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Bridging the Gap: Access to Genetic Testing in a Community Sample of Individuals with Autism Spectrum Disorder



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Bridging the Gap: Access to Genetic Testing in a Community Sample of Individuals with Autism Spectrum Disorder



ELS FOR AUTISM

Icahn School of Medicine at Mount Sinai

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BACKGROUND

- While the American College of Medical Genetics recommends genetic testing for individuals with autism spectrum disorder (ASD), access to testing and physician referrals remain limited.
- Testing for Fragile X syndrome and high-resolution chromosomal microarray are the first-tier genetic tests for individuals with ASD (Schaefer & Mendelsohn, 2013); however, the extent to which they are pursued varies widely.
- In April 2018, the Seaver Autism Center for Research and Treatment in New York, NY partnered with the Els for Autism Foundation in Jupiter, FL in order to integrate research into a community setting, where the majority of individuals with ASD are served.
- The Seaver Autism Center is a medical-center based autism research center that carries out comprehensive genetic and clinical evaluations for several hundred individuals each year.
- Els for Autism Foundation is a nonprofit organization established in 2009 by world-class pro golfer Ernie Els and his wife Liezl. The foundation's 26-acre campus is comprised of two public charter schools and offers recreational, therapeutic, and adult services for several hundred individuals with ASD per year.
- The joint institute, The Seaver Els Institute, provides genetic testing, facilitated by the research group, to individuals within the school and the broader community.

Objective: To characterize and assess the access and barriers to receiving the recommended genetic testing in a community sample of individuals with ASD.

