Pre- and Post-Test Parent Perceptions of Genetic Testing for Children with Autism Spectrum Disorder (ASD)

Thesis

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By

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Abstract

Many children who are given a diagnosis of autism spectrum disorder (ASD) are offered a chromosomal microarray and often other genetic tests for conditions like Fragile X syndrome, as a routine component of a diagnostic evaluation. However, not every family has the opportunity to meet with a genetic counselor or other genetic provider to discuss the process, benefits and limitations, and the results of genetic testing for ASD. The purpose of this study was: 1) to assess the perceptions and attitudes of parents surrounding the genetic testing process, and 2) to see if these perceptions differed based on the provider that counseled the family. Participants were divided into those who had already completed genetic testing (Group A) and those who had not yet (Group B). Group A was sent one 16-question survey and Group B was sent an 8-question survey before and after testing. Responses in Group A were split into three categories: those who saw a genetic counselor, a non-genetic provider, or an unknown provider. All Group B participants saw a genetic counselor. In Group A, there was a statistically significant difference between the provider groups in participants’ ratings of the quality of the testing explanation, the explanation quality and understanding of results, and overall satisfaction with the process. The Group B data appeared consistent with these findings. However, the themes identified in the short answer survey questions were not exclusive to one provider group. Many participants displayed a limited understanding of the result
interpretation, cited concerns outside of the testing discussion, or indicated the desire for
greater follow-up regardless of which provider counseled them. While these data support
the benefit of involving a genetic counselor, several changes could be made in this clinic
to improve patient satisfaction and understanding of the genetic testing process.
Dedication

This document is dedicated to my family, whose support I could not have gone without.
Acknowledgements

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Fields of Study

Major Field: Genetic Counseling
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Chapter 1: Introduction and Background

**Autism Prevalence, History, and Genetic Causes:**

In recent decades, a greater awareness has been brought to autism spectrum disorder and the signs of this condition are being recognized at a younger age. Recent figures estimate the prevalence of autism spectrum disorders (ASDs) to be approximately 1 in 68 children (Christensen et al, 2016), with almost four times as many cases observed in males than females (Werling, 2016). “Autism spectrum disorders describe individuals with persistent deficits in communication and social interaction, and repetitive, restricted behaviors and/or interests”, with or without some degree of intellectual disability (Carter et al, 2013). It used to be thought that autism was caused by “refrigerator mothers”, or more recently vaccines, but we have now shifted to a recognition that ASD is multifactorial and that genetics is a major contributing factor (Carter et al, 2013; Chahrour et al, 2016). This has been evidenced by various twin and sibling studies (Heil and Schaaf, 2013; Ozonoff et al, 2011), by higher incidence of ASDs in single gene disorders, and by the identification of de novo copy number variations and mutations in autism candidate genes (Bauer and Msall, 2011). Autism can be diagnosed as syndromic, a feature of a condition such as Fragile X or Rett syndrome, or idiopathic, meaning the autism diagnosis is unrelated to an underlying syndrome. At times, making such a distinction in a child can be difficult. Carter and colleagues estimate that 75% of individuals with ASD are thought to be non-syndromic, while 25% have syndromic or
“complex” autism (2013). Attention deficit disorders are common comorbidities for individuals with ASDs, as are other modifiers such as depression, anxiety, and other neuropsychiatric conditions (Lord and Bishop, 2015). Because individuals with ASDs often present with comorbid mental health issues or impaired intellectual function, some in the autism field think of it all as a spectrum of symptoms under the umbrella of “developmental brain dysfunction”, rather than as individual diagnoses (Finucane and Myers, 2016). Other features of non-syndromic autism include: seizure activity, gastrointestinal issues, sleep problems, regression, tantrums, and hypersensitivity to stimuli, among others (Carter et al, 2013). Many of these features can overlap with those of potentially syndromic or complex autism. Other features of syndromic autism include: overgrowth, hypotonia, ataxia, hand or foot abnormalities, dysmorphic facies, and multiple congenital anomalies (Carter et al, 2013). The behavioral hallmarks of ASD can start to become apparent at a young age, often close to eighteen months old (Christensen et al, 2016). While a diagnosis can often be made confidently around two years of age, Christensen and colleagues found “the median age at earliest known comprehensive evaluation [for autism] was 40 months, and 43% of children had received an earliest known comprehensive evaluation by age 36 months” in the United States (2016). In the past, the American Psychiatric Association recognized several subtypes of autism as separate diagnoses rather than one disorder with a broad range of phenotypes. The most recent version of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) released in 2013 did away with these subtypes such as Asperger’s syndrome, autistic disorder, and PDD-NOS (Lord and Bishop, 2015). These subtypes were consolidated into
what is now recognized as autism spectrum disorder. This is due in part to the fact that these separate diagnoses were found to be given with great inconsistency across providers, which did little more than to provide “a general index of severity” (Lord and Bishop, 2015). In fact, the practice in which a provider worked had a greater influence on the type of autism diagnosis given than any particular clinical feature of the child, due to each clinic’s individual method of differentiating subtypes.

A great deal has been discovered, and is continuing to be revealed daily, regarding genetic contributors and causes of autism spectrum disorders. While no genetic variants have been found in association with autism alone, hundreds of genes and copy number variants (CNVs) have been implicated in the pathogenesis of autism and other neurodevelopmental and neuropsychiatric conditions (Carter et al, 2013). In many cases, it is likely that another genetic aberration yet to be identified is contributing to a phenotype, especially a more severe phenotype, along with a known CNV identified in an individual (Wolf et al, 2013). “The genetic architecture of ASD at a population level is so complex that risk is most likely conferred by rare mutations and common variants at hundreds of independent loci” (Chahrour et al, 2016). Ji and colleagues postulate that there is a higher frequency of pathogenic variants in essential genes (genes that are imperative for development and survival of an individual, specifically in brain development) in probands with ASD (2016). Additionally, a large number of genes that have been identified in association with autism risk are also essential genes (studied within human orthologues of mouse genes) (Ji et al, 2016). Finally, another important aspect in autism genetics, epigenetics, is just beginning to be more thoroughly
investigated. As we learn more, epigenetics will likely come to occupy a larger role in understanding autism pathogenesis, as it is the link between genetic and environmental factors at play (Hall and Kelley, 2014).

The most common single-gene disorders associated with autism are Fragile-X syndrome, Rett syndrome, Tuberous Sclerosis Complex, and PTEN mutations, consisting of about 5% of cases (Carter et al, 2013). Collectively, CNVs make up a much greater number of ASD cases. The most common copy number variations found on microarray include the chromosome regions 16p11.2, 15q11-13, and 22q11.2, though many more pathogenic and likely pathogenic CNVs have been identified (AlSagob et al, 2015; Carter et al, 2013). Duplications in 15q11-13 and deletions and duplications in 16p11.2 account for approximately one percent each of all cases of autism (Carter et al, 2013; Heil and Schaaf, 2013). These common CNVs show considerable phenotypic variability as well as reduced penetrance, and are frequently inherited from a parent that exhibits no symptoms (AlSagob et al, 2015; Heil and Schaaf, 2013). Logically, larger CNVs contain a greater number of genes that have been deleted or duplicated and therefore are likely to cause more significant symptoms (Heil and Schaaf, 2013). These susceptibility loci are challenging to counsel because of the difficulty in predicting phenotype for future children or other family members (Wolf et al, 2013). Outside of genetic factors contributing to an autism diagnosis, epilepsy, significantly low birth weight, significant prematurity, or other conditions could put one at an increased risk to develop autism as well (Lord and Bishop, 2015).
Despite changes to how medical professionals view autism, and broader knowledge of genetic etiologies, there has been no clear explanation for the sex disparity in diagnoses of ASD. It could be that affected females are being underdiagnosed, or that ASD diagnostic criteria are biased toward affected males. It could be that females are better able to “camouflage” their symptoms of autism, or that females are less susceptible to X chromosome mutations and copy number variants (Werling, 2016). This conundrum only stands true for apparently non-syndromic cases of autism however. For cases of ASD that have been attributed to a specific syndrome, such as PTEN-related disorders, the sex disparity does not exist; the male to female ratio is one to one (Bauer and Msall, 2011).

With respect to recurrence risk for families with a child with ASD, providers can often only offer estimates based on previous research, family history, and suspected multifactorial inheritance. Recent studies suggest the heritability of autism spectrum disorders to be between 37-67%, lower than previous estimates (Hall and Kelley, 2014). A 2014 Swedish study estimated that “for an individual, the risk of autism is increased tenfold if a full sibling has the diagnosis [ASD or autistic disorder] and about twofold if a cousin has the diagnosis” (Sandin et al, 2014). For those parents that have at least one child with apparently non-syndromic ASD, data gathered in Ozonoff and colleagues’ prospective study suggest their chance to have another child with ASD is approximately 19% (2011). If a couple has two or more children with non-syndromic ASD, recurrence risk increases to estimates between 32-36% (Ozonoff et al, 2011; Finucane and Myers, 2016). Based on Ozonoff and colleagues’ study, the sex of an older sibling with ASD did
not significantly increase or decrease the risk of a younger sibling to receive an autism diagnosis (2011). This provides evidence against the multifactorial threshold model, which suggests that the recurrence risk would be higher for families whose first child diagnosed with ASD is female (Ozonoff et al, 2011). For those families that opt for genetic testing and are able to identify a single gene cause for autism, a clearer risk estimate can be given based on the pattern of inheritance of that disorder. However, as alluded to earlier, risk estimates for developing autism and associated features for families with identified CNVs is not always as straightforward.

**Genetic Testing, Indications, and Diagnostic Yield:**

Before chromosomal microarrays (CMAs) became routinely used, the recommendation for genetic testing for autism was often a G-banded karyotype along with Fragile X testing (Bauer and Msall, 2011; McGrew et al., 2012). However, a karyotype is only able to identify visible chromosome deletions, duplications, or rearrangements with an approximately 2-5% yield (Carter et al, 2013). Within the last decade, the American College of Medical Genetics and Genomics (ACMG) as well as the International Standard Cytogenomic Array Consortium revised their guidelines to recommend chromosomal microarray as the first-tier test for autism over a karyotype (McGrew et al, 2012; Shea et al, 2014). Microarrays can not only identify the same chromosomal aberrations as a karyotype (aside from balanced rearrangements), but they also allow for the detection of smaller-scale copy number variations (CNVs). As a result, diagnostic yield for autism genetic testing is significantly higher. Despite these improvements, however, some studies report the diagnostic yield of microarrays to be
below 20%, meaning no clear genetic cause for autism is identified in the majority of cases (Tammimies et al., 2015; Carter et al., 2013). In one cohort of 68 patients in Hong Kong who had microarrays, researchers found an approximately 22% detection rate for CNVs overall, and a diagnostic yield of approximately 12%, for those CNVs that were identified to be clinically significant (Siu et al, 2016). Those children who are more severely affected, or who exhibit dysmorphic features or other symptoms suggesting complex ASD, are more likely to receive a genetic diagnosis (Bauer and Msall, 2011; Tammimies et al, 2015). In the study conducted by Tammimies and colleagues, the diagnostic yield for CMA for those children in the “complex” ASD category was almost 25%, while those in the “essential” or idiopathic ASD group had a diagnostic yield of 4% with the same test (2015). This suggests that determining the category into which a child with autism is expected to fall (essential, equivocal, or complex) may help determine who is most appropriate to test, as the diagnostic yield for those with apparently idiopathic autism, especially without intellectual disability, may be quite low. However, because so many children go through a diagnostic assessment at an age too young to accurately assess cognitive functioning, ACMG guidelines still recommend genetic testing for any child with ASD (Schaefer et al, 2013). For young boys on the autism spectrum (and girls for whom there is a suspicion of the disorder), testing for Fragile X syndrome is recommended. Testing for MECP2 mutations in children with autism and global developmental delay (particularly in females), and testing for PTEN mutations in those with macrocephaly are also recommended as second-tier tests (Carter et al, 2013; Schaefer et al, 2013).
Genetic Counseling and Access to Services:

Now that genetic testing has become much more common for children with autism, many different types of medical providers are now ordering these tests. As a result, referrals to genetics providers are coming in from a variety of specialties and at various stages in the diagnostic process (Finucane and Myers, 2016). However, many parents are never referred or do not have access to a geneticist or genetic counselor.

