**Symposium Title**: Co-occurring autism in Down syndrome: Screening, diagnostic, and symptom monitoring tools

**Overview**: Autism co-occurs in individuals with Down syndrome (DS) at a higher rate than in the general population (CDC, 2024; Glennon et al., 2017). However, accurately screening for and diagnosing autism spectrum disorder (ASD) in this population that also has co-occurring intellectual disability and carries its own phenotype related to social communication remains challenging. This symposium brings together research groups who have addressed this challenge in various ways to learn more about how to best apply the current gold-standard ASD screening and diagnostic tools as well as explore other promising tools for screening and monitoring symptoms over time in individuals with DS from early childhood through young adulthood.

**Paper 1 of 3**

**Paper Title**: Autism Screening and Symptom Monitoring Tools for Youth with Down Syndrome

**Introduction**: As many as 1 in 5 individuals with Down syndrome (DS) meet criteria for co-occurring autism spectrum disorder (ASD; Glennon et al., 2017). Yet it is under-diagnosed in community settings. For example, in one recent study, caregivers of children with a dual diagnosis of DS and ASD reported frustrations in the diagnostic process, citing frequent dismissal of their initial concerns resulting in delayed referrals, with an average time to diagnosis of 4.65 years (Spinazzi et al., 2024). Delayed diagnosis leads to missed opportunities for early intervention and access to services that can address the unique support needs of those with DS+ASD (Versaci et al., 2021). One barrier is the lack of evidence for reliable and valid screening tools that measure ASD symptoms among individuals with DS. That is, the presence of intellectual disability and the hallmark phenotypic difficulties in language associated with DS make it difficult to differentiate whether specific behaviors characterized in ASD screeners are indicative of ASD or, more broadly, characteristic of DS (Glennon et al., 2017). The current study addressed this barrier by evaluating the psychometric properties and utility of three common ASD symptom measures in youth with DS.

**Method**: We conducted a national online survey of 149 caregivers of youth with DS ages 6-18 years old (*M* = 12.0, *SD* = 3.5; 53.7% male, 46.3% female; 81.9% White, 9.4% Multi-racial, 4.0% Black, 3.4% Asian, 1.3% Other; 7.4% Hispanic). In this sample, 26% reported that their child had received a diagnosis of ASD. Of those who had not received a diagnosis, 14.9% reported that they think their child has ASD, with another 16.8% reporting that they were not sure if their child has ASD. The survey was administered in REDCap and included the *Social Communication Questionnaire (SCQ)*, *Social Responsiveness Scale (SRS-2)*, and the *Autism Impact Measure (AIM)* along with developmental and health questionnaires. Caregivers completed the SCQ, SRS-2, and AIM again 2-4 weeks later for test-retest reliability. To examine the utility of each standardized measure, we asked caregivers: “*Did you feel that any of these questions were inappropriate for or did not apply to your child?*” (yes/no). If they selected ‘yes,’ we asked an open-ended question: “*How did you respond to/rate those questions (e.g., rated them all as Not True, rated them all as Almost Always True)? Please explain.”*

**Results**: Internal consistency was strong for each measure (Cronbach’s *α* = SCQ: 0.89, SRS-2: 0.96, AIM: 0.98). Test-retest reliability was also strong (Intra-Class Correlation Coefficient [ICC] = SCQ: 0.95 [0.91-0.96], SRS-2: 0.97 [0.95-0.98], AIM: 0.95 [0.93-0.97]; Spearman’s *r* = SCQ: 0.91, SRS-2: 0.92, AIM: 0.93). Notably, test-retest reliability was stable across all levels of ASD symptoms. Convergent validity was also established among the measures (range = 0.78-0.88). We also conducted item analyses for each measure to determine (1) the correlation of each item with the total score (item-rest correlation) and (2) items that were over-/under-endorsed by more than 80% of the sample (endorsement rate). There were some items on each measure with low item-rest correlation coefficients, meaning that those items do not measure the same trait as the other items on the scale. Further, some items had very high/low endorsement rates across the sample, indicating that they do not differentiate high/low ASD symptoms among individuals with DS. More information on these items will be presented. Regarding the utility of each measure, caregiver appropriateness ratings revealed that some of the questions were inappropriate for their child (20% for SCQ, 38% for SRS-2, 30% for AIM). Interestingly, for the SRS-2 and AIM, the proportion of caregivers who indicated inappropriateness was significantly higher for those whose child had a diagnosis of ASD (SRS-2: +ASD = 63.9%, -ASD = 28.2%; AIM: +ASD = 50.0%, -ASD = 20.4%); however, there was no significant difference in the caregivers who reported inappropriateness for the SCQ (+ASD = 19.4%, -ASD = 20.4%).