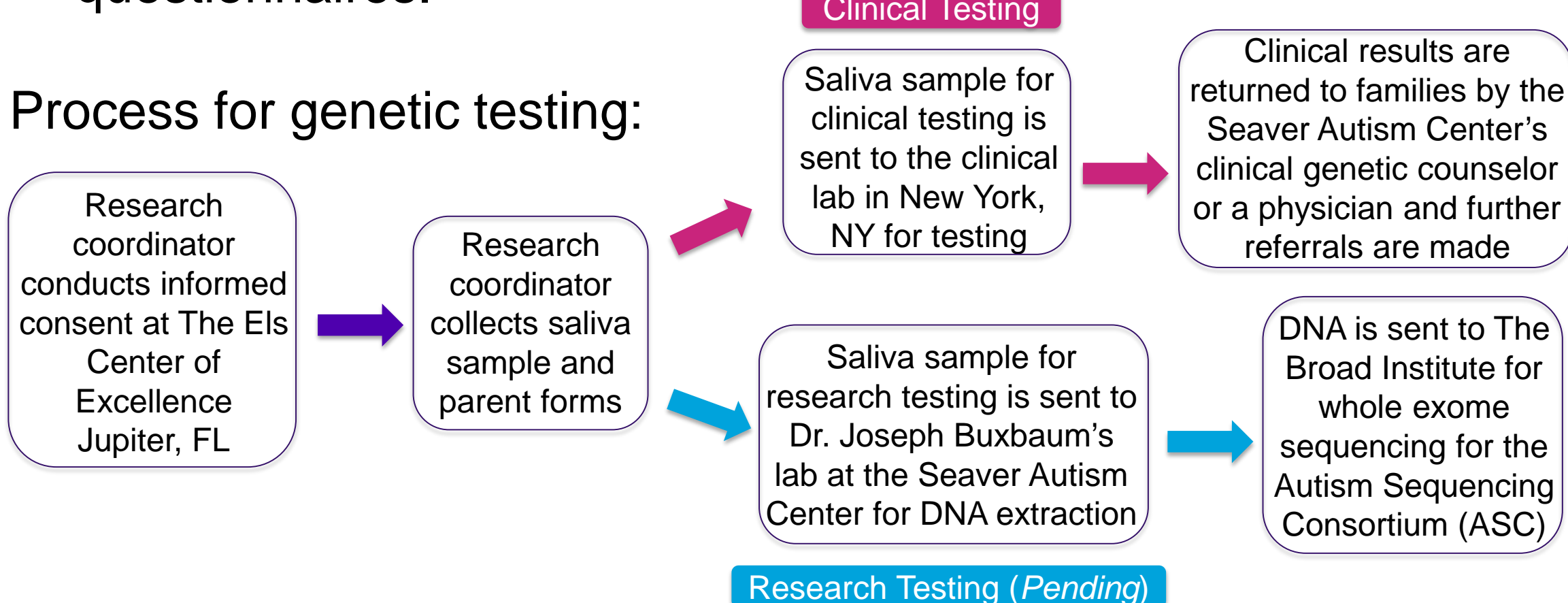
METHODS

Participants:

- Between August 2018 and April 2019, 31 individuals were enrolled. The 31 individuals (22.58% female) ranged in age from 2 to 23 years and all carried Individualized Education Plan (IEP) classifications of ASD and/or a documented diagnosis from medical records.

	Age (years)	Sex
ASD	M = 10.9; SD = 5.5	24 M; 7 F

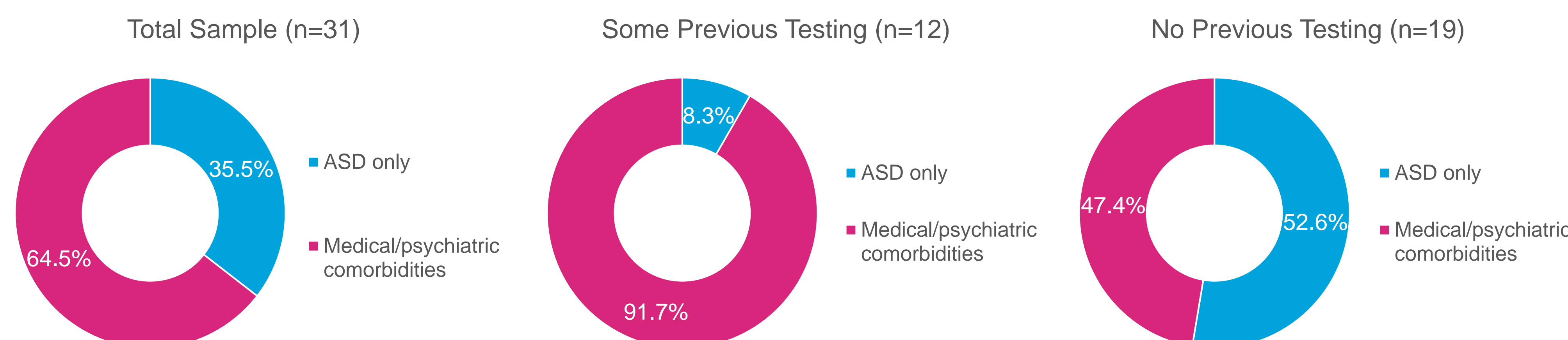
- Results from previous genetic testing were obtained, and testing was ordered for those who had not had recommended testing.
- Saliva samples were collected at the Jupiter, FL center, and DNA extraction and testing was facilitated by the research institute.
- Phenotype data were collected through parent report including demographic, social communication, and adaptive behavior questionnaires.