Several survey- and interview-based studies of parents of children with ASD consistently demonstrated that approximately 20% saw a genetic specialist, while the vast majority did not (Cuccaro et al., 2014; Vande Wydeven et al., 2012). This significant underutilization of genetic specialists for families with autism spectrum disorder exists largely because of a general lack of awareness or understanding of such services on behalf of the parents and their children’s providers (Vande Wydeven et al., 2012).

Another reason for the small number of families referred to genetics for genetic testing could be that other non-genetic providers are ordering and interpreting these tests (Cuccaro et al., 2014; Vande Wydeven et al., 2012). Not surprisingly, those that were not referred to genetics were generally less likely to be offered genetic testing (Cuccaro et al., 2014). Additionally, the level of a child’s functioning on the autism spectrum affected whether or not families were offered genetic consultation or testing. In one study, those children that were lower functioning were much more likely to be referred to genetics, while those that were higher functioning were much less likely to have seen genetics and undergone genetic testing (Cuccaro et al, 2014). In a study conducted by Li and colleagues, most of the parents interviewed reported that their provider gave them no
information regarding genetic testing for their child with autism (though most were interested), and those that did get information about genetic testing, from their provider or elsewhere, did not feel the information was sufficient (2016). Chen and colleagues’ study revealed that a majority of parents whose child never had genetic testing stated that they were unaware that the option of genetic testing existed (2016). This was particularly true for participants with a lower level of education (high school diploma or lower) or a lower economic status (a household income below $35,000 a year). Those that had heard of it did not receive the information from a medical provider, but rather from media outlets or articles (Chen et al., 2013). Families of children with ASD who are able to secure a genetics referral and/or undergo genetic testing almost certainly benefit from more specialized knowledge about autism genetics. In interviews with several autism professionals from Belgium, one stated there could be usefulness in having any ASD family see a genetic professional to learn about the genetics of autism and limits in knowledge, even if they believed not every one of them should receive genetic testing (Hens et al., 2016). However, genetic specialists are in relatively short supply, and many non-genetic providers that are helping to address the demand for testing may lack the appropriate training and knowledge to be able to accurately explain and interpret genetic testing for autism (Li et al., 2016).

Genetic counselors are particularly well suited to address this need for more specialized assessment. “Genetic counselors can play a pivotal role in helping families by providing accurate, up-to-date information regarding ASDs…providing an accurate recurrence risk estimate for parents and their children, and identifying a cause, when
possible” (Selkirk et al., 2009). The fact remains, however, that many families still lack knowledge of or access to these services. Therefore, Li and colleagues argue it is important to appropriately educate non-genetic professionals on how to discuss the options of genetic testing for their autism families (2016). Beyond discussions with providers regarding autism genetic testing and genetic diagnoses, specialized knowledge is also important for identifying patient-friendly resources outside of clinic. While much is known and many resources are available for several single gene causes of autism such as Fragile X syndrome, that is not necessarily the case for many of the CNVs or mutations in known autism risk genes now routinely identified on microarray and other genetic tests (Finucane and Myers, 2016). In general, genetic counselors could have a vital role in training non-genetic providers in the ordering, interpretation, and discussion surrounding autism genetic testing.

**Parent and Professional Perceptions:**

Multiple studies have been done to assess the perceptions of both parents and medical professionals regarding the genetic testing process as well as suspected etiology or other aspects of ASDs. Across several studies, most parents reported that they wanted to know about potential genetic contributors for their child with autism and reported positive attitudes toward genetic testing (Cucaro et al, 2014; Chen et al, 2013; Reiff et al, 2015; Xu et al, 2016). In a study about concordance in beliefs about autism conducted by Fischbach and colleagues, parents and scientists largely agreed about wanting to know if a genetic contributor to their child’s autism had been found (2015). Parents generally had similar ideas across studies regarding what they believed was the cause of ASD. In
Cuccaro and colleagues’ study, about half of participants thought their child’s autism was mainly caused by “genetic influences” while almost one third believed the main cause was vaccines (2014). In Fischbach and colleagues’ study, a similar proportion of parents named genetics as the main contributor to ASDs, while 13% believed vaccines were to blame (2015). Several studies consistently show that many parents greatly overestimate their recurrence risk, which has an effect on family planning for some (Chen et al., 2013; Selkirk et al, 2009). In Selkirk and colleagues’ research, over two-thirds of participants with one child with autism believed their recurrence risk to be 25% or more (2009).

Despite the opinions that some parents had already formed, many of those in favor of genetic testing wanted to know the cause of their child’s autism and wanted the information for family planning and informing other members of the family. Parents also cited that genetic testing may be useful in obtaining early medical interventions and services, contribution to research, and potential treatments for autism (Chen et al, 2013; Reiff et al, 2015; Xu et al, 2016).

As with any potentially controversial subject, both parents and providers in several studies identified concerns with genetic testing for autism. Xu and colleagues states “CMA is controversial due to possible ambiguous test findings, uncertain clinical implications, and other social and legal issues related to the test” (2016). More specifically, these issues could include fear of genetic discrimination, loss of confidentiality, or psychological distress caused by potential uncertainty (Xu et al, 2016). For some families, these concerns were significant enough to discourage them from moving forward with testing. Several autism providers thought genetic counseling and
testing had the potential to either relieve or create parental guilt and family conflict, depending on whether or not inheritance can be proven or if blame had been placed on certain family members (Hens et al, 2016). This was found to be the case for some parents surveyed by Reiff and colleagues who underwent genetic testing, though this study did not quantify these responses (2015). Some parents did not investigate a genetics evaluation due to concerns about cost, while some did not anticipate any benefit to their child’s management or in their family planning (Chen et al, 2013; Vande Wydeven et al, 2012). Others worried about discomfort or other risks from the testing, such as the pain or emotional ordeal of a blood draw, as well as apprehension about the results (Xu et al, 2016).

Of those that completed genetic testing in the aforementioned studies, mixed feelings were noted. “Among parents who had taken their children for ASD genetic testing, some had negative experiences and low confidence in their providers’ ability to interpret test results” (Chen et al, 2013). For many of the families in these studies (approximately 80%), genetic testing was offered to them and interpreted by non-genetic providers such as pediatricians. However, in Reiff and colleagues’ research, in which all participants completed genetic testing, 60% of parents surveyed said that their child’s microarray test results were helpful to some degree, and many still found value in the testing even if it didn’t change management or care (Reiff et al, 2015).

Purpose and Hypotheses:

The purpose of this study was to assess the perceptions and attitudes of parents surrounding the procedure and results of genetic testing (specifically a chromosomal
microarray) for their child with an autism spectrum disorder diagnosis before and after the test is conducted. Additionally, this study aimed to see how those perceptions are influenced by the medical professional who explained and ordered the testing (a genetic counselor versus a non-genetic provider). We hypothesized that parents who did not meet with a genetic counselor would not fully recognize the limitations of the testing and will expect a higher likelihood of finding something definitive to explain their child’s autism, which would subsequently lead to more feelings of frustration and dissatisfaction with the testing process. We also hypothesized that those parents who met with a genetic counselor through the testing process will have a better understanding and higher satisfaction with the explanations given about the testing and the results than those families who met with a non-genetics specialist. If we are able to show that parents’ understanding of their child’s genetic testing is better in those that met with a genetic counselor, it would illustrate the importance of genetic counselors and may lend more support to increasing the availability and utilization of genetics services for ASD families as part of the initial diagnostic process.
Chapter 2: Methods

The Ohio State University Institutional Review Board ceded authority to the Nationwide Children’s Hospital Institutional Review Board which approved this study (Study #: IRB16-00407). We identified and surveyed two cohorts of parents that had at least one child with an autism spectrum disorder diagnosis and for whom genetic testing was recommended through the Child Development Center/Autism Center at Nationwide Children’s Hospital (CDC/Autism Center).

**Group A Participants and Survey:**

The retrospective cohort, Group A, consisted of parents whose child had undergone genetic testing (specifically a chromosomal microarray, with or without additional testing) between January 1, 2015 and August 31, 2016. These families were identified through a medical record review of families who saw medical providers at the CDC/Autism Center and had genetic testing within the aforementioned timeframe. Those families that were non-English speaking, not seen at the CDC/Autism Center, or whose child did not receive an official autism diagnosis were excluded from the study. Additionally, those who were found to have a likely pathogenic/pathogenic microarray finding, Fragile X, or PTEN mutation and/or were seen by a geneticist in the Genetics clinic at Nationwide Children’s Hospital were excluded from the study. This is because we expected that these families would have received more detailed counseling surrounding their genetic test results and would therefore not have a comparable
experience to those with negative or uncertain results that did not have more extensive counseling. These families chosen from the medical record review represented an even mix of those who met with a genetic counselor to discuss genetic testing for the autism diagnosis, and those who received counseling for genetic testing from a different provider at the CDC/Autism Center. The non-genetic providers were developmental behavioral pediatricians, nurse practitioners, and neurologists.

The families eligible to participate in Group A were mailed an anonymous survey comprised of sixteen questions. Participants were also provided with a link to complete the survey online, if they chose to do so. Four of the questions were multiple choice, and they were meant to determine basic demographic information (gender, age, race, income, and education) and the reason participants pursued testing. They also assessed the type of result that participants expected before testing was completed, as well as what they recalled their actual result to be post-testing. Seven of the questions were Likert scale, with 1 indicating poorest understanding or satisfaction, and 5 indicating best understanding or satisfaction. These questions assessed the participants’ perceived quality of the explanation of the testing process and results, as well as their understanding of the testing and results. They also gauged participants’ perceived likelihood of getting the result that they expected, and how well their expected result matched with their actual one. The last Likert scale question asked the respondents to rate their overall satisfaction with the testing process. Finally, five of the questions were short answer. The first asked for the age of the child at which he or she was tested, and the second asked which provider counseled the family about genetic testing. The other short answer questions
asked respondents to explain their test result in their own words, explain their overall satisfaction rating, and indicate what they wish they had known prior to testing. For the purposes of data analysis, those that participated in Group A were further differentiated into three groups: those that indicated they received counseling about genetic testing from a genetic counselor, a non-genetic specialist, or an unknown provider.

