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Assessing the Gaps and Potential Solutions to Improve Access to Genetic Testing for Autistic Individuals

Nisha Dhiren Pandya

ASSESSING THE GAPS AND POTENTIAL SOLUTIONS TO IMPROVE ACCESS TO GENETIC TESTING FOR AUTISTIC INDIVIDUALS

By

Nisha Dhiren Pandya

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Accepted by:

Crystal Hill-Chapman, Director of Thesis

Michelle Macias, Reader

Aubrey Rose, Reader

Lucy Drayson, Reader

Cheryl Addy, Interim Vice Provost and Dean of the Graduate School

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ABSTRACT

The prevalence of Autism Spectrum Disorder (ASD) continues to increase. Numerous genetic syndromes increase the risk of ASD. Professional organizations have published guidelines on the genetic testing recommended for Autistic individuals. However, healthcare providers do not unanimously offer genetic testing or refer for a genetics evaluation. Notably, parents of Autistic individuals express interest in learning about genetic testing as an option for their children.

This study aimed to identify gaps to improve access to genetic evaluations for Autistic individuals and their families. A survey was sent to healthcare providers across the United States that currently see Autistic individuals. We expected to see variable responses from healthcare providers on their perspectives of the role of genetic counseling, the clinical utility of genetic testing for Autistic individuals, and the current published professional guidelines. Of all participants (n=58), 44.1% were developmental and behavioral pediatricians (DBPs), 32.2% were psychologists, and 13.6% were pediatricians. Other fields represented include pediatric/child psychiatry and social work.

Overall, more than half of the healthcare providers indicated that they were comfortable (32.8%) or very comfortable (27.6%) with the professional guidelines about genetic testing for Autistic individuals. Additionally, only 57.1% of providers selected the correct first-tier genetic testing recommended by the American College of Medical Genetics (ACMG) and American Academy of Pediatrics (AAP) guidelines. Most providers believe genetic counselors are an available resource (74.1%); however, not all

are familiar with the full scope of genetic counselors. Due to the gaps identified, there is a need to increase support for healthcare providers routinely seeing Autistic individuals. Maximizing efficient communication between these healthcare providers and genetic counselors can improve ordering appropriate tests and referral rates. Utilizing society/professional organizations and seminars that provide CME credits to communicate practice guidelines will hopefully improve levels of comfort and familiarity. To sustainably provide this support to healthcare providers, the field of genetic counseling must continue to grow. If genetic counselors are an increasingly available resource and communication and interpretation of practice guidelines is improved, then healthcare providers may feel more equipped to provide their patients with increased access to genetic evaluations.

TABLE OF CONTENTS

LIST OF FIGURES

CHAPTER 1: BACKGROUND

1.1 Autism Spectrum Disorder

Autism Spectrum Disorder (ASD) is a neurodevelopmental disorder that is defined by deficits in social and communication skills and repetitive and restricted behaviors (American Psychological Association, n.d.). There is significant variability within the presentation of ASD (Schaefer et al., 2013). The prevalence of ASD is increasing in the United States and is now estimated to be 1 in 44 (Maenner et al., 2021).

A diagnosis of ASD can be established as early as 18 to 24 months of age (Lipkin et al., 2020). Therefore, the American Academy of Pediatrics (AAP) recommends screening for ASD at 18 months and 24 months of age. Patients benefit from early diagnosis of ASD. If an increased risk is recognized, referrals are recommended to allow for evidence-based early intervention (Hyman et al., 2020). Although a diagnosis can be made as early as 18 months of age, the current median age of diagnosis in the United States is 50 months of age, according to the most recent United States epidemiologic study (Council on Children with Disabilities et al., 2006; Lipkin et al., 2020; Maenner et al., 2021). With the prevalence of ASD on the rise, it is important for patients and families to be receiving the recommended resources and healthcare.

1.2 Identifying an Etiology for ASD

ASD is largely considered to have multifactorial inheritance (Kreiman & Boles, 2020). There is increasing evidence that genetics plays a significant role in ASD due to

The high heritability of 0.7 to 0.9 (Schaefer, 2016). Furthermore, a number of genetic syndromes that increase risk for ASD have been identified, including *FMR1* repeat disorder, *MECP2*-related disorders, *PTEN*- related disorders, Angelman syndrome, CHARGE syndrome, Prader-Willi syndrome, Tuberous Sclerosis Complex, Cornelia de Lange syndrome, *MED12* disorders, Smith-Lemli-Opitz syndrome, Smith-Magenis syndrome, Sotos syndrome, and 22q11.2 deletion syndrome (Schaefer et al., 2013). In addition to ASD, genetic syndromes can be associated with medical concerns that, if recognized, can inform screening, prevention, and management recommendations (Schaefer, 2016; Schaefer et al., 2013).