**Discussion**: This was the first study to systematically characterize psychometric properties and caregiver rating data on the SCQ, SRS-2, and AIM in a large sample of youth with DS. Overall, the psychometric properties were strong for each ASD symptom measure. However, item-level analyses revealed some items on each measure with low item-rest correlation coefficients and some with high/low endorsement rates; further consideration should be given for the use of these items in youth with DS. Also, some caregivers reported that some of the questions were not appropriate for or applicable to their child, especially those who have a diagnosis of ASD, warranting additional examination into why. These findings have clinical implications for the use of the SCQ and SRS-2 as ASD screening tools and the use of the SRS-2 and AIM as symptom monitoring tools and potential outcome measures in youth with DS.

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**Paper 2 of 3**

**Paper Title**: Co-Occurring Autism Spectrum Disorder in Preschool-Aged Children with Down syndrome: Rates and Adaptive Profiles

**Introduction**: Children with Down syndrome (DS) are at an elevated risk for developing co-occurring autism spectrum disorder (ASD) with rates converging around ~18%1. Differential diagnosis of ASD in the context of intellectual disability (ID) can be challenging due to the early delays associated with eventual ID and some limitations of available diagnostic tools for these populations2,3. We sought to characterize rates within a sample of preschool-aged children with DS and describe functional profiles across children with DS-only, those with DS+ASD, and those with DS without co-occurring ASD that exceeded cutoffs on gold standard diagnostic tools (DS-O+).

**Method**: Participants included 45 children with DS between 34–64 months of age (*Mage* (months)=45.41, *SDAge*=9.55). The Mullen Scales of Early Learning (MSEL) indexed nonverbal cognition (*MNVDQ*=48.6 *SDNVDQ*=10.02), the Autism Diagnostic Observation Schedule 2nd Edition (ADOS-2) measured ASD symptoms; and the Vineland Adaptive Behavior Scales-2nd Edition (VABS-II) captured functional profiles. Clinical best estimate (CBE) procedures included full case-reviews to consider developmental and adaptive skills with gold standard ASD measures and clinical judgement.

**Results**: Results identified discrepant co-occurring ASD rates across the ADOS and CBE outcomes. According to the ADOS-2, 44% met ASD criteria, versus just 16% per CBE. Thirteen participants (29%) were misidentified for DS+ASD according to ADOS cutoff-scores (DS-O+). Functional profile comparisons identified large differences between the DS-Only and the DS+ASD and DS-O+ groups in all domains. The DS+ASD and DS-O+ groups showed moderate differences in Motor and Daily Living domains (*d* range=.59-.64), and small differences in Socialization and Communication (*d* range=.10-.19).

**Discussion**: Our findings revealed rates of DS+ASD that were consistent with prior studies. Results also provide evidence that solely relying on clinical cutoff scores specified on gold standard ASD diagnostic measures can skew estimated rates of co-occurring ASD in DS, and, consequently, contribute to a variable characterization of the DS+ASD phenotype depending on diagnostic or grouping methodology. Interestingly, similarities in adaptive behavior profiles emerged across the DS+ASD and DS-O+ groups emerged, highlighting the influence ID may have in diagnostic overshadowing and ASD evaluation in neurogenetic populations.