**Group B Participants and Surveys:**

The prospective cohort, Group B, consisted of parents who had not yet undergone genetic testing for their child’s autism diagnosis and who were meeting with a genetic counselor to begin the genetic testing process. These participants were consented in the CDC/Autism Center after receiving genetic counseling and agreeing to genetic testing for their child. Participants consented for Group B were asked to complete one eight-question survey before their child had blood drawn or saliva collected for genetic testing, and one eight-question survey after they had been informed about the results of the testing. The first survey included three multiple choice questions, which assessed the same demographic information, reason for testing, and expected result as the Group A survey. Three of the questions were Likert scale (scaled 1 to 5, with 1 indicating poorest understanding or satisfaction, and 5 indicating best understanding or satisfaction) that asked participants to rate the quality of the testing explanation, their understanding of the testing, and their perceived likelihood to get their expected result. Lastly, there were two short answer questions; one asked for the child’s age and the other asked for the participant’s biggest concern regarding the genetic testing. The second survey involved one multiple choice question about the type of result that the family received. Four of the
questions were Likert scale (1 to 5), and they addressed the participants’ perceived quality of the results explanation, understanding of the result, consistency between their expected and their actual result, and overall satisfaction with the testing process. Finally the post-test survey had three short answer questions. These questions asked respondents to describe their result in their own words, and to indicate what they wish they had known prior to testing and what would have made the testing process better for them. Participants were given the choice of completing each survey either on paper or online. Each family was provided a paper copy of the pre-test survey and the electronic survey link immediately following consent to the study. Once the first survey was returned and the family was notified about the child’s genetic test results, the paper version of the post-test survey and electronic link to the online version was mailed to the family. In order to link the pre- and post-test surveys and make the responses anonymous during data analysis, each family in Group B was assigned a study ID number to put on each survey. If a survey was not returned within two weeks of being given or sent to the family, a reminder letter was sent. For those that had already received one reminder for the post-test survey but had still not completed the survey, one final reminder with another copy of the survey was mailed two weeks later. Pre-test surveys that were returned were analyzed and incorporated into the final results regardless of whether or not the second post-test survey was completed.

**Data Analysis:**

For data analysis of the surveys, various themes were identified and described in each short answer question, such as variants of uncertain significance or negative results.
received, or feeling frustrated about aspects of the testing process. Examples of each theme were highlighted and were related to the demographic information provided and the type of provider seen. The answers to the multiple choice survey questions for Group A addressing the explanation and understanding of the testing process and results, as well as overall satisfaction, were compiled and significance was determined using Fisher’s exact test. The threshold for determining statistical significance was set at a value of p=0.05. The data gathered from the multiple choice questions was compiled and used to further describe both groups in the study.

The two Likert scale questions assessing the likelihood of receiving the expected result and the comparison of their expectation to the actual result were thrown out and not analyzed for either cohort. This is because most participants indicated that they did not know what to expect for a result or had no expectation, and were therefore unable to answer these two Likert scale questions.
Chapter 3: Results

**Group A Quantitative Findings:**

For Group A, a total of 301 potential participants were identified during the initial medical record review. However, 29 families identified did not have a current mailing address listed in Nationwide Children’s Hospital’s electronic medical records system or had the address of a Child & Family Services agency or courthouse listed as the mailing address. A total of 272 families were deemed eligible and mailed a copy of the Group A survey. Twelve surveys were returned as undeliverable. In this cohort, a total of 44 surveys were returned (a response rate of 17%). One of these surveys was left mostly incomplete and was returned by a parent who stated her child never completed testing, so it was excluded from the data analysis. The remaining 43 completed surveys were used for data analysis. Of the 43 respondents, 40 (93%) of the respondents were female and 3 (7%) were male. The majority of respondents were white (81%) and were age 30 or older (88.4%). Nearly half of participants had a combined household income of $50,000 or more (48.8%), and 58.1% had an undergraduate degree or higher. Finally, participants were asked how old their child was when he or she underwent testing. The mean age of the children was 6.2 years old; the youngest child tested was 21 months old and the oldest was 16 years old. A complete description of Group A’s demographics is illustrated in Table 1.
<table>
<thead>
<tr>
<th>Group A (n=43)</th>
<th>Number</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>40</td>
<td>93%</td>
</tr>
<tr>
<td>Female</td>
<td>3</td>
<td>7%</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;20</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>20-29</td>
<td>6</td>
<td>13.9%</td>
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<tr>
<td>30-39</td>
<td>23</td>
<td>53.5%</td>
</tr>
<tr>
<td>40-49</td>
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<td>≥50</td>
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<tr>
<td><strong>Race</strong></td>
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<tr>
<td>White</td>
<td>35</td>
<td>81%</td>
</tr>
<tr>
<td>Black/African American</td>
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<tr>
<td>Hispanic/Latino</td>
<td>1</td>
<td>2.3%</td>
</tr>
<tr>
<td>Asian/Pacific Islander</td>
<td>2</td>
<td>4.7%</td>
</tr>
<tr>
<td>Native American/American Indian</td>
<td>1</td>
<td>2.3%</td>
</tr>
<tr>
<td>Other</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td><strong>Household Income</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$25,000</td>
<td>10</td>
<td>23.3%</td>
</tr>
<tr>
<td>$25,000-$34,999</td>
<td>8</td>
<td>18.6%</td>
</tr>
<tr>
<td>$35,000-$49,999</td>
<td>4</td>
<td>9.3%</td>
</tr>
<tr>
<td>$50,000-$74,999</td>
<td>4</td>
<td>9.3%</td>
</tr>
<tr>
<td>$75,000-$99,999</td>
<td>7</td>
<td>16.3%</td>
</tr>
<tr>
<td>$100,000-$149,999</td>
<td>5</td>
<td>11.6%</td>
</tr>
<tr>
<td>≥$150,000</td>
<td>4</td>
<td>9.3%</td>
</tr>
<tr>
<td><strong>Education</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Some high school</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>High school graduate/GED</td>
<td>9</td>
<td>20.9%</td>
</tr>
<tr>
<td>Some college</td>
<td>6</td>
<td>14%</td>
</tr>
<tr>
<td>Associate’s degree</td>
<td>4</td>
<td>9.3%</td>
</tr>
<tr>
<td>Undergraduate degree</td>
<td>17</td>
<td>39.5%</td>
</tr>
<tr>
<td>Master’s degree or higher</td>
<td>7</td>
<td>16.3%</td>
</tr>
</tbody>
</table>

Table 1. Group A responses to demographic questions. *An asterisk indicates that one participant did not provide an answer for the question.

In order to compare understanding and satisfaction with the genetic testing process, participants were asked which provider counseled them about the testing. Their responses were divided into three categories: those who were counseled by a genetic counselor, those who were counseled by a non-genetic provider (developmental
behavioral pediatrician, nurse practitioner, etc.), and those who did not know who provided their counseling. Statistical analysis of the data was done based on these three categories. Of the 43 respondents, 18 (41.9%) reported that they were counseled by a genetic counselor, 15 (34.9%) by a non-genetic provider, 9 (20.9%) were unsure which provider they saw, and one did not answer.

Participants were asked to choose from the following four options for why they decided to pursue genetic testing for their child: 1) it was recommended by a medical provider, 2) I want to know the cause of my child’s autism, 3) I want to know what my chance is to have another child with autism, and 4) other. They were asked to select only one answer. Of those families that met with a genetic counselor, 50% (n=9) said they did testing because it was recommended, 44% (n=8) said they wanted to know the cause of their child’s autism, and 6% (n=1) chose “other”. Of those who saw a non-genetic provider, 67% (n=10) pursued testing because it was recommended, 27% (n=4) said they wanted to know the cause for their child’s autism, and 7% (n=1) said they wanted to better understand their recurrence risk. Finally, of those who were unsure of which provider they saw, 44% (n=4) reported they did testing because it was recommended, 22% (n=2) said they wanted to know the cause of their child’s autism, and 33% (n=3) chose “other”. These data, as well as responses to the other multiple choice questions, are shown in Table 2.
Participants were also asked to choose what kind of result they expected to see before the testing was completed (Table 2). This was asked in an attempt to gauge realistic expectations of the testing. We hypothesized that parents would be more likely to expect a negative result given that during the testing discussion with a genetic counselor, it is explained that there is a 15-20% chance of getting a positive result. Twenty-two percent (n=4) of the genetic counseling group, 7% (n=1) of the non-genetic provider group, and none in the unknown provider group reported that they expected a positive result. Twenty-two percent (n=4) of the genetic counseling group, 13% (n=2) of the non-genetic provider group, and none in the unknown provider group reported that they
expected a negative result. Six percent (n=1) of the genetic counseling group, 7% (n=1) of the non-genetic provider group, and 11% (n=1) in the unknown provider group reported that they expected a variant of uncertain significance. Finally, 50% (n=9) of the genetic counseling group, 73% (n=11) of the non-genetic provider group, and 89% (n=8) in the unknown provider group reported that they had no expectation or did not know what to expect for a result. Given that the majority of respondents indicated no particular expectation regarding results, statistical analysis was not done for this question.

There was a statistically significant difference between the three provider groups and the participants’ rating of how well they felt the testing was explained to them (p=0.015). Those who were counseled by a genetic counselor gave the highest rating of the testing explanation. The genetic counseling group had a mean Likert scale rating of 4.4 out of 5 (SD=0.6) and 16 (89%) of them stated that they understood the explanation very well (a rating of 4) or extremely well (a rating of 5). In contrast, those counseled by a non-genetics provider had a mean rating of 3.6 (SD=1.1) with only 8 (53%) reporting their understanding as a 4 or 5; and those in the third group had a mean rating of 3.1 (SD=1.7) with only 3 (38%) rating their understanding at a 4 or 5. However, there appeared to be no significant difference between the three groups when asked how well they understood the genetic tests that were being ordered and what these tests were looking for (p=0.13). The group that received genetic counseling had an average understanding rating of 4.0 out of 5 (SD=1.0) and 67% (n=12) gave a rating of 4 or 5. Those in the non-genetic counseling group reported a very similar level of understanding, with a mean rating of 3.9 (SD=1.0) and 67% (n=10) giving a rating of 4 or 5. The last
group had the lowest reported level of understanding of the testing, with an average rating of 2.8 (SD=1.6) and 25% (n=2) giving a rating of 4 or 5.

Of the 43 respondents, 30 (69.8%) reported that they received a negative result, 9 (20.9%) reported a variant of uncertain significance, 2 (4.7%) reported a positive result, and 2 (4.7%) did not answer the question (Table 2). Participants were also asked to rate the quality of the explanation they received about their child’s genetic test results and their understanding of the results. The difference between the three groups’ ratings of the results explanation was statistically significant (p=0.011). Those who were resulted by a genetic counselor gave the highest ratings; the average rating was 3.6 (SD=1.4) out of 5 and 11 (61%) gave a rating of 4 or 5. The group that was resulted by a non-genetic provider had a mean rating of 2.9 (SD=1.2) and 6 (40%) gave a rating of 4 or 5, while those resulted by an unknown provider reported the lowest quality of results explanation. This group gave an average rating of 2.0 (SD=1.1) with no one giving a rating of 4 or 5. The difference between the counseling provider and the participants’ level of understanding of their child’s test results also reached statistical significance (p=0.016). Once again, the group that received genetic counseling reported the highest levels of understanding, with a mean rating of 3.8 (SD=1.2) out of 5 and 72% (n=13) giving a rating of 4 or 5. The group resulted by a non-genetic provider had a mean rating of 3.3 (SD=1.4) and 47% (n=7) gave a rating of 4 or 5. The last group had the lowest levels of understanding, with a mean rating of 2.4 (SD=1.5) and 13% (n=1) giving a rating of 4 or 5.
Finally, there was a statistically significant difference between the three groups and the participants’ overall satisfaction with the testing process (p=0.025). Participants who saw a genetic counselor during the testing process had an average satisfaction rating of 3.5 (SD=1.1) out of 5, and 10 (56%) of them gave a rating of 4 or 5 (very satisfied or extremely satisfied). Participants who met with a non-genetics provider had an average rating of 3.3 (SD=1.2) with 7 (47%) giving a rating of 4 or 5, and those who were unsure which provider they saw had an average satisfaction rating of 2.3 (SD=0.9) and none of them gave a rating of 4 or 5. These findings are represented in Table 3.