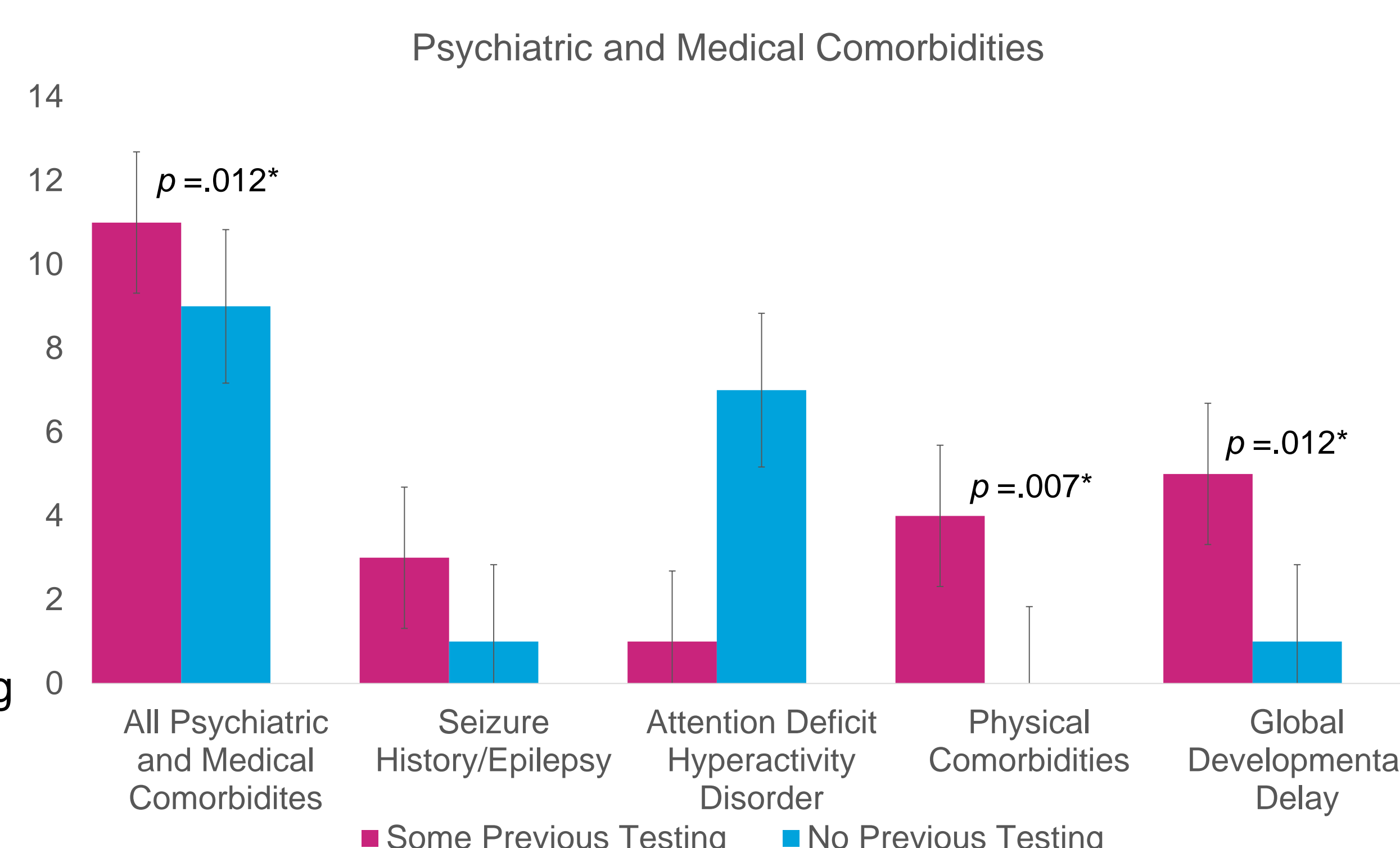
RESULTS

Medical and Psychiatric Comorbidities:

- 20 of 31 individuals in the sample (64.5%) had medical or psychiatric comorbid diagnoses.
- Physical medical comorbidities included: congenital anomalies (perforated bowel, tethered spinal chord, eye movement disorder, gonadal dysgenesis), and chronic diseases (eosinophilic esophagitis).
- Psychiatric/neurological comorbid diagnoses included: global developmental delay (GDD), seizure activity/epilepsy, attention deficit hyperactivity disorder (ADHD), and encephalopathy.
- Of the 12 individuals who had some previous genetic testing (Fragile X, chromosomal microarray, karyotype, or whole exome sequencing), 11 of them (91.7%) had an additional medical or psychiatric comorbidity. 47.4% of the group with no previous testing had additional comorbid diagnoses.