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**Paper 3 of 3**

**Paper Title**: Neurobehavioral Patterns in the Diagnosis of Autism Spectrum Disorder in Down Syndrome

**Introduction**: Down syndrome (DS) is one of the most common chromosomal disorders, with an incidence of 1 in every 700 live births in the United States1. Autism spectrum disorder (ASD) in children with DS (DS+ASD) is common, with an estimated prevalence between 12 to 41% 2,3,4. There are no standardized screening/assessment tools for evaluating ASD in DS. This study aimed to (1) utilize the ND-PROM5,6 to investigate item-level differences in developmental skills and behaviors among children with DS only, DS+ASD, and ASD only and to (2) determine which symptoms and behaviors are most specific to those with a co-occurring diagnosis of ASD within the DS population.

**Method**: We utilized a novel validated questionnaire, the ND-PROM, to investigate differences in developmental skills and behaviors among children with DS only, ASD only, and DS+ASD. The ND-PROM includes 93 Likert scale-type questions on a 5-point scale of Never, Rarely, Sometimes, Often, Always, indicating the demonstration of skill frequency or maladaptive behavior. It assesses the following skill-based domains (higher scores indicate demonstration of that skill at higher frequencies): Expressive Language, Receptive Language, Non-verbal Communication, Social Emotional Understanding, Social Interaction, Independent Play, Adaptive/Toileting, and the following behavioral areas (higher scores indicate more frequent occurrence): Restrictive and Repetitive Behaviors and Interests, Sensory Processes, Challenging Behaviors, Mental Health, and Impulse/Attention Deficit Hyperactivity Disorder (ADHD). Outside of these domains, the ND-PROM asks two communication-related questions which were included in this study: primary communication type (words, pictures, signs, or augmentative communication device); how many words, signs, or pictures the child puts together to communicate (does not communicate; one at a time, two, three, full sentences)5,6. Caregivers of all people seen in the DS clinic of a large, pediatric referral hospital provided information prior to their clinical visit, including completion of the ND-PROM. Descriptive statistics were used to report demographic and clinical data between groups. Data were analyzed using the Analysis of Variance (ANOVA) test for unequal group sizes. Power for the ANOVA test was estimated for the above sample sizes and was estimated to be 99% for a medium effect size (i.e., f=0.25). The required total sample size for power levels equal to 80% was n=125 participants. Post hoc tests involved the Tukey honestly-significantly difference test, at an alpha level of 5%. Comparisons were made for ND-PROM for domains that are consistent with DSM-5 criteria and those that are common co-occurring symptoms and behaviors. We consider differences in excess of one as reflecting a large effect size based on Cohen as domain scores are standardized with a mean of zero and a standard deviation (SD)=1. Thus, a value of one indicates differences in excess of one SD.

**Results**: In total, 53 individuals with DS+ASD (age range 1-24), 385 individuals with DS only (ages 0-24) and 246 individuals with ASD only (ages 2-21) were included. Data analysis using ANOVA tests and post-hoc t tests revealed item-level differences between groups in domains specific to ASD (Non-verbal Communication, Social-Emotional Understanding, Social Interaction, Independent Play, Restrictive and Repetitive Behaviors and Interests, and Sensory Processes) and not specific to ASD (Expressive Language, Receptive Language, Adaptive/Toileting, Challenging Behaviors, Mental Health, and Impulse/ADHD).

**Discussion**: This study utilized a freely available clinical tool to characterize developmental and behavioral functioning among individuals with DS. Notable differences were seen between DS+ASD, DS only, and ASD only groups, highlighting many signs, symptoms, and patterns of deficits that may help caretakers and clinicians better recognize individuals who require further evaluation for ASD. ASD-specific symptoms best distinguished DS only and DS+ASD groups, while non-ASD symptoms best distinguished ASD only and DS+ASD groups. Items that best differentiate groups are presented.

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