<table>
<thead>
<tr>
<th></th>
<th>Genetic Counselor (n=18)</th>
<th>Non-Genetic Counselor (n=15)</th>
<th>Unknown Provider (n=9)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Testing Well explained</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td># Giving 4 or 5 Rating</td>
<td>16 (89%)</td>
<td>8 (53%)</td>
<td>3 (38%)</td>
<td>0.015*</td>
</tr>
<tr>
<td>Testing Well Understood</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td># Giving 4 or 5 Rating</td>
<td>16 (89%)</td>
<td>10 (67%)</td>
<td>2 (25%)</td>
<td>0.13</td>
</tr>
<tr>
<td>Result Well Explained</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td># Giving 4 or 5 Rating</td>
<td>11 (61%)</td>
<td>6 (40%)</td>
<td>0 (0%)</td>
<td>0.011*</td>
</tr>
<tr>
<td>Result Well Understood</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td># Giving 4 or 5 Rating</td>
<td>13 (72%)</td>
<td>7 (47%)</td>
<td>1 (13%)</td>
<td>0.016*</td>
</tr>
<tr>
<td>Overall Satisfaction</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td># Giving 4 or 5 Rating</td>
<td>10 (56%)</td>
<td>7 (47%)</td>
<td>0 (0%)</td>
<td>0.025*</td>
</tr>
</tbody>
</table>

Table 3. Group A responses to Likert scale questions. Means of the Likert scale ratings are given with the standard deviation in parentheses. A rating of 4 corresponded to a response of “Very Well” or “Very Satisfied” while a rating of 5 corresponded to a response of “Extremely Well” or “Extremely Satisfied”. The numbers and percentages given for these responses are out of the number of participants who were counseled by each type of provider. Significance was determined by Fisher’s exact test and significance was set at p=0.05. An asterisk indicates that a statistically significant difference between the three provider categories was found.
Group B Quantitative Findings:

Thirty-three families were consented and enrolled to participate in Group B and total of 19 pre-test surveys were returned (58% response rate). Only participants who completed the initial survey, had their child’s blood drawn for genetic testing, and had been notified of their results were sent the final survey. Twelve post-test surveys were mailed and one of these was returned as undeliverable, leaving 11 follow-up surveys that were sent. Of these 11 surveys, 4 post-test surveys were returned (36% response rate). Among the 19 pre-test surveys completed, sixteen (84.2%) of the respondents were female and 3 (15.8%) were male. The majority of respondents were white (84.2%) and were age 30 or older (68.4%). Approximately two-fifths of participants had a combined household income of $50,000 or more (42.1%), and 31.6% had an undergraduate degree or higher. All participants in this group received pre-test counseling from a genetic counselor. The mean age of the child being tested was 6.2 years old; the youngest child was 2 years old and the oldest was 17 years old at the time of testing. A complete description of Group B’s demographics is illustrated in Table 4.
<table>
<thead>
<tr>
<th></th>
<th>Group B (n=19)</th>
<th>Number</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td></td>
<td>16</td>
<td>84.2%</td>
</tr>
<tr>
<td>Female</td>
<td></td>
<td>3</td>
<td>15.8%</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;20</td>
<td></td>
<td>1</td>
<td>5.3%</td>
</tr>
<tr>
<td>20-29</td>
<td></td>
<td>5</td>
<td>26.3%</td>
</tr>
<tr>
<td>30-39</td>
<td></td>
<td>10</td>
<td>52.6%</td>
</tr>
<tr>
<td>40-49</td>
<td></td>
<td>2</td>
<td>10.5%</td>
</tr>
<tr>
<td>≥50</td>
<td></td>
<td>1</td>
<td>5.3%</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td></td>
<td>16</td>
<td>84.2%</td>
</tr>
<tr>
<td>Black/African American</td>
<td></td>
<td>1</td>
<td>5.3%</td>
</tr>
<tr>
<td>Hispanic/Latino</td>
<td></td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>Asian/Pacific Islander</td>
<td></td>
<td>1</td>
<td>5.3%</td>
</tr>
<tr>
<td>Native American/American Indian</td>
<td></td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td>1</td>
<td>5.3%</td>
</tr>
<tr>
<td>Household Income</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$25,000</td>
<td></td>
<td>5</td>
<td>26.3%</td>
</tr>
<tr>
<td>$25,000-$34,999</td>
<td></td>
<td>1</td>
<td>5.3%</td>
</tr>
<tr>
<td>$35,000-$49,999</td>
<td></td>
<td>5</td>
<td>26.3%</td>
</tr>
<tr>
<td>$50,000-$74,999</td>
<td></td>
<td>2</td>
<td>10.5%</td>
</tr>
<tr>
<td>$75,000-$99,999</td>
<td></td>
<td>2</td>
<td>10.5%</td>
</tr>
<tr>
<td>$100,000-$149,999</td>
<td></td>
<td>3</td>
<td>15.8%</td>
</tr>
<tr>
<td>≥$150,000</td>
<td></td>
<td>1</td>
<td>5.3%</td>
</tr>
<tr>
<td>Education*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Some high school</td>
<td></td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>High school graduate/GED</td>
<td></td>
<td>2</td>
<td>10.5%</td>
</tr>
<tr>
<td>Some college</td>
<td></td>
<td>4</td>
<td>21.1%</td>
</tr>
<tr>
<td>Associate’s degree</td>
<td></td>
<td>6</td>
<td>31.6%</td>
</tr>
<tr>
<td>Undergraduate degree</td>
<td></td>
<td>5</td>
<td>26.3%</td>
</tr>
<tr>
<td>Master’s degree or higher</td>
<td></td>
<td>1</td>
<td>5.3%</td>
</tr>
</tbody>
</table>

Table 4. Group B responses to demographic questions. *An asterisk indicates that one participant did not provide an answer for that question.

Participants in Group B were asked the same questions as Group A regarding why they decided to pursue genetic testing and what kind of result they expected to receive.

They were asked to select only one answer. Fifty-eight percent (n=11) reported that they
did genetic testing because their child’s medical provider recommended it, and 42% (n=8) said they wanted to know the cause of their child’s autism. No other reason was listed as the primary reason parents chose to go forward with testing. Sixteen percent (n=3) of respondents said they expected a positive result, none expected a negative result, 16% (n=3) expected a variant of uncertain significance, and 68% (n=13) said they had no expectation or did not know what to expect for a result.

In the pre-test survey, when asked how well they felt the genetic testing was explained to them, 16 participants (84%) gave a rating of 4 (very well) or 5 (extremely well) with a mean rating of 4.4 (SD=0.8). However, only 13 (68%) rated their understanding of the tests being done as a 4 or 5, with a mean rating of 3.9 (SD=1.1). The average ratings in the participants’ feelings about the quality of the testing explanation and their understanding of the testing are consistent with those of the Group A cohort who saw a genetic counselor. The responses to the multiple choice and Likert scale questions in the pre-test survey are illustrated in Table 5.
Table 5. Group B pre-test survey responses. Means of the Likert scale ratings are given with the standard deviation in parentheses. A rating of 4 corresponded to a response of “Very Well” while a rating of 5 corresponded to a response of “Extremely Well”.

In the post-test survey, only 4 responses were recorded. Of these respondents, 2 received a negative result and 2 received a variant of uncertain significance. When asked how well they felt they understood their result, 3 (75%) gave a rating of 4 or 5, with an average rating of 4 out of 5. All four respondents, however, gave a rating of 4 or 5 for how well they felt the results were explained to them, with an average rating of 4.5. Finally, when asked about their overall satisfaction with the testing process, 3 (75%) of the respondents gave a rating of 4 or 5 with an average rating of 4.3. One respondent did not answer this question. Due to the small number of responses, no quantitative comparison of the answers on the post-test Group B survey could be done.
Themes Identified in Short Answer Survey Questions:

Themes identified in the short answer questions of all group surveys along with quotations illustrating those themes are included in Tables 6-9. Details of these themes and the questions that prompted them are described below. Within these tables, genetic counselor is abbreviated as “GC”.

In an effort to assess understanding of the genetic test results, participants in both groups were asked to explain their result in their own words (Table 6). Within these explanations, several themes emerged: 1) no mutation or genetic factor was found, 2) their child’s autism has no genetic component and their recurrence risk is lower, 3) the cause of their child’s autism is still unknown due to limitations in current testing and knowledge, 4) the significance of the result was unknown, 5) their child had an extra chromosome, or 6) they were unsure of their result or how to explain it.
<table>
<thead>
<tr>
<th>Theme</th>
<th>Illustrated Quote</th>
</tr>
</thead>
<tbody>
<tr>
<td>No mutation or genetic factor found</td>
<td>“There was no genetic mutation found.” (saw GC)</td>
</tr>
<tr>
<td></td>
<td>“My son did not have any abnormal genetic test results.” (saw non-GC)</td>
</tr>
<tr>
<td>Child’s autism is not genetic</td>
<td>“The cause was not genetic and I have a lower chance of my next child having autism.” (saw GC)</td>
</tr>
<tr>
<td></td>
<td>“The result means that my child’s genetics did not cause his autism.” (saw non-GC)</td>
</tr>
<tr>
<td>Unknown cause due to limitations in testing and knowledge of autism</td>
<td>“My child tested negative for the specific genetic mutations the test was looking for, but this does not mean that there might not be other genetic mutations that she might have that were not included on the test.” (unknown provider)</td>
</tr>
<tr>
<td></td>
<td>“With the genetic testing, technology, and information/knowledge currently available, it was not possible to determine the genes/mutations responsible for my child’s autism.” (saw GC)</td>
</tr>
<tr>
<td>Unknown significance</td>
<td>“It means my child has a mutation, but the significance of it has not been identified.” (saw non-GC)</td>
</tr>
<tr>
<td></td>
<td>“There was a weak link or gene missing in the DNA but not enough to have caused his autism” (saw non-GC)</td>
</tr>
<tr>
<td>Extra Chromosome</td>
<td>“My child has an extra chromosome.” (saw non-GC)</td>
</tr>
<tr>
<td></td>
<td>“He has more chromosomes than needed – this doesn’t cause the autism but might be a factor.” (saw GC)</td>
</tr>
<tr>
<td>Unsure of result</td>
<td>“We didn’t get the results, probably the results are in the hospital archive.” (unknown provider)</td>
</tr>
<tr>
<td></td>
<td>“I was told just that the significance was uncertain and I could make an appointment with genetic counselor to know more.” (saw non-GC)</td>
</tr>
</tbody>
</table>

Table 6: Parents’ explanations of their child’s genetic test results.

After participants were asked to rate their overall satisfaction with the genetic testing process, they were prompted to give an explanation for their level of satisfaction (Table 7). The themes identified in their responses include: 1) they were satisfied with the
results and/or testing process, 2) they felt there was confusion, lack of explanation or lack
of follow-up, 3) they gained nothing from the testing, 4) they had issues with outside
factors (blood draw, insurance, etc.), 5) they were unsatisfied with the result or current
testing and knowledge., or 6) miscellaneous.