PTEN-related disorders, for example, can be associated with benign and malignant tumors and macrocephaly. There are specific surveillance recommendations that start in childhood for early identification and treatment of tumors in patients with pathogenic *PTEN* variants (Yehia, 2021). It is estimated that about 25% of individuals with *PTEN*-related disorders either meet criteria for ASD or have ASD-like features (Cummings et al., 2022). Therefore, children with macrocephaly and ASD or developmental delay should be evaluated for *PTEN*-related disorders (Yehia, 2021).

Establishing a genetic diagnosis in Autistic individuals can help patients and families feel better educated regarding additional related medical concerns and recurrence risks. Additionally, identification of a genetic cause for symptoms can lead to important changes in management and surveillance, and can prevent gratuitous testing (Schaefer, 2016; Schaefer et al., 2013; Shafqat et al., 2022).

One recent retrospective study of 500 Autistic toddlers using *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5)* criteria found that 59.8%

of families chose to pursue genetic testing for their toddler (Harris et al., 2020). The study found the diagnostic yield for chromosomal microarray (CMA) and *FMR1* repeat testing to be 12% for Autistic individuals. Out of the patients with pathogenic variants, about 72% had relevant clinical recommendations associated with genetic testing results. Overall, 8.7% of all patients in this study had relevant clinical recommendations. Examples of clinical recommendations included echocardiograms, renal ultrasounds, audiology evaluations, ophthalmology evaluations, and epilepsy management. These findings highlight the clinical utility of genetic testing for Autistic individuals (Harris et al., 2020).

For Autistic individuals, the American College of Medical Genetics (ACMG) estimates a diagnostic yield of 10% for CMA, 1-5% for *FMR1* repeat testing, 4% for *MECP2* analysis in females, 5% for *PTEN* analysis, 3% for karyotype, and 10% for additional genetic testing. However, the overall diagnostic yield for Autistic individuals that receive a genetics evaluation, which includes family history, physical examination, and the appropriate genetic tests is estimated to be 30-40% (Schaefer et al., 2013). If healthcare providers that routinely see Autistic individuals are familiar with the diagnostic yield of genetic evaluations, they may become more comfortable with communicating the clinical utility with their patients.

1.3 Professional Guidelines on Genetic Testing for Autistic Individuals

In 2013, ACMG published guidelines recommending that every Autistic individual be offered a genetic evaluation. An in-depth genetic evaluation includes discussing family history, conducting a physical examination to assess features present, and offering first-tier and second-tier genetic testing as indicated. Additionally, ACMG

recommends that all patients who receive a genetic evaluation also receive genetic counseling. The guidelines also state that the referring provider, typically the primary care provider, should provide background information prior to the genetic evaluation, including expectations for the appointment. After the genetics evaluation has been completed, it is recommended that each patient have a primary care medical home and that the primary care provider and clinical geneticist collaborate with follow-up care (Schaefer et al., 2013).

Cytogenetic testing used to be the first-tier test recommended by ACMG for identifying the etiology of ASD (Manning et al., 2010; Schaefer et al., 2013). CMA has increased the diagnostic yield and is now recommended by ACMG as first-tier testing for Autistic individuals, replacing karyotype, combined with *FMR1* repeat testing for males. It is important to note that if a patient has clinical features of certain genetic syndromes that have known associations with ASD, such as *PTEN*-related disorders, targeted testing should be considered (Schaefer et al., 2013). Several other professional organizations have published guidelines for healthcare providers independently. The AAP published recommendations in 2020 stating that all Autistic individuals should be offered genetic evaluations including a detailed family history and physical examination, with CMA and *FMR1* repeat testing as first-tier tests, similar to the ACMG guidelines. However, the AAP also states that whole exome sequencing (WES) can be considered if initial testing is negative (Hyman et al., 2020). The National Society of Genetic Counselors (NSGC) published practice guidelines for *FMR1* repeat disorder, recommending that both Autistic males and females should be offered *FMR1* repeat testing (Finucane et al., 2012). The American Academy of Child and Adolescent Psychiatry (AACAP) published guidelines

in 2014 stating that clinicians should offer a medical evaluation to all Autistic individuals, including genetic testing. Although they state that CMA is the first-tier test that medical geneticists recommend and include supporting evidence of the diagnostic yield, the guidelines do not say that CMA should be offered to all Autistic individuals (Volkmar et al., 2014). In addition, the American Academy of Neurology (AAN) published guidelines in 2000 recommending karyotype and *FMR1* repeat testing for certain patients; however, those guidelines are now retired (American Academy of Neurology, n.d.; Filipek et al., 2000). The timing of professional organizations' guideline publications, and the specific recommendations and phrasing of their guidelines differ. Therefore, there is no standard protocol available for all healthcare providers to follow.