- Analysis revealed that having a medical or psychiatric comorbid diagnosis had a statistically significant effect on likelihood of having previous testing: $\chi^2 = 6.30, p = .012$.
- Having a physical comorbid diagnosis also had a significant effect: $\chi^2 = 7.27, p = .007$, as did having GDD: $\chi^2 = 6.244, p = .012$.
- Individuals with ADHD were marginally less likely to have had previous testing: $\chi^2 = 3.122, p = .077$



Sibling with ASD

- No statistically significant relation was found between having a sibling with ASD and having had previous genetic testing: $\chi^2 = 0.07, p = .80$.

Communication Scores

- Individuals without phrase speech (answered 'no' to *Social Communication Questionnaire* (SCQ), item 1: 'Is she/he now able to talk using short phrases or sentences?') were marginally more likely to have had previous genetic testing: $\chi^2 = 3.16, p = .075$.
- The *Vineland-III* communication scores did not differ significantly between those who had previous testing and those who did not: $t(21) = 1.06, p = .30$.

Parental Highest Level of Education Achieved:

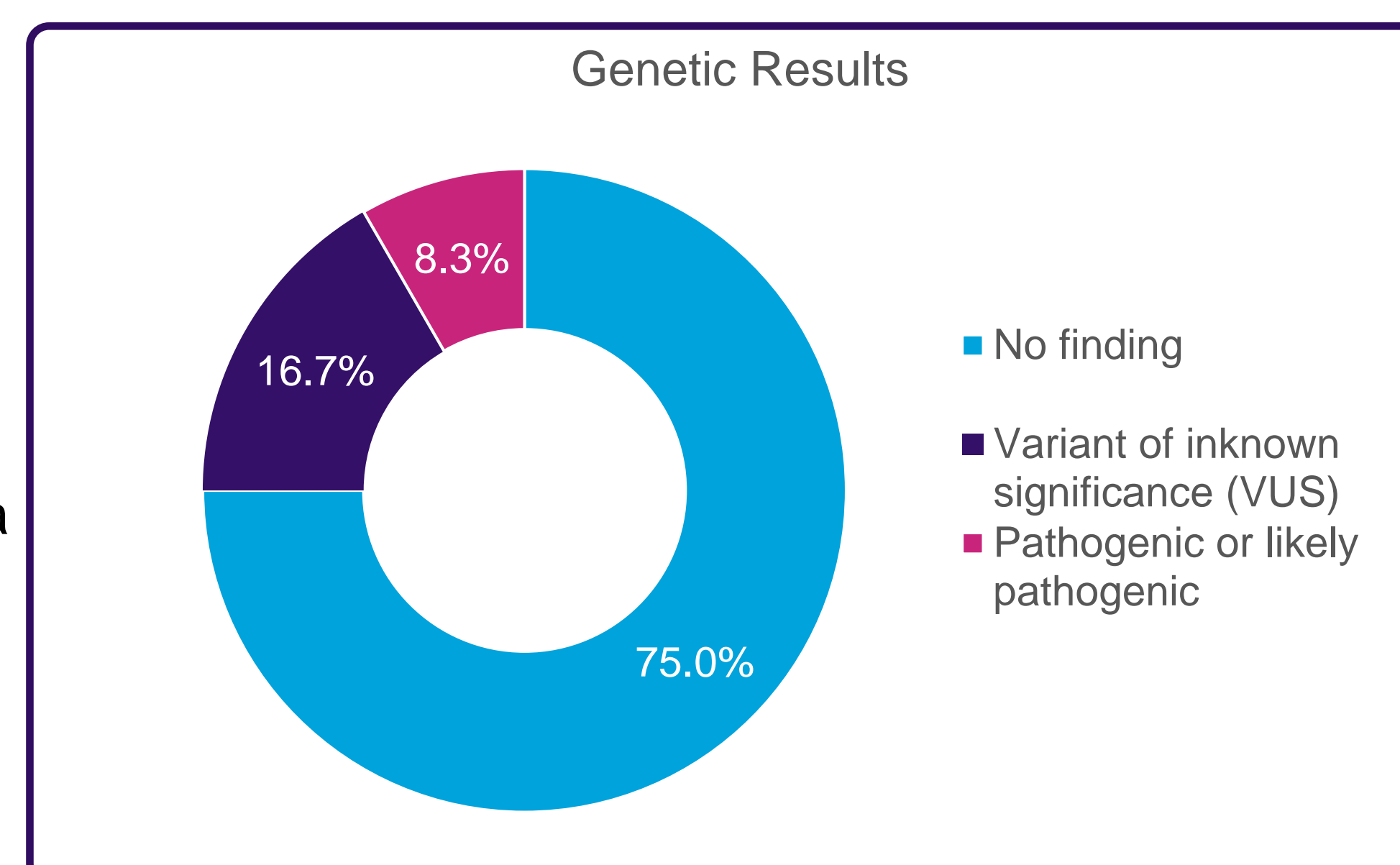
- Level of maternal education had no significant relation to having had previous genetic testing: $\chi^2 = 2.38, p = .50$.
- Level of paternal education also had no significant relation to having had previous genetic testing: $\chi^2 = 0.28, p = .96$.

