that psychiatric disorders in parents, especially when both are affected, significantly raise the likelihood of autism in children. |

| 18 | NIMH | **Nominated article:** Gulsrud AC, Shih W, Paparella T, Kasari C. Comparative efficacy of an early intervention "parent and me" program for infants showing signs of autism: The Baby JASPER model. *Infant Behav Dev*. 2024 Apr 27;76:101952. [Read Abstract Here] | **Justification from IACC member who nominated article:** Despite significant progress in early autism detection, there are still few proven interventions for children under two years old. Caregiver-
mediated interventions may be particularly effective because they support both the child and family. This study expands on existing research by enrolling a large group of infants (80 infants total, between the ages of 12-22 months old) showing early traits of autism into a randomized controlled intervention program. Infants and parents participated in a group-based program using a standard early childhood curriculum. Additionally, families were randomly assigned to receive either parent-mediated Joint Attention Symbolic Play Engagement and Regulation (JASPER) training or psychoeducation. Over an 8-week period, infants in both groups made significant improvements in social communication, play, and cognition, with an average increase of over 10 points in developmental quotient (DQ) and improvements in standardized social communication and play measures. These gains were maintained at a 2-month follow-up. The group that received JASPER training showed increased child-initiated joint engagement and play during interactions with their parents, while the psychoeducation group showed increased joint attention during a standardized assessment. This study highlights the potential of early interventions to achieve positive outcomes for young children and their families.


**Justification from IACC member who nominated article:**
In this study, parent-led cognitive behavioral therapy (CBT) emerged as a promising treatment for anxiety disorders in autistic youth aged 7 to 13 years. The research compared two formats of CBT delivery: one with minimal therapist contact (four 30-minute telehealth calls) and another with standard therapist contact (ten 60-minute telehealth calls). Both groups showed significant reductions in anxiety, functional impairment, and autism-related features over the 12-week therapy period, with no significant differences between the two formats. Participants and their families reported high satisfaction with the interventions, with slightly higher ratings for the standard-contact CBT. Responder rates, indicating treatment success, were high across both groups at post-treatment and 3-month follow-up. Importantly, low-contact CBT was found to be significantly more cost-effective than standard-contact CBT, offering potential economic benefits without compromising therapeutic outcomes.


**Justification from IACC member who nominated article:**

Dena Gassner
Researchers analyzed data from 144 studies involving 9,038 young autistic children to determine if the amount of early childhood autism intervention (daily intensity, duration, cumulative intensity) was associated with improved development. The analysis found no significant association between the amount of intervention and developmental outcomes. This suggests that intensifying early childhood interventions does not necessarily increase their benefits, and practitioners should consider what amounts are developmentally appropriate.

## Services and Supports

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<td><strong>Justification from IACC member who nominated article:</strong> This cohort study investigated mental health (MH) conditions and access to community MH services among transition-age autistic youth (TAYA), focusing on Black, indigenous, and other diverse communities. Using Medicare-Medicaid data from 2012, the study found that compared to White TAYA, Black, Asian/Pacific Islander, and Hispanic TAYA were less likely to have diagnoses of substance-use, depressive, anxiety, ADHD, or PTSD. They were also less likely to have accessed community MH services in the past year, even after accounting for various factors. Factors enabling greater community MH service use included dual enrollment in Medicare and Medicaid, and longer enrollment in specific Medicaid waivers. The study highlights disparities in MH diagnosis and service access among diverse TAYA populations, suggesting a need for improved service delivery and equitable coverage across different demographic groups.</td>
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<tr>
<td>22</td>
<td>NIMH</td>
<td>Brusilovskiy E, Salzer MS, Pomponio Davidson A, Feeley C, Pfeiffer B. Using GPS and Self-Report Data to Examine the Relationship Between Community Mobility and Community Participation Among Autistic Young Adults. <em>Am J Occup Ther</em>. 2024 May 1;78(3):7803205160. <a href="#">Read Abstract Here</a> <a href="#">Free Full Text Article</a></td>
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<td><strong>Justification from IACC member who nominated article:</strong> This study investigates the connection between community participation and community mobility among autistic young adults. Using GPS data and self-reports from 63 participants in Philadelphia, the study found significant links between various aspects of community mobility and initial levels of community participation. However, changes in mobility over time did not correspond to changes in participation. These findings underscore the importance of addressing mobility barriers to enhance community engagement for autistic individuals, suggesting tailored...</td>
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interventions and policies could improve their quality of life and health outcomes.

