**Title:** The eXtraordinarY Babies Study: Early Developmental and Adaptive Functioning Skills of Infants and Toddlers with Prenatally Identified Sex Chromosome Trisomies

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**Introduction:** Children with sex chromosome trisomies (SCTs: i.e. XXY, XYY, XXX) are at risk for cognitive, language, social, and motor deficits (Tartaglia, et al., 2020). Advances in non-invasive prenatal testing (NIPT) have led to higher rates of prenatal identification of SCT, which provides opportunity to study early developmental features in these infants. The eXtraordinarY Babies Study is an ongoing prospective natural history study of health and neurodevelopment in prenatally-diagnosed infants with SCT with aims to identify predictors of positive and negative outcomes. Neurodevelopmental profiles are characterized utilizing a combination of direct developmental assessment and parental report of adaptive skills and behaviors in their naturalistic environment. Results have significant impact for guiding genetic counseling, care recommendations, and intervention research, and here we present early developmental data from the first 100+ participants enrolled.

**Method:** Participants included infants and toddlers identified prenatally by NIPT as having XXY, XYY, and XXX and enrolled before 12-months of age at either the 2, 6, or 12 months visit. Participants were assessed with the Bayley scales of Infant Development – 3rd Edition (Bayley, 2006) and the Vineland-3 Adaptive Behavior Scales (Sparrow, et al,. 2016) at 6 months (n = 109), 12 months (n = 103), and 24 months of age (n = 56). One sample t-tests were conducted with the entire cohort to compare the sub-domain scores on these measures at 6, 12, and 24 months of age to the population mean of 10 (Bayley-3 scaled scores) or 100 (Vineland-3 standard scores). Paired samples t-tests were conducted to compare sub-domain composites as well as expressive vs. receptive language and fine vs. gross motor at each timepoint. Finally, repeated measures ANOVAs were used to explore scores across time in a subgroup of children who had data for all 3 timepoints (n=26).

**Results:** On direct assessment using the Bayley-3, there were no differences in cognitive skills compared to the population mean at all timepoints (Cognitive scale means (SD): 6 month ss= 9.9 (2.5); 12 months ss= 10.5 (1.9); 24 months ss= 10.8 (2.6)). At all 3 timepoints, expressive language and gross motor scales were lower than the population mean (p ≤ .001), but with mean scores still in the average range. Similarly, the receptive language scale was lower at the 6 and 12 month timepoints (p ≤ .001), and the fine motor scale was lower at 12 months (p < .05), but mean scaled scores were in the average range. Across the entire cohort, gross motor skills were lower than fine motor skills at 6 and 12 months (p ≤ .001), and a trend was seen at 24 months (p = .10). Expressive language was lower than receptive language at 6 and 24 months (p < .05). Secondary analyses with 23 children with data at all timepoints showed that receptive language was lower at the 12 month assessment compared to the 6 and 24 month assessment (p < .05). Scaled scores were stable across timepoints for all other Bayley-3 scales.

In comparison, on the Vineland-3, all 4 sub-domain composite standard scores and the adaptive behavior composite standard score were significantly lower than the population mean at the 6, 12 and 24 month timepoints (all p-values < .01), with the exception of the Daily Living Skills sub-domain at 12-months which was at the population mean. Within-sample comparisons of sub-domains at 6 months showed that communication was significantly lower than the other 3 sub-domains (p < .01). At 12 months, the communication and motor sub-domains were lower than daily living skills (p < .001) and communication was lower than social skills (p ≤ .001). Finally, at 24 months, there were no statistical differences across sub-domains. Specific analyses looking at differences within the communication and motor sub-domains were conducted. At 6 and 12 months, receptive language skills were significantly lower than expressive language skills (p < .05). At 24 months, the opposite pattern was observed with expressive being lower than receptive (p ≤ .001). At 6 and 12 months, gross motor was significantly lower than fine motor (p ≤ .001), but at 24 months, there was no significant difference. Secondary analyses were conducted with 26 children who have data at all 3 timepoints. In this longitudinal sub-sample, communication skills were significantly lower at 6 months than at 12 and 24 months (p < .05), with no difference seen between 12 and 24 months. The social and motor sub-domains, as well as the adaptive behavior composite, were stable across time.

**Discussion:** This is the largest prenatally-identified SCT cohort that has been studied from infancy, and initial results from this ongoing study demonstrate interesting neurodevelopmental profiles. While cognitive skills remain stable throughout early development, scores on language and gross motor scales using both direct assessment and parent-report are statistically lower compared to the population mean, although overall mean scores still fall within the average range. Similarly, on parent-report using the Vineland-3, statistical differences from the population mean are noted in all sub-domains; however, overall mean

scores remain in the average range across all timepoints.  Results show relative weaknesses in communication and motor skills. Specifically, children scored lower on receptive language than on expressive language through 12 months of age, but at 24 months, the opposite was true. This switch is consistent with findings that show that these children have speech sound disorder and expressive language deficits as they get older (St John, et al., 2019). Finally, in looking at the 26 children with data at all 3 timepoints, children's communication skills lag at 6 months of age, but improve over time. Next steps include analysis of the role of early interventions, medical history, and other factors such as early hormone levels in developmental trajectories and outcomes.

**References:**

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