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# Family History of Autism Spectrum Disorder in the Preconception/Prenatal Genetic Counseling Session

Denise Cutillo MS, LCGC; Amy Cronister MS, LCGC; Denise Ramsey, Alan Donnenfield MD; Theresa Boomer MS, CG/MB(ASCP), CGC
Integrated Genetics, Laboratory Corporation of America®Holdings

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LabCorp Specialty Testing Group

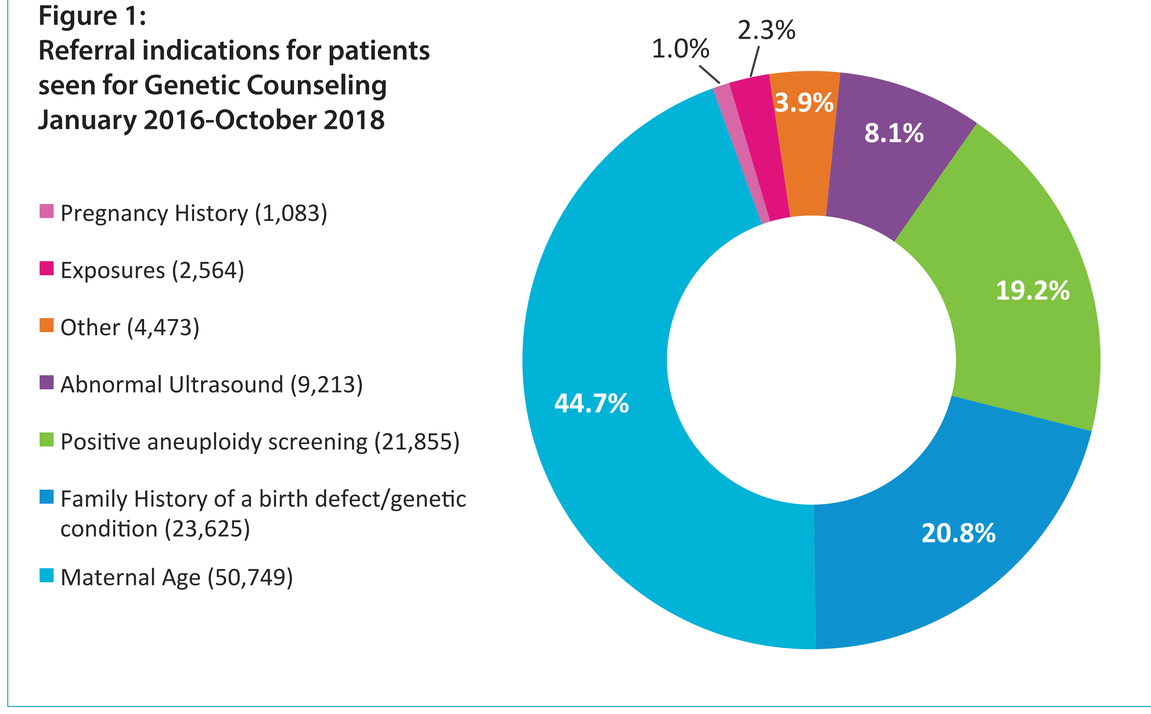
## I. Introduction and Purpose

In April 2018, the Centers for Disease Control and Prevention (CDC) released their latest estimate of the prevalence of autism spectrum disorder (ASD) among children in the United States (US). This number was based on data collected in 2014 and is estimated to be 1 in 59 US children. Previously, based on data collected in 2012, the prevalence of autism in US children was estimated to be 1 in 69. The 2014 data indicated a 15% increase in prevalence. Symptoms of ASD typically exhibit in the first two years of life, and both genetic (copy number and single nucleotide variants have been implicated) and environmental factors contribute to the disorder. Risk factors include a sibling with ASD, advanced paternal age, assisted reproductive technologies, low birthweight and genetic conditions such as Down syndrome, Fragile X syndrome, and Rett syndrome. The purpose of this retrospective study was to evaluate the frequency of reported family histories of ASD in a large reproductive genetic counseling population.

## II. Methods

The study evaluated 102,474 patients seen for preconception/prenatal genetic counseling from January 1, 2016 through October 31, 2018. Referral indications for genetic counseling for this patient population are shown in **Figure 1**:

**Figure 1:**
**Referral indications for patients seen for Genetic Counseling January 2016-October 2018**




The genetic counseling session included family history data collection for each patient/partner and creation of a minimum three generation pedigree. All reports of a family history of ASD were self-reported by the patient and/or partner. Reports of ASD in greater than second degree relatives to the patient and/or partner were excluded from this study. All patients were physician referred for genetic counseling. Geographic distribution includes multiple states across the US regions including the Northeast, Southeast, Midwest and West. Genetic counseling was provided by American Board of Genetic Counseling certified/active candidate genetic counselors with state licensure as required by the individual states. When a family history of ASD was detected during the genetic counseling session, discussion included, as applicable, 1) recurrence risk for ASD, 2) ASD risk factors, and 3) etiology of ASD.