As genetic testing methodologies advance, the diagnostic yields for ASD continue to increase. Studies have investigated the benefits of WES for Autistic individuals. Du et al. (2018) found a 9.2% diagnostic yield of WES for Autistic individuals that had prior non-diagnostic CMA results. An additional study found the WES diagnostic yield to be 14.6% for Autistic individuals, while the diagnostic yield for CMA was 2.9% and for *FMR1* repeat testing was 0.9% (Arteche-López et al., 2021). Due to swift advances in this field, the guidelines will likely update again in the coming years (Schaefer, 2016). Given these fast-paced changes, WES might be a future first-tier test for Autistic individuals. Therefore, clinical processes and protocols will need to adapt so healthcare providers can efficiently implement changes in genetic testing practice guidelines (Arteche-López et al., 2021; Schaefer, 2016).

1.4 Compliance to Professional Guidelines on Genetic Testing for Autistic Individuals

Although there are published guidelines with specific recommendations, studies have shown that genetic evaluations and genetic testing are not offered to all Autistic individuals (Barton et al., 2018; Rutz et al., 2019; Tchaconas & Adesman, 2017). Additionally, the overall utilization of genetic testing is low (Shafqat et al., 2022). A study of 108 Utah pediatricians demonstrated that 24% do not discuss genetic etiology of ASD with families, and only 9% discuss it routinely (Rutz et al., 2019). Only 24% of the providers surveyed believe that genetic testing should be offered to all Autistic children. However, 55% expressed that they were familiar with the ACMG practice guidelines, stating that every Autistic individual should be offered a genetics evaluation. Therefore, there is discordance between healthcare providers' self-reported familiarity with genetic testing guidelines and their adherence to them (Rutz et al., 2019).

In an interview-based study of families and providers, a developmental pediatrician stated that there is no standard protocol they follow to decide when to refer Autistic patients to a geneticist. In addition, some providers expressed that they only refer their Autistic patients to genetics clinics based on various factors such as the number of features present and the provider's level of comfort. Healthcare providers also expressed discordance with the different guidelines and did not fully understand the clinical utility of genetic testing for Autistic individuals (Barton et al., 2018).

Given two scenarios, Autistic individuals with intellectual disability and Autistic individuals without intellectual disability, 267 developmental pediatricians and child neurologists were asked which tests they would order (Tchaconas & Adesman, 2017).

For both scenarios, over 75% of providers said they would order one or more tests discordant with guidelines. The types of tests selected included MRIs, CT scans, EEGs, karyotypes, and metabolic tests. Overall, the published guideline compliance rate was 18.4% for the Autistic individuals and intellectual disability scenario and 16.9% for the Autistic individuals without intellectual disability (Tchaconas & Adesman, 2017). Results of these studies emphasize that healthcare providers are practicing differently regarding offering genetic testing to Autistic individuals and do not consistently follow the guidelines published by professional organizations (Barton et al., 2018; Tchaconas & Adesman, 2017). Additionally, some providers stated that there is no standard protocol due to the variability in guidelines published by different professional organizations (Barton et al., 2018). The gap present between healthcare providers' practice and the guidelines for seeing Autistic individuals is evident based on these prior reports.

To further understand potential reasons why this gap exists, Rutz et al. (2019) assessed the barriers physicians experience ordering genetic testing. Some common barriers included wait times for appointments with geneticists, insurance coverage and test prices, and minimal confidence in ordering tests, interpreting results, and discussing the results with patients. Thirty percent of physicians in this study cited lack of professional guidelines. Additionally, 10% of physicians ordering genetic testing reported minimal communication with genetic counselors as a barrier (Rutz et al., 2019). Therefore, resources for accessing support and education are critical for improved patient outcomes.

1.5 Parental Perspective on Genetic Testing for Autistic Children

Studies assessing parents' perspectives on genetic testing for their Autistic children show that parents are interested in access to genetic testing (Chen et al., 2013; Zhao et al., 2019; Zhao et al., 2021). One study identified that about 44% of 552 parents were either not aware of or minimally aware of genetic testing, even though most were open to learning about it (Zhao et al., 2019). In a study of 1280 Autistic individuals from 2013 to 2019, only 16.5% had genetic testing. Out of those patients that received genetic testing, 3% self-reported having both *FMR1* repeat testing and CMA (Moreno-De-Luca et al., 2020). In Chen et al. (2013), 30 out of 42 parents did not pursue genetic testing for their children. Of those parents that did not pursue testing, 63% were not familiar with genetic testing as an option. Additionally, 69% of the parents in this study had positive attitudes toward genetic testing. Some of the reasons they supported genetic testing included access to interventions, a known etiology, and family planning (Chen et al., 2013). A genetic diagnosis can provide resources to families through increased education and support groups. In Barton et al. (2018), a family that pursued genetic testing and obtained a genetic diagnosis connected with a support group that provided additional resources specific to their child's genetic diagnosis. Some parents shared concerns about genetic testing and believed there is lack of clinical utility, and it could potentially harm their children or families (Chen et al., 2013). Another study showed that 90% of 397 parents agreed that genetic testing has clinical utility and 86% were interested in additional information about the genetics of ASD. However, despite the interest level, in this study only about 40% of Autistic individuals had genetic testing (Cuccaro et al., 2014).