<table>
<thead>
<tr>
<th>Theme</th>
<th>Illustrative Quote</th>
</tr>
</thead>
<tbody>
<tr>
<td>Satisfied</td>
<td>“I’m glad that we had it done, I’m happy with the result, and all of my questions were answered.”</td>
</tr>
<tr>
<td></td>
<td>(Extremely satisfied (5), saw non-GC)</td>
</tr>
<tr>
<td>Confusion, lack of information or follow-up</td>
<td>“There was a lot happening the day my son was diagnosed. Some things went in one ear and out the other. I do wish someone would have followed-up on this topic. Maybe had them meet with us again after he was diagnosed and explain it all. I don’t think I fully understood all the info and that it all sunk in that day. We walked away from a multiple hour appointment with a diagnosis of autism. We were scared, unsure, anxious. Not everything we heard that day went home with us. Some things, unfortunately, were not absorbed.” (somewhat satisfied (3), saw GC)</td>
</tr>
<tr>
<td></td>
<td>“I wasn’t really expectant of a result either way, but I would have liked a little more information about what is known about genetic markers presently, and what they were actively looking for.” (somewhat satisfied (3), unknown provider)</td>
</tr>
<tr>
<td>Gained nothing from testing</td>
<td>“While it is interesting to know that my child does not have certain genetic mutations, this knowledge is fairly irrelevant to how we approach helping her achieve the best outcome possible.” (slightly satisfied (2), unknown provider)</td>
</tr>
</tbody>
</table>

Table 7: Parents’ explanation of their level of satisfaction with the testing process.
Table 7 continued

<table>
<thead>
<tr>
<th>Problems with outside factors</th>
<th>“The nurse that took my son’s blood was very mean. He was not kind and screamed at my autistic son to calm down. I yelled back at him and told him not to scream at my son again.” (not satisfied at all (1), saw GC)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>“The actual blood draw was AWFUL! Putting a kid with autism through that was not good. Before we were told very little about it but were told it was our choice and then we got the results and I felt like it still didn’t make sense – I wish someone would just say exactly what it means and what caused his autism.” (very satisfied (4), saw GC)</td>
</tr>
</tbody>
</table>

| Unsatisfied with their result, current testing or knowledge         | “I was satisfied with the services provided at the CDC. My disappointment stems from the current state of genetic testing in general. Based on the specific incidence of autism in my family, and on my knowledge of autism statistics in general, it seems to me that the odds of my child’s autism NOT being genetic are quite astronomical. I look forward to continuing advances in genetic testing and am confident that one day we will have the answers we seek.” (slightly satisfied (2), saw GC) |
|                                                                     | “I expected the testing to give us an answer as to why our child is autistic. The test did not provide an answer.” (somewhat satisfied (3), saw GC) |

| Miscellaneous                                                       | “I was not expecting anything from genetic testing one way or another. I just wanted to make sure we had explored every outlet for assistance.” (very satisfied (4), saw non-GC) |
|                                                                     | “There was no finding of any genetic issue, but I honestly wasn’t expecting there to be one.” (somewhat satisfied (3), saw non-GC) |

Both groups were asked what they wish they had known or had been clarified before the testing was completed (Table 8). Similar themes to the previous question
arose: 1) issues with outside factors (time, cost, insurance, blood draw, etc.), 2) more explanation of the testing process (benefits/limitations) and possible results, 3) the usefulness of having genetic test results, 4) more information about autism etiology and other testing options, or 5) none, they were satisfied.

<table>
<thead>
<tr>
<th>Theme</th>
<th>Illustrative Quote</th>
</tr>
</thead>
<tbody>
<tr>
<td>Problems with outside factors</td>
<td>“Well what difference would it have made if there was something genetically found. I really feel it wasn’t beneficial to me or my son. We have information without context. It benefits research or maybe the science but does nothing to give families comfort, direction, security, etc. I had to go through denials from my insurance, apply for grants, and prepare my son for testing. A lot of frustration and preparation for no clarity. I had to hold my crying son as he begged ‘please mommy make it stop’ FOR NOTHING!” (unknown provider)</td>
</tr>
<tr>
<td>More explanation of testing and possible results</td>
<td>“What we might/might not see and the full scope of the test.” (saw non-GC)</td>
</tr>
<tr>
<td>Usefulness of genetic test result</td>
<td>“I wish I was told why a little bit more – like why it was important or why this applied to my son. We also had never been told what the possible results could be and what that would mean.” (saw GC)</td>
</tr>
<tr>
<td></td>
<td>“I’d like a better explanation of how this could affect my child’s possible children in the future.” (saw non-GC)</td>
</tr>
<tr>
<td>More information about etiology and testing options</td>
<td>“If we had more ways of finding out what caused him to have autism other than chance.” (unknown provider)</td>
</tr>
<tr>
<td></td>
<td>“I still wish I knew if he got the disorder from his immunizations (like some of the readings I have read say) or if it’s from his father’s side of the family (he has an autistic uncle).” (unknown provider)</td>
</tr>
<tr>
<td>None (satisfied)</td>
<td>“Nothing – we were all well-prepared. It would have been nice to be able to point to something, as the cause of our son’s autism is a mystery to us – but we are also glad to have confirmation that he is a healthy kid who just happens to be autistic.” (saw non-GC)</td>
</tr>
</tbody>
</table>
One question was addressed only to Group B in the pre-test survey. Participants were asked what, if any, was their biggest concern regarding the genetic testing (Table 9). Again, several main themes were identified: 1) that there could be more serious health concerns revealed 2) getting blood drawn, 3) implications for reproductive decisions and future children, 4) there could be little or no information available, 5) miscellaneous, or 6) no concerns. Seven of the respondents identified the last theme on their responses, either by writing “no concerns” or “none”.

<table>
<thead>
<tr>
<th>Theme</th>
<th>Illustrative Quote</th>
</tr>
</thead>
<tbody>
<tr>
<td>Additional health problems</td>
<td>“I’m concerned if there is a positive result, that there may be other issues later medically, besides ASD.”</td>
</tr>
<tr>
<td></td>
<td>“Are there other issues we will have to deal with later in our daughter’s life.”</td>
</tr>
<tr>
<td>Blood draw</td>
<td>“The drawing of the blood. My son hates needles.”</td>
</tr>
<tr>
<td></td>
<td>“His reaction to the blood draw.”</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>“My only concern is that they will find a mutation in the genes but won't be able to specify it because that will just put me back to where I started.”</td>
</tr>
<tr>
<td></td>
<td>“Not finding out anything.”</td>
</tr>
<tr>
<td>Reproductive decisions</td>
<td>“Decision on having another child.”</td>
</tr>
<tr>
<td></td>
<td>“That I will find out there is a genetic mutation and my other son may be affected and possible future children.”</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>“Cost.”</td>
</tr>
</tbody>
</table>

Table 9: Parents’ concerns about genetic testing.

In the Group B cohort, respondents were also asked what they wish they had known before the testing was completed. Only one respondent answered the question, stating: “All of my questions were answered.” Finally, Group B participants were asked
what would have made the genetic testing process easier or better for them. Again, only one participant responded: “*I felt the process was easy*.”
Chapter 4: Discussion

Overall, participants in the retrospective cohort (Group A) who received counseling about the genetic testing from a genetic counselor generally reported higher satisfaction with and understanding of the testing process and results [testing explanation (p=0.015), results explanation (p=0.011), results understanding (p=0.016), and overall satisfaction (p=0.025)]. These data suggest that having a genetic counselor in this clinic is beneficial for the families, in that they feel better informed about the testing and may have a more positive view of the testing process. Previous studies have illustrated the importance of having a genetic counselor involved in the testing process in other clinical settings. Within the cancer specialty of genetic counseling, one study found that patients’ test results were frequently misinterpreted (especially variants of uncertain significance) and many felt they received inadequate counseling from their doctors (Brierley et al, 2010). Another study in the cancer field found that 80-90% of patients who received genetic counseling for a particular syndrome reported the pre-test counseling to be fairly useful or very useful and the post-test counseling to be sufficient (Aktan-Collan et al, 2000). However, approximately one-fifth of respondents in Group A did not know who counseled them about the testing. It is likely that some of the respondents who fell into this category did in fact see a genetic counselor, which could have made a difference in explanation, understanding, and satisfaction ratings for the genetic counseling group. Had
it been possible to determine which providers the unsure group saw, a more direct statistical analysis could have been done to determine the significance in ratings between genetic and non-genetic providers. Several trends noted in the socioeconomic status of respondents between the provider groups could perhaps partially explain the differences in the ratings participants gave. Specifically, those that saw a genetic counselor tended to have a higher level of education and household income than those who saw a non-genetic provider. Approximately 59% of the participants that received genetic counseling had a combined income of $50,000 or more and 50% had an undergraduate degree or higher, compared to only 33% with an income of $50,000 or more and 20% with an undergraduate degree or higher in the group that saw a non-genetic provider. Interestingly, despite the fact that 67% of those who saw an unknown provider had an income of $50,000 or more and 67% had an undergraduate degree or higher, ratings of explanation, understanding, and overall satisfaction tended to be much lower than the other two groups. Statistical analysis of the relationship between socioeconomic status and type of provider seen was not done, therefore, future studies may help in determining how strongly the participants’ income and education influenced these responses.

Another interesting finding was the type of results that participants indicated they expected. It was not necessarily surprising that most respondents had no specific expectations, or did not know what to expect for a test result. However, what was surprising was that more participants in the genetic counselor group tended to expect a positive result more often than in the other provider groups. This was the opposite of what was expected because those that saw a genetic counselor would have been informed
that there is only a 15-20% chance of finding a genetic explanation for their child’s autism as opposed to potentially being given no estimate. There are several potential explanations for this finding. One could be that families may perceive a 15-20% likelihood for a positive result as being a high likelihood, or higher than they expected before their appointment. Another explanation could be that those who spoke with a genetic counselor assumed that their meeting with a genetic specialist meant that there was a greater suspicion of an underlying genetic cause for their child’s autism diagnosis.

It appears that the responses to the short answer question asking parents to explain their child’s genetic test result in their own words fits with the more neutral ratings that participants gave for their understanding of the result. Many of the respondents’ explanations did not illustrate a clear understanding of their genetic test results or did not reflect an understanding of the limitations of the testing performed. Explanation of the variants of unknown significance proved particularly difficult for some participants. Several of them reported that their child had “an extra chromosome”, presumably illustrating a chromosomal microduplication. Several respondents believed that a negative test result for a microarray and possibly Fragile X or PTEN testing meant that their child’s autism had no genetic etiology. This reflected a lack of understanding of the full scope and limitations of the testing being offered at the CDC/Autism Center. Additionally, the selected quotes illustrate that the type of provider who counseled the family about the genetic testing and possibly the results may not strongly correlate with the family’s ability to accurately explain the result interpretation. It appeared that those who saw a genetic counselor were just as likely to struggle to explain their results
accurately as those who saw a non-genetic or unknown provider. For example, parents who described their child’s variant of uncertain significance as his or her having an extra chromosome, or who interpreted a negative result to mean that their child's autism was not genetic, were found in both the genetic counselor and non-genetic provider group (Table 6).

Some respondents’ overall satisfaction rating for the genetic testing process seemed to be influenced to varying degrees by factors outside of the control of the counseling providers. For example, several participants quoted unfortunate experiences with getting their child’s blood drawn or issues with insurance coverage that factored into their perception of the testing process. This was particularly interesting since none of the participants should have received a bill for the genetic testing. The majority of families who underwent testing through the CDC/Autism Center would not have been balance billed for the testing or would have been eligible for supplemental insurance based on institutional policy. Other respondents conveyed disappointment about their child’s test result and questioned the usefulness of the testing, thinking it only benefited future research. While a genetic test result could give families useful information for estimating recurrence risk or guiding current management for their child, receiving an uncertain or negative result may leave families feeling unsatisfied. Another recurrent theme identified in participant’s overall satisfaction was a lack of information or follow-up on behalf of the providers, especially for those who received negative results. For example, one parent expressed a desire for the genetic testing subject to be revisited or to meet with the genetic counselor at a future appointment because of how much information was
provided in general at the initial appointment (Table 7). This suggests that the length of the initial diagnostic assessment appointment in which genetic testing is discussed likely influenced some participant’s responses and overall satisfaction. For most families, this appointment is over two hours long and multiple providers assess the child and discuss recommendations with the parents, in addition to the genetic counseling component. For this reason, participants may have reported not being told or given a full explanation of certain parts of the testing process when in reality they were saturated with information. In a similar vein, many respondents who received a negative result took this to mean that their child’s autism was not genetic, illustrating a poor understanding of the scope and limitations of the testing. It is likely not realistic to have these patients come back in and meet with a genetic counselor separately as the aforementioned respondent suggested, both because of the time commitment that would be required of the counselor and because of the potential for service billing issues in the future. Therefore, one suggestion for counselors may be to provide families with a detailed handout or access to an online education tool that families can reference after their appointment. This resource could include content such as why the test is being recommended, the possible results and the type of information they would provide, and the benefits and limitations of the testing. It may also benefit patients to include some information about what is known about autism etiology currently, as that was another topic brought up by several participants.