Age at Diagnosis

- Age at diagnosis did not significantly differ between those who had previous testing and those who did not have previous testing: $t(29) = .08, p = .94$.

Genetic Results

- Previous literature indicates that chromosomal microarray testing (CMA) has a diagnostic yield of 10% in the genetic evaluation of individuals with ASD, and Fragile X testing has a diagnostic yield of 1-5% (Schaefer & Mendelsohn, 2013).
- Genetic testing was completed for 24 individuals (results remain pending for 7), where 8.3% of individuals had a pathogenic or likely pathogenic finding resulted from the chromosomal microarray.



CONCLUSIONS

- Preliminary results suggest that genetic testing and referrals in the community remain limited.
- Our results suggest that additional medical and psychiatric comorbidities may significantly influence physician referrals for genetic testing and/or willingness to undergo testing.
- Comorbid diagnoses of GDD and medical problems, such as congenital anomalies, significantly increased likelihood of having had previous genetic testing, whereas having an ADHD diagnosis (a psychiatric condition) seemed to decrease likelihood of having previous testing.
- These findings further emphasize the need for physicians to provide genetic testing referrals to children with ASD, regardless of the presence or absence of additional medical or psychiatric conditions.
- Having a sibling with ASD, age at diagnosis, and parental level of education achieved all had no significant impact on the proband with ASD had had previous genetic testing.
- In our sample, *Vineland-III* communication scores did not significantly differ between those who had testing and those who did not, but those who did not have phrase speech were marginally more likely to have had previous genetic testing.
- Our preliminary genetic results reinforce previous findings that chromosomal microarray testing (CMA) has a diagnostic yield approaching 10% in individuals with ASD (8.3% in our sample). This finding emphasizes the importance of genetic testing for ASD individuals of all ages and phenotypic presentations.

Future Directions:

- Research whole exome sequencing (WES) is pending for participants, and enrolled participants are actively being consented for second-tier clinical testing, which includes a comprehensive neurodevelopmental panel of over 400 genes thought to be related to autism and epilepsy.
- Recruitment and enrollment is ongoing. As our sample increases it will be important to investigate additional phenotypic variables influencing referrals including IQ, receptive and expressive language, and adaptive behavior.
- As our sample increases, demographic factors such as parental educational achievement and income should also be analyzed to identify additional barriers to genetic testing in community settings where the majority of individuals with ASD are served.

REFERENCES

Schaefer, G.B., Mendelsohn, N.J.; for the Professional Practice and Guidelines Committee (2013). Clinical genetics evaluation in identifying the etiology of autism spectrum disorders: 2013 guideline revisions. *Genetics in Medicine* 15, 399-407. doi:10.1038/gim.2013.32.