| 23 | NIMH | **Nominated article:** Burke MM, Johnston AN, Cheung WC, Li C, Monárrez E, Aleman-Tovar J. Exploring the Perspectives of Parents of Individuals with Autism from Low-Resourced Communities to Inform Family Navigator Programs. *J Dev Phys Disabil*. 2024 Apr;36(2):271-292. [Read Abstract Here] [Free Full Text Article]

**Justification from IACC member who nominated article:**
As the use of Family navigator programs become more widely utilized by families of children with autism in order gain access necessary evaluations and services, more research is need about how these navigator programs are developed. This study explored the experiences of 12 parents from low-income communities to inform these programs. Findings suggest that navigators need training to address barriers like limited knowledge and difficulty accepting an autism diagnosis. Programs should focus on educating families, connecting them with peer support, and covering services and advocacy strategies. Systemic changes are also needed to improve service access for all autistic children.


**Justification from IACC member who nominated article:**
Transitioning to a new school can be particularly difficult for students on the autism spectrum. And to date, we lack well-established interventions to help these students and their families navigate school transitions. To address this problem, researchers developed Building Better Bridges (BBB), a coaching program for caregivers that includes training on school communication, educational rights, advocacy, and child preparation. In this study, investigators followed 170 participants from diverse, under-resourced communities, where BBB students (n=83) were compared to a resource-only group n=87). The results showed that caregivers and teachers who participated in BBB reported more positive transitions for the students, suggesting that this low-cost intervention can significantly aid families and students facing challenging school transitions.


**Justification from IACC member who nominated article:**
This study explored how a culturally tailored parent education program, using a peer-to-peer mentoring model, impacted depressive symptoms among Latina mothers of autistic children. In a randomized waitlist-control study across two sites with 109 mother-child pairs, the intervention aimed to boost mothers' self-efficacy and use of effective strategies. Depressive symptom scores (CES-D) were measured at baseline, post-intervention (Time 2), and 4 months later (Time 3). Results indicate that mothers in the intervention group experienced a significant reduction in depressive symptoms at Time 2, and this improvement was sustained at Time 3 with moderate effect sizes. The intervention showed consistent benefits across both study sites, suggesting that "Parents Taking Action" effectively reduces depressive symptoms in this population.

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<th>Lifespan</th>
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<td>Justification from IACC member who nominated article: Researchers sought to explore how autistic children faired before and during the pandemic when compared to the broader group of children with special health care needs (SHCN), and those without SHCN as it relates to economic hardship and safety net program utilization. Notably, it spotlights the importance and reliance of safety net program utilization among children, as it specifically examines differences across utilization of cash assistance, including Temporary Assistance for Needy Families (TANF) and Supplemental Security Income (SSI), as well as Supplemental Nutrition Assistance Program (SNAP) and Special Supplemental Nutrition Program for Women, Infants, and Children (WIC) and purposefully considers impacts on children with autism. Findings included, a) decreased risk of medical hardship, foregone work, and multiple hardship during the pandemic, when compared to before the pandemic; and b) increased food insecurity risks, c) higher rates of safety program utilization during COVID when compared to children with no SCHN.</td>
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| Justification from IACC member who nominated article: Later autism diagnosis has been linked to higher mental health risks. Factors like sex assigned at birth, gender identity, and gender diversity affect when autism is diagnosed. This study looked at age at diagnosis across three groups of autistic individuals, finding significant delays for |
females, those identifying as female, and gender-diverse individuals compared to males and cisgender individuals. These findings stress the need for tailored diagnostic approaches and more research on autism diagnosis in adulthood.

**Nominated article:**

**Justification from IACC member who nominated article:**
Prior research has demonstrated that girls and women are diagnosed with autism later than boys and men. And among those with a late life ASD diagnosis, girls and women are more likely to have higher levels of anxiety and depression. This study examined two ASD groups: one from a large clinic-based sample and the other from a research-based sample diagnosed with ASD via strict research criteria, in order to explore the links between the age of diagnosis, gender, and mental health. In both groups, later diagnosis was linked to more anxiety and depression, with anxiety not varying by gender. In the large clinic-based group, girls were diagnosed later than boys and had more anxiety and depression. In the research sample, girls had more depressive symptoms than boys. The findings highlight the need for early autism diagnosis, particularly for girls and women, to address mental health disparities.

**Infrastructure and Prevalence**
*There were no nominations covering this topic from April - July 2024.*