Parents have also expressed that their healthcare providers never discussed genetic testing. In Cuccaro et al. (2014), 21.3% of 397 parents of Autistic children received a genetics referral and 41.2% of parents stated that their children received genetic testing. In another study by Zhao et al. (2019), out of all parents that had heard of genetic testing, only about 35% learned about it from physicians. The other ways parents learned about genetic testing included the internet, support groups, research articles, and other parents. In this study, parents were interested in learning more about the accuracy, cost, benefits, logistics, eligibility, and concerns of genetic testing (Zhao et al., 2019). Overall, these studies show the importance of healthcare providers having the resources and knowledge to answer questions and discuss concerns accurately with parents and families. Furthermore, it is salient for parents to receive education on all aspects of genetic testing and the potential implications for them to decide whether they want to move forward with genetic evaluations or testing (Schaefer, 2016). To improve access to genetic testing for patients and families, healthcare providers must be well-informed and proficient regarding genetic testing practice guidelines.

1.6 Purpose

Since there are gaps in healthcare providers' knowledge and familiarity regarding professional guidelines and recommending genetics referrals or testing to Autistic patients, it is important to identify potential solutions so that testing guidelines can be more easily accessible for and utilized by healthcare providers. It is also crucial to understand current patterns of referencing genetic testing guidelines, knowledge, and level of comfort with the guidelines, and resources that providers find helpful. The current study aimed to include relevant provider specialties across the nation and add the

perspective of which tools providers would prefer as solutions to these gaps in care regarding ASD and genetic testing.

Rutz et al. (2019) exhibited several gaps in understanding of guidelines and beliefs about whether providers should discuss genetics referrals or testing with their patients. Furthermore, some providers expressed that they had never worked with a genetic counselor in their career. Additionally, this study highlighted barriers that are present for providers, such as knowledge of insurance coverage and test prices and lack of access to genetic counselors (Rutz et al., 2019). The current investigation was conducted to obtain a more recent, national participant pool inclusive of more specialties that care for Autistic individuals. It also included a focus on which tools providers find helpful to improve these gaps in care. Barton et al. (2018) highlighted several gaps expressed by healthcare providers, including limited standard protocol, discordance with the guidelines and what they learned in training, and a limited understanding concerning the clinical utility of testing. These results show that it is essential that healthcare providers understand the clinical utility and professional guidelines to meet the needs of patients and their families (Barton et al., 2018).

With how rapidly advancements are occurring for genetic testing methodologies such as whole exome sequencing or whole genome sequencing, it is likely that the professional guidelines will continue to be updated frequently (Schaefer, 2016). If there are still gaps in healthcare providers' implementation of genetic testing guidelines, solutions need to be identified to address these gaps and to enhance access to genetics evaluations for patients and families affected by ASD.

Since there is interest from parents, a low utilization of genetic testing, and a lack of clinical practice aligning with national guidelines, this research study aimed to identify gaps to improve access to genetic evaluations for Autistic patients and their families. This study had the following objectives: (1) Evaluate the practice gap concerning offering genetic evaluations for health care providers seeing Autistic individuals, (2) Assess healthcare providers' implementation of genetic testing practice guidelines, (3) Investigate healthcare providers' perspectives of the role of genetic counseling, (4) Identify healthcare providers' perspectives of the clinical utility of genetic testing for Autistic individuals, and (5) Explore tools to improve confidence and familiarity with offering genetic testing for Autistic individuals.

We expected to see variable responses from healthcare providers on their perspectives of the role of genetic counseling, the clinical utility of genetic testing for Autistic individuals, and the professional guidelines. Additionally, we expected to learn what providers prefer as methods to improve the gaps in care.

CHAPTER 2: ASSESSING THE GAPS AND POTENTIAL SOLUTIONS TO IMPROVE ACCESS TO GENETIC TESTING FOR AUTISTIC INDIVIDUALS[1]

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2.1 Abstract

The prevalence of Autism Spectrum Disorder (ASD) continues to increase. Numerous genetic syndromes increase the risk of ASD. Professional organizations have published guidelines on the genetic testing recommended for Autistic individuals. However, healthcare providers do not unanimously offer genetic testing or refer for a genetics evaluation. Notably, parents of Autistic individuals express interest in learning about genetic testing as an option for their children.

This study aimed to identify gaps to improve access to genetic evaluations for Autistic individuals and their families. A survey was sent to healthcare providers across the United States that currently see Autistic individuals. We expected to see