It is also possible that those who saw a non-genetic provider were unaware that genetic testing was being done or they were told very little about it. However, some of this dissatisfaction may be attributable to the operation of the clinic at the CDC/Autism
Center. In this clinic, the protocol indicates that families who receive a negative test results are called by the nursing staff, and not by the counseling provider. If these families are not reached via phone, a letter is mailed to the family’s residence or is released as correspondence within Nationwide Children’s Hospital’s electronic medical records system. This likely explains why some respondents reported that they never received results or were told very little about them. This is another factor that played into participant satisfaction that is not an accurate reflection of the quality of counseling provided by the genetic counselor or non-genetic provider. Therefore, it may benefit the families to have the genetic counselor call out the negative results as well, and for the genetic counselor to write the letter explaining the results. However, in a clinic with only one genetic counselor on staff (such as this one) or no genetic provider at all, this may not be feasible. This is another reason why a handout or online education tool for families could be helpful.

Participants in the prospective cohort (Group B) highly rated the explanations and their understanding of the testing and results, as well as their overall satisfaction with the genetic testing process. For the most of these Likert scale responses, the ratings matched quite closely to those of the Group A cohort that were seen by a genetic counselor based on qualitative comparison. This lends more support to the idea of a higher quality of counseling about genetic testing offered by a genetic counselor. Additionally, the explanations of the results they received and the concerns they identified with the testing in the short answer questions were also similar. This consistency in responses between Group B and the genetic counseling cohort of Group A is also likely attributed to the fact
that there is currently only one genetic counselor in this clinic. To some degree, the responses from this cohort may further strengthen the trend of higher genetic counselor ratings in Group A because this group did not have as high an income or level of education. In fact, only 42% (n=8) reported a combined income of $50,000 or more and 33% (n=6) had an undergraduate degree or higher.

Due to the small number of participants that completed the final survey (Group B post-test), no statistical analysis could be done and no true trends could be extrapolated from the post-test survey. Not only was the response to the final survey poor, but of those that did return this survey only one completed the short answer questions assessing desired knowledge and improvements to the testing process. One explanation for this small post-test response rate is the slow or absent uptake of the genetic testing, as many of the families enrolled had not had their child’s blood drawn by the time data analysis had begun. Many of those who completed a pre-test survey were never sent the post-test survey because they had not had blood drawn for testing by the time the data collection period was ending. Finally, only 33 families were recruited for participation in Group B. If this study could be repeated with a longer recruitment and data collection timeframe, many more survey responses could be collected and stronger comparisons could be made.

**Limitations:**

This study had several limitations. The questions used in all three surveys were developed specifically for this project and have not been validated, nor was the survey piloted in the study population prior to the study implementation. Therefore, there may have been questions that were misinterpreted by participants, or the questions may not
have accurately measured what they were intended to measure. Another factor that likely influenced the participants’ responses is the long appointment time and the great deal of information given by various providers in the initial diagnostic appointment. It is reasonable that families may not have remembered much about the testing discussion in this setting. A third limitation that potentially affects all the responses of the Group A surveys is recall bias. Some participants in this cohort completed their child’s testing as much as two years prior to the completion of the survey, which may have affected their ability to accurately reflect on their perceptions before and after the testing was completed, as well as their ability to explain their test result. A fourth limitation of this study is that there is only one genetic counselor providing counseling to patients in this clinic. If there were several genetic counselors in this clinic or if similar levels of understanding and satisfaction were found in another clinic with a different genetic counselor, that could further strengthen the findings of this study. Finally, we were unable to verify that the genetic test result that participants reported was the actual genetic test result they received. Therefore, we are unable to determine accuracy of their recall. This limitation is evident in the two respondents in Group A who reported a positive result, which we know is inaccurate because those with positive genetic test results were excluded from the study. This does not exclude the possibility that a variant of uncertain significance was found which may have been interpreted as contributing to the child’s autism diagnosis. However, based on their short answer responses, it appeared that these two participants may not have understood the questions being asked. For
example, the explanation one of these respondents gave for her child’s positive result was “we were unsure of what it meant for our child and what we were getting into”.

**Conclusions:**

Our data did not support our first hypothesis, that parents who did not meet with a genetic counselor would not fully recognize the limitations of the testing and would expect a higher likelihood of finding something definitive to explain their child’s autism. Most participants indicated that they had no expectation or did not know what to expect from the testing. For those that did indicate a specific type of result, no clear pattern was identified based on the counseling provider. However, the highest number of people that reported they expected a positive result were among those that saw a genetic counselor, which is not what was expected. Our second hypothesis, that those parents who met with a genetic counselor through the testing process will have a better understanding and higher satisfaction with the explanations given about the testing and the results than those families who met with a non-genetics specialist, was supported by the statistically significant findings in these data. Despite the limitations of this study, the data demonstrate that those who received genetic counseling reported a higher quality explanation and subsequent understanding of the testing process and results, as well as an overall higher satisfaction with the testing process. This illustrates the importance of having a genetic counselor available to meet with these families during the genetic testing process. However, trends in these data suggest that there are aspects of the counseling process that could be improved. Many participants in Group A described a lack of follow-up or general lack of information about the testing process. Therefore, having
another way to access important information about the testing process, in the form of a handout or online resource, could be a reasonable solution to address this issue. Another component of the counseling process that could be improved would be how negative results are handled. Many respondents indicated that they never received their results, or that they were only told that the result was negative with no further explanation. This is why having the genetic counselor involved in discussing negative results could also be beneficial. While this dataset was small, we were able to identify several trends in patient understanding and satisfaction and potential areas for improvement in the testing process. To further assess the strength of these trends and to gather more perspectives of families undergoing this testing, this study should be replicated at other autism clinics, and with a longer timeframe for recruitment and collection of surveys.
References


Fischbach RL, Harris MJ, Ballan MS, Fischbach GD, and Link BG. 2015. Is there
concurrence in attitudes and beliefs between parents and scientists about autism spectrum disorder? *Autism* pii: 1362361315585310.


Appendix A: Group A Survey

**Study Title:** Pre- and Post-Test Parent Perceptions of Genetic Testing for Children with Autism Spectrum Disorder

**OSU PI:** Dawn Allain, M.S., LGC  
**NCH PI:** Emily Hansen-Kiss, MS, MA, LGC  
**Key Personnel:** Hayley Winslow

GROUP A SURVEY

1. Demographic Questions:
   a) What is your gender? Please check one.
      
      ___ Male  ___ Female  ___ Transgender  ___ Other: ________________

   b) What is your age? Please check one.
      
      ___ Younger than 20  ___ 20-29  ___ 30-39  ___ 40-49  ___ 50 or older

   c) What is your ethnicity? Please check one.
      
      ___ White          ___ Black or African American
      ___ Hispanic or Latino   ___ Asian/Pacific Islander
      ___ Native American or American Indian  ___ Other: ________________

   d) What is your combined household income? Please check one.
      
      ___ Less than $25,000  ___ $25,000-$34,999  ___ $35,000-$49,999
      ___ $50,000-$74,999  ___ $75,000-$99,999  ___ $100,000-$149,999
      ___ $150,000 or more
e) What is your highest level of education? Please check one.

___Some high school  ___High school graduate/GED

___Some college     ___Associate degree

___Undergraduate degree ___Master’s degree or higher

___Other: ________________________

2. Why did you choose to pursue genetic testing for your child with autism? Choose the one answer that best fits.
   a) It was recommended by my child’s medical provider.
   b) I want to know the cause of my child’s autism diagnosis.
   c) I am interested in learning what my chance is for having another child with an autism diagnosis.
   d) Other (please explain):

3. How old was your child when genetic testing was completed?

4. What kind of medical professional counseled you about testing options, procedures, and results (genetic counselor, pediatric doctor, other)?

5. On a scale from 1 to 5, how well do you feel the provider explained the genetic testing to you before the testing was ordered? Please circle one.

<table>
<thead>
<tr>
<th>Not well at all</th>
<th>Slightly Well</th>
<th>Somewhat well</th>
<th>Very Well</th>
<th>Extremely Well</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

6. On a scale from 1 to 5, how well do you feel you understood the genetic tests that were done and what they were looking for? Please circle one.

<table>
<thead>
<tr>
<th>Not well at all</th>
<th>Slightly Well</th>
<th>Somewhat well</th>
<th>Very Well</th>
<th>Extremely Well</th>
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<tr>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>
7. What kind of result did you expect to see from the genetic testing (positive, negative, or VUS)? Please choose one.
   a) Positive (a mutation/genetic change that explains the autism)
   b) Negative (no mutation/genetic change was detected)
   c) VUS (a mutation/genetic change with uncertain significance)
   d) I had no expectation/I didn’t know what to expect

8. On a scale from 1 to 5, how likely did you think it would be to get the result you chose in question 7?

   Not likely at all  Slightly Likely  Somewhat likely  Very likely  Extremely likely
   1                  2                   3                   4                   5

9. What was the test result that you actually received (positive, negative, VUS)? Please choose one.
   a) Positive (a mutation/genetic change that explains the autism)
   b) Negative (no mutation/genetic change was detected)
   c) VUS (a mutation/genetic change with uncertain significance)

10. On a scale from 1 to 5, how well do you feel you understand what this result means?

    Not well at all  Slightly Well  Somewhat well  Very Well  Extremely Well
    1                  2                   3                   4                   5

11. In your own words, please describe what this result means.

12. On a scale from 1 to 5, how well did this result compare with your expectation from before testing was completed?

    Not at all what I expected  Slightly what I expected  No expectation  Somewhat what I expected  Exactly what I expected
    1                  2                   3                   4                   5
13. On a scale from 1 to 5, how well do you feel the genetic testing result *was explained* to you after testing was completed?

Not well at all  Slightly Well  Somewhat well  Very Well  Extremely Well
1                2                  3                4              5

14. On a scale from 1 to 5, how did you feel about the overall genetic testing experience?

Not satisfied at all  Slightly satisfied  Somewhat satisfied  Very satisfied  Extremely satisfied
1                      2                          3                      4                      5

15. Please explain your answer to question 14.

16. What do you wish you had known or had been clarified about the testing process before it was completed?
Appendix B: Group B Initial Survey

**Study Title:** Pre- and Post-Test Parent Perceptions of Genetic Testing for Children with Autism Spectrum Disorder

**OSU PI:** Dawn Allain, M.S., LGC  
**NCH PI:** Emily Hansen-Kiss, MS, MA, LGC  
**Key Personnel:** Hayley Winslow

**GROUP B PRE-TESTING SURVEY**

PLEASE WRITE YOUR ASSIGNED STUDY NUMBER HERE: __________________

1. Demographic Questions:

   a) What is your gender? Please check one.

      ___Male  ___Female  ___Transgender  ___Other:_________________

   b) What is your age? Please check one.