## III. Results

In this time period, a total of 7,020 (6.9%) patients reported a family history of ASD (for the purpose of this study 'patients' reflects a family history identified in the patient and/or partner). **Figure 2** indicates the increasing reported histories of ASD by year: 2016, 2,415 (6.5%) patients reported a family history of ASD, in 2017, the number was 2,453 patients (6.9%) and in 2018 (thru October 31, 2018) 2,152 (7.2%) patients reported a family history of ASD. **Figure 3** demonstrates the increasing trend of reported histories of ASD per year by percentage. The increase in reports of ASD family histories from January 1, 2016 to October 31, 2018 is highly statistically significant with a p value of <0.001.

**Figure 2:**
**Number of patients reporting a family history of autism**

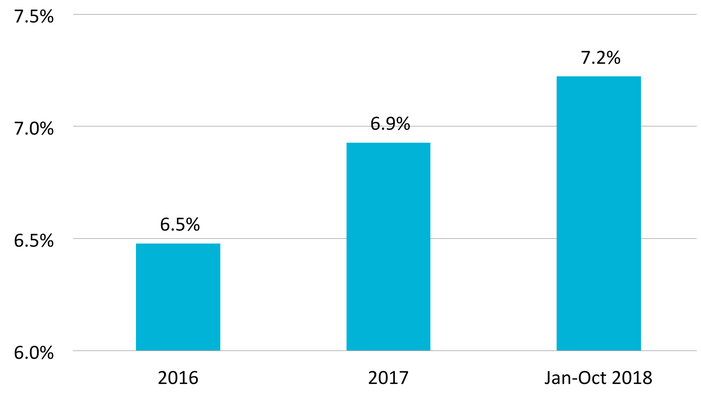
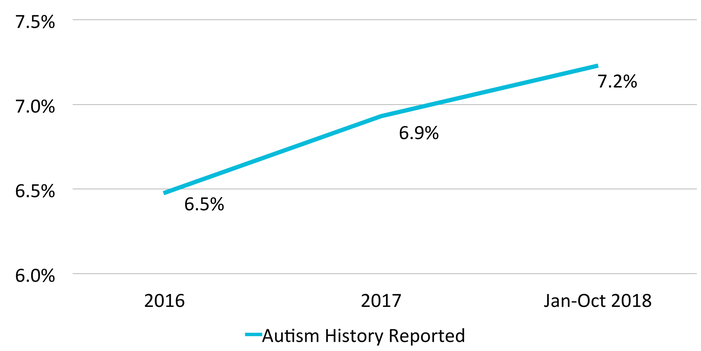



**Figure 3:**
**Autism Spectrum Disorder Reporting Trend**

p value <0.001 (two sided proportional Z test used for analysis)




An interesting additional set of data from the most recent time period studied, January 1, 2018 thru October 31, 2018, revealed in **Table 1** that a family history of ASD was reported in 13.9% of all genetic counseling sessions. This data includes any reported family history of autism, and was not restricted to second degree relatives or greater.

**Table 1: Reported Family Histories in Patients seen for Genetic Counseling January-October 2018 (29,792)**

| Family History | % | Total Reported |
|---|---|---|
| Cystic fibrosis | 4.2% | 1,265 |
| Epilepsy (seizures) | 4.6% | 1,356 |
| Sickle cell anemia | 4.9% | 1,468 |
| Down syndrome | 7.8% | 2,331 |
| Congenital Heart Defect | 9.3% | 2,761 |
| Intellectual Disability | 10.6% | 3,160 |
| Pregnancy loss/multiple miscarriages | 10.7% | 3,202 |
| Autism Spectrum Disorder | 13.9% | 4,131 |
| Infant Death (including stillbirth) | 14.6% | 4,356 |
| Advanced Paternal Age | 17.7% | 5,279 |

## IV. Discussion and Conclusion

Genetic counseling is an important component of healthcare for many patients during the preconception and prenatal time period. This data indicates an increasing trend in reported family histories of ASD identified during the genetic counseling session. With the increasing prevalence of ASD in the US population, it is expected this trend will continue. Patients in this reproductive time period are often focused on understanding a wide spectrum of genetic risk factors personalized to their specific history.

Genetic counselors need to be prepared to discuss the potential genetic causes of ASD, the importance of a clinical genetics evaluation for affected individuals, and to provide a risk assessment for ASD. Even in family histories where a specific recurrence risk for ASD is not possible, patients may have questions about ASD that need to be addressed. The current ACMG Practice Guideline "Clinical genetics evaluation in identifying the etiology of autism spectrum disorders" is a useful resource when managing a family history of ASD. The genetics of ASD is a rapidly evolving area of study and there will be an increasing expectation for genetic counselors to understand the genetic etiologies and genetic testing options.

## IV. References

Prevalence of Autism Spectrum Disorder Among Children Aged 8 years-Autism and Developmental Disabilities Monitoring Network 11 sites, United States 2014. Centers for Disease Control and Prevention, April 27, 2018.

Risk and Protective Environmental Factors associated with ASD: Evidence-Based Principles and Recommendations. Gialloreti, et al. *J Clin Med*, 2019 Feb.

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