      ___Younger than 20  ___20-29  ___30-39  ___40-49  ___50 or older

   c) What is your ethnicity? Please check one.

      ___White  ___Black or African American  
      ___Hispanic or Latino  ___Asian/Pacific Islander  
      ___Native American or American Indian  ___Other:_________________

   d) What is your combined household income? Please check one.

      ___Less than $25,000  ___$25,000-$34,999  ___$35,000-$49,999  
      ___$50,000-$74,999  ___$75,000-$99,999  ___$100,000-$149,999
$150,000 or more

e) What is your highest level of education? Please check one.

___Some high school   ___High school graduate/GED

___Some college   ___Associate degree

___Undergraduate degree   ___Master’s degree or higher

___Other:_______________________

2. Why did you choose to pursue genetic testing for your child with autism? Choose the one answer that best fits.
   a) It was recommended by my child’s medical provider.
   b) I want to know the cause of my child’s autism diagnosis.
   c) I am interested in learning what my chance is for having another child with an autism
diagnosis.
   d) Other (please explain):

3. How old is your child?

4. On a scale from 1 to 5, how well do you feel the genetic counselor explained the genetic testing to you before the testing was ordered? Please circle one.

   Not well at all  Slightly Well  Somewhat well  Very Well  Extremely Well
   1  2  3  4  5

5. On a scale from 1 to 5, how well do you feel you understand the genetic tests that will be done and what they are looking for? Please circle one.

   Not well at all  Slightly Well  Somewhat well  Very Well  Extremely Well
   1  2  3  4  5

6. What kind of result do you expect to see from the genetic testing (positive, negative, VUS)? Please choose one.

   a) Positive (a mutation/genetic change that explains the autism)
   b) Negative (no mutation/genetic change was detected)
c) VUS (a mutation/genetic change with uncertain significance)
d) I have no expectation/I don’t know what to expect

7. On a scale from 1 to 5, how likely do you think it would be to get the result you chose in question 7?

<table>
<thead>
<tr>
<th>Not likely at all</th>
<th>Slightly Likely</th>
<th>Somewhat likely</th>
<th>Very likely</th>
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8. What, if any, is your biggest concern regarding genetic testing for your child?
Appendix C: Group B Final Survey

Study Title: Pre- and Post-Test Parent Perceptions of Genetic Testing for Children with Autism Spectrum Disorder

OSU PI: Dawn Allain, M.S., LGC
NCH PI: Emily Hansen-Kiss, MS, MA, LGC
Key Personnel: Hayley Winslow

GROUP B POST-TESTING SURVEY

PLEASE WRITE YOUR ASSIGNED STUDY NUMBER HERE: ____________________

1. What was the test result that you received (positive, negative, VUS)? Please choose one.
   a) Positive (a mutation/genetic change that explains the autism)
   b) Negative (no mutation/genetic change was detected)
   c) VUS (a mutation/genetic change with uncertain significance)

2. On a scale from 1 to 5, how well do you feel you understand what this result means?
   Not well at all 1 Slightly Well 2 Somewhat well 3 Very Well 4 Extremely Well 5

3. In your own words, please describe what this result means.

4. On a scale from 1 to 5, how well did this result compare with your expectation from before testing was completed?
   Not at all what I expected 1 Slightly what I expected 2 No expectation 3 Somewhat what I expected 4 Exactly what I expected 5
5. On a scale from 1 to 5, how well do you feel the genetic testing result was explained to you after testing was completed?

- Not well at all (1)
- Slightly Well (2)
- Somewhat well (3)
- Very Well (4)
- Extremely Well (5)

6. On a scale from 1 to 5, how do you feel about the overall genetic testing experience? Explain.

- Not satisfied at all (1)
- Slightly satisfied (2)
- Somewhat satisfied (3)
- Very satisfied (4)
- Extremely satisfied (5)

7. What do you wish you had known or had been clarified about the testing process before it was completed?

8. What would have made the genetic testing process easier or better for you and your family?
CONSENT TO PARTICIPATE IN A CLINICAL RESEARCH STUDY

STUDY TITLE: Pre- and Post-Test Perceptions of Genetic Testing for Children with Autism Spectrum Disorder (ASD)

PRINCIPAL INVESTIGATOR: Emily Hansen-Kiss, MS, LGC

CONTACT TELEPHONE NUMBER: 614-355-7536

SUBJECT'S NAME: _______________________
DATE OF BIRTH: _______________________

NOTE: The words “you” and “your” are used in this consent form. These words refer to the study volunteer whether a child or an adult.

1) INTRODUCTION

We invite you to be in this research study because your child has received a diagnosis of autism spectrum disorder (ASD) and you have chosen to do genetic testing.

Participation is voluntary. Using this form as a guide, we will explain the study to you. If you have any questions about the study, please ask. Once you understand this study, we will ask you to decide whether you would like to participate or not. By signing this form, you agree to be in this study. If you do not want to be involved with this study, all regular and standard medical care will still be available to you here or at another institution. You also have the right to leave this study at any time, even if you agree to join now.

You will be given a signed and dated copy of the consent form.

2) WHY ARE WE DOING THIS RESEARCH STUDY?

This study is being done to gain a better understanding of how parents feel about the process of genetic testing when their child has been diagnosed with autism spectrum disorder, and assess how this process may be improved in the future. It is also being done to find out whether seeing a genetic counselor makes a difference in the testing experience for parents.
3) **WHERE WILL THE STUDY BE DONE AND HOW MANY SUBJECTS WILL TAKE PART?**

This study will be done at the Child Development Center/Autism Center clinic at Nationwide Children’s Hospital and we hope to enroll about 100 participants, including 75 participants completing a post-testing survey only and 25 participants in the pre-testing and post-testing survey group (this is the group that you have the chance to participate in).

4) **WHAT WILL HAPPEN DURING THE STUDY AND HOW LONG WILL IT LAST?**

If you choose to take part in this study, you will complete two online or paper surveys that are about 8-12 questions long. These questions will ask you about your perceptions and understanding of the information you received regarding genetic testing for your child with autism spectrum disorder before the test was done, and questions about how you feel about the result and counseling you received after the test was completed. The first survey and link to the online survey will be given to you at the appointment when you are consented and genetic testing is ordered. You will be mailed a link and a paper copy of the second survey after you are called with your results of the genetic test. You will also be assigned a study ID number that you will need to write on both surveys so that we can link them together when they are done.

The survey will be anonymous. We will not be collecting any private health information, and once you complete the second survey your name and contact information will no longer be connected with your study ID number and they will not be able to be reconnected with your survey answers.

We expect that each survey will take 10 minutes or less to complete.

5) **WHAT ARE THE RISKS OF BEING IN THIS STUDY?**

We believe that there is very little chance that bad things will happen as a result of being in this study.

It is possible that you could feel upset when answering questions about your child’s diagnosis and your experiences, but it may be more likely that you find the questions or feedback process a little boring. If you do find any of the questions upsetting or don’t want to answer a question, you don’t have to, and the study coordinator will be available to discuss this with you further.

Although we will take every precaution, there is a small chance of loss of confidentiality of your study information.

If you are worried about anything while in this study, please call the Principal Investigator or study coordinator at the telephone number on page 1.

This study involves questions or surveys that may make you feel depressed. You should call the Principal Investigator at 614-355-7536 immediately if you notice any changes in your mood, ideas, or behavior. Common warning signs that might be a signal for risk of suicide include talking or thinking about wanting to hurt oneself or end one’s life. Other signs include withdrawing from friends and family, becoming depressed or a worsening of depression, becoming preoccupied with death and dying, and giving away prized possessions.
Immediate help is available if thoughts or feelings of hurting oneself come up. If these thoughts or feelings occur, you should immediately call one of the numbers below or go to the closest Emergency Room.

Nationwide Children’s Psychiatric Emergency Evaluation Center  614-722-1800
Hopeline/Lifeline – 1-800-784-2433 or 1-800-SUICIDE

There may be other risks of being in this research study that are not known at this time.

6) ARE THERE BENEFITS TO TAKING PART IN THIS STUDY?
Although there will likely be no benefit to you from being in this study, we hope to learn something that could help others.

9) WHAT ARE THE COSTS AND REIMBURSEMENTS?
All costs related to the research parts of this study will be covered by the research team. However, the parts of the study that would be done for routine clinical care will be billed to you and to your insurance company or third party payer. You may have to pay any costs that the insurance company or third party payer does not pay. The study team will discuss these costs with you.

We do not anticipate any costs to you in this study. If you choose to fill out a paper survey instead of the online version, the return envelope for that survey will be pre-paid.

You will not be compensated for participating in this study.

10) WHAT HAPPENS IF BEING IN THIS STUDY CAUSES INJURIES?
We believe that there is very little chance that injuries will happen as a result of being in this study.

12) WHAT HAPPENS IF I DO NOT Finish THIS STUDY?
It is your choice to be in this study. You may decide to stop being in this study at any time. If you decide to stop being in this study you must call the Principal Investigator. If you stop being in the study, there will not be a penalty or loss of benefits to which you are otherwise entitled.

If at any time the Principal Investigator believes that this study is not good for you, the study staff will contact you about stopping. If the study instructions are not followed, participation in the study may also be stopped.

13) OTHER IMPORTANT INFORMATION
If you are an employee of Nationwide Children’s Hospital or the Research Institute at Nationwide Children’s Hospital, your job or performance appraisal will not be affected in any way if you decline to participate or withdraw your consent to participate in this study.
The final study results will not be shared with you individually.

Nationwide Children’s Hospital is a teaching hospital and we are committed to doing research. Doing research will enable us to learn and provide the best care for our patients and families. You may be asked to participate in other research studies in the future. You have the right to decide to participate or decline to participate in any future studies. We will not share your contact information with researchers outside Nationwide Children’s Hospital.

14) **HOW WILL MY STUDY INFORMATION BE KEPT PRIVATE?**

Information collected for this study will be kept confidential. Information will be stored in a password-protected electronic database and access will be given only to study personnel. All written records will be stored in a locked filing cabinet.

Efforts will be made to keep your study-related information confidential. However, there may be circumstances when this information must be released. For example, personal information regarding your participation in this study may be disclosed if required by state law.

Your records may be reviewed by the following groups (as applicable to the research):
- PI and study staff
- The Nationwide Children’s Hospital Institutional Review Board (the committee that reviews all human subject research)
- Nationwide Children’s Hospital internal auditors

If you have a bad outcome or adverse event from being in this study, the Principal Investigator and staff or other health care providers may need to look at your entire medical records. We expect that the results from this study may be published in the future but your identity will not be revealed.

**PHI that may be used or disclosed:**
PHI that may be used includes first and last names and mailing addresses. Your assigned study ID number will also be associated with your name until you finish both the pre- and post-test surveys.

**Reason(s) why the use or disclosure is being made:**
PHI will be accessed and used only to mail you information for the surveys. Your assigned study ID number will be associated with your name only until we have finished recruiting and collecting data for this study. All PHI and records of your study ID number will be destroyed and will not be connected to you in any published data. Once this information is destroyed there will be no way to associate your survey and study ID number with your contact information again.

You may decide not to authorize the use and disclosure of your PHI. However, if it is needed for this study, you will not be able to be in this study. If you agree to be in this study and later decide
to withdraw your participation, you may withdraw your authorization to use your PHI. This request must be made in writing to the Principal Investigator at 187 West Schrock Rd., Westerville, OH 43081. If you withdraw your authorization, no new PHI may be collected and the PHI already collected may not be used unless it has already been used or is needed to complete the study analysis and reports.

There is a risk that someone could get access to the information (data) we have collected about you. If those data suggested something serious about your health, it could be misused. For example, it could be used to make it harder for you to get or keep a job or insurance. The Genetic Information Nondiscrimination Act of 2008 (GINA) says that group and individual health insurers may not use your genetic information to determine whether you are eligible for insurance, how much you have to pay, nor can they request or require that you take a genetic test. We cannot guarantee that this will fully protect you. Your privacy and the confidentiality of your data are very important to us. We will make every effort to protect them.

PHI will only be shared with the groups listed above, but if you have a bad outcome or adverse event from being in this study, the Principal Investigator and staff or other health care providers may need to look at your entire medical records. In the event of any publication regarding this or any future studies, your identity will not be revealed.

The PHI collected or created under this research study will be used or disclosed as needed until the end of the data collection. Your authorization to use or disclose your PHI will not expire.

16) WHOM SHOULD I CALL IF I HAVE QUESTIONS OR PROBLEMS?

If you have questions, concerns, or complaints about anything while on this study or you have been injured by the research, you have access during regular business hours to talk to the Principal Investigator at 614-355-7536.

If you have questions about anything while on this study or you have been injured by the research, you may contact the Principal Investigator at 614-355-7536, Monday – Friday, between 8am-5pm.

If you have questions, concerns, or complaints about the research; if you have questions about your rights as a research volunteer; if you cannot reach the Principal Investigator; or if you want to call someone else - please call (614) 722-2708, Nationwide Children's Hospital Institutional Review Board, (IRB, the committee that reviews all research involving human subjects at Nationwide Children’s Hospital).

Subject’s Name _______________________________
Date of Birth _____________________________
SUBJECT or SUBJECT’S PARENT OR PERSON AUTHORIZED TO CONSENT ON BEHALF OF THE CHILD (SUBJECT TO THE SUBJECT’S GENERAL MEDICAL CARE)

I have read this consent form and I have had an opportunity to ask questions about this research study. These questions have been answered to my satisfaction. If I have more questions about participating in this study or a research-related injury, I may contact the Principal Investigator. By signing this consent form, I certify that all health information I have given is true and correct to the best of my knowledge.

I have been given a copy of the Nationwide Children's Hospital Notice of Privacy Practices. If allowed by law, I understand that my right to any information that is created or collected by Nationwide Children's Hospital for this study can be temporarily suspended if necessary for the purposes of this research project. I also understand that my right to access to this information from this study will be reinstated upon completion of this research unless I have been told by the Principal Investigator that I will not receive study results.

I agree to participate in this study or I give permission for my child to participate in this study. I will be given a copy of this consent form with all the signatures for my own records.

CONSENT SIGNATURES

SUBJECT or SUBJECT’S LEGAL REPRESENTATIVE
_________________________ DATE & TIME  AM/PM

SUBJECT'S SECOND LEGAL REPRESENTATIVE
_________________________ DATE & TIME  AM/PM
Permission of the second parent not obtained because (select all that apply):
____ Not required by the IRB (risk level 1 or 2).
____ Other parent is deceased.
____ Other parent is unknown.
____ Other parent is not reasonably available.
____ Only one parent has legal responsibility for the care and custody of subject.

PERSON OBTAINING CONSENT
_________________________ DATE & TIME  AM/PM
I certify that I have explained the research, its purposes, and the procedures to the subject or the subject’s legal representatives before requesting their signatures.
Appendix E: Group A Invitation to Participate Letter

Invitation to Participate in a Research Study Regarding Parent Perceptions of Genetic Testing for Their Children with an Autism Spectrum Disorder

Dear ________________ Family,

I am Hayley Winslow, a genetic counseling student at The Ohio State University working with Emily Hansen-Kiss, LGC, a genetic counselor at the Child Development Center/Autism Center at Nationwide Children’s Hospital. We would like to invite you to participate in our research. You are being contacted because you have completed genetic testing for your child with an autism spectrum disorder diagnosis in the last year through Nationwide Children’s Hospital.

We are hoping to learn more about parents’ experiences with genetic testing for their children with an autism spectrum disorder.

We want to know how you felt about the information and the counseling that you received both before the testing and after you got the genetic test results back. We are doing this study because we want to know parent’s opinions so that we can make this process even better for families in the future.

If you choose to participate in this study, we ask you to please fill out the survey that is included with this letter. The survey contains questions that will ask you about basic demographic information like your age and ethnicity, as well as some questions about your decision to do testing. We will also ask you how you felt about the testing process and the information you were given by the genetic counselor or other medical professional that coordinated the genetic testing. We expect that this survey will take about 15 minutes to complete.

This survey will be completely anonymous and we will not ask you for any identifying information. If any question makes you uncomfortable or upset, you do not need to answer it. Please do not put any names or identifying information in your survey responses.

You can choose to fill out the paper survey provided, which you can send back in the stamped return envelope that has been included, OR

You can fill out the survey online by following the link provided here:
If you have any questions or concerns, please contact Emily Hansen-Kiss, MS, LGC at 614-355-7536 between the hours of 8am-5pm Monday-Friday.

We thank you for your participation in this study.

Sincerely,
Hayley Winslow

**OSU PI:** Dawn Allain, MS, LGC  
**NCH PI:** Emily Hansen-Kiss, MS, MA, LGC  
**Key Personnel:** Hayley Winslow
Appendix F: Group B Study Instructions Letter

Title: Pre- and Post-Test Parent Perceptions of Genetic Testing for Children with Autism Spectrum Disorder (ASD)

OSU PI: Dawn Allain, MS, LGC
NCH PI: Emily Hansen-Kiss, MS, MA, LGC
Key Personnel: Hayley Winslow

Study ID Number: ____________

Invitation to Participate in a Research Study Regarding Parent Perceptions of Genetic Testing for Their Children with an Autism Spectrum Disorder

I am Hayley Winslow, a genetic counseling student at The Ohio State University working with Emily Hansen-Kiss, LGC, a genetic counselor at the Child Development Center/Autism Center at Nationwide Children’s Hospital. You have been invited to participate in this study because your child has been recently diagnosed with an autism spectrum disorder and genetic testing was recommended. We will be requesting that you fill out a survey (8 questions) before the genetic testing is completed and a second survey (8 questions) after you receive the results.

Both surveys are completely anonymous and the only link between them will be your family’s study ID number. After we have finished collecting all survey responses, any documentation linking your family with your assigned study ID number will be destroyed. At that point, we will be unable to link your family back to your survey responses.

You can choose to fill out the paper survey provided, which you can send back in the stamped return envelope that has been included,
OR
You can fill out the first survey online by following the link provided here: http://bit.ly/1Tul5f9

After you are called with the results of your child’s genetic testing, you will be mailed the link to the second survey, along with a paper copy and stamped return envelope. You have the choice of completing these surveys either online or on paper, but please only complete one option.
To remain in the study, we need to have received the completed initial survey before your child has blood drawn for the genetic testing. Results of the second survey will need to be received no later than Friday, November 11th, 2016 in order to allow enough time to analyze the data. If you have not completed a survey within two weeks of initial notification, you will be mailed one reminder letter.

This is your assigned study ID number: _______________
Please enter this number on your survey where it is indicated. This study number will stay the same for both surveys that you complete so that they can be linked and compared.

If any question makes you uncomfortable or upset, you do not need to answer it. Please do not put any names or identifying information in your survey responses.

If you have any questions or concerns, please contact Emily Hansen-Kiss, MS, LGC at 614-355-7536 between the hours of 8am-5pm Monday-Friday.

Thank you again for agreeing to participate in our research study.

Sincerely,

Hayley Winslow
Appendix G: Group B Final Survey Letter

Title: Pre- and Post-Test Parent Perceptions of Genetic Testing for Children with Autism Spectrum Disorder (ASD)

OSU PI: Dawn Allain, MS, LGC
NCH PI: Emily Hansen-Kiss, MS, MA, LGC
Key Personnel: Hayley Winslow

Study ID Number: __________

Invitation to Participate in a Research Study Regarding Parent Perceptions of Genetic Testing for Their Children with an Autism Spectrum Disorder

I am Hayley Winslow, a genetic counseling student at The Ohio State University working with Emily Hansen-Kiss, LGC, a genetic counselor at the Child Development Center/Autism Center at Nationwide Children’s Hospital. You have been invited to participate in this study because your child has been recently diagnosed with an autism spectrum disorder and genetic testing was recommended. We will be requesting that you fill out a survey (8 questions) before the genetic testing is completed and a second survey (8 questions) after you receive the results.

Both surveys are completely anonymous and the only link between them will be your family’s study ID number. After we have finished collecting all survey responses, any documentation linking your family with your assigned study ID number will be destroyed. At that point, we will be unable to link your family back to your survey responses.

You have recently been called with the results of your child’s genetic testing. Included in this letter is the link to the second survey, along with a paper copy and stamped return envelope. You have the choice of completing this survey either online or on paper, but please only complete one option.

You can choose to fill out the paper survey provided, which you can send back in the stamped return envelope that has been included,

OR

You can fill out the first survey online by following the link provided here:

To remain in the study, we need to have received the completed final survey no later than Friday, November 11th, 2016 in order to allow enough time to analyze the data. If you have not completed this survey within two weeks of initial notification, you will be mailed one reminder letter.

This is your assigned study ID number: _______________
Please enter this number on your survey where it is indicated. This study number will stay the same for both surveys that you complete so that they can be linked and compared.

If any question makes you uncomfortable or upset, you do not need to answer it. Please do not put any names or identifying information in your survey responses.

If you have any questions or concerns, please contact Emily Hansen-Kiss, MS, LGC at 614-355-7536 between the hours of 8am-5pm Monday-Friday.

Thank you again for agreeing to participate in our research study.

Sincerely,

Hayley Winslow
Appendix H: Group B Reminder Letters

Reminder to Participate in a Research Study Regarding Parent Perceptions of Genetic Testing for Their Children with an Autism Spectrum Disorder

Dear _________ Family,

You were provided a link and a paper copy of the “Parent Perceptions of Genetic Testing for Their Children with an Autism Spectrum Disorder” survey on _________ date. We have not yet received your response and we are sending this letter as a reminder.

Below is the link to the survey:
First survey: http://bit.ly/1Tul5f9
OR

Please complete the survey before your child has blood drawn for the genetic testing/by no later than Friday, November 11th, 2016.

If you have any questions or concerns, please contact Emily Hansen-Kiss, MS, LGC at 614-355-7536 between the hours of 8am-5pm Monday-Friday.

Sincerely,

Hayley Winslow

**OSU PI:** Dawn Allain, MS, LGC  
**NCH PI:** Emily Hansen-Kiss, MS, MA, LGC  
**Key Personnel:** Hayley Winslow
Reminder to Participate in a Research Study Regarding Parent Perceptions of Genetic Testing for Their Children with an Autism Spectrum Disorder

Dear _____________ Family,

You were mailed a link and paper copy of the “Parent Perceptions of Genetic Testing for Their Children with an Autism Spectrum Disorder” survey after you received results for your child’s genetic testing. You were also mailed a reminder letter. We have not yet received your response. This letter serves as your FINAL REMINDER to please respond to this second survey.

You may fill out the paper survey provided,
OR
Complete the survey online at the link below:

Please complete the survey by no later than Friday, November 11th, 2016.

As a reminder, your study ID number is ______.

If you have any questions or concerns, please contact Emily Hansen-Kiss, MS, LGC at 614-355-7536 between the hours of 8am-5pm Monday-Friday.

Sincerely,

Hayley Winslow

**OSU PI:** Dawn Allain, MS, LGC
**NCH PI:** Emily Hansen-Kiss, MS, MA, LGC
**Key Personnel:** Hayley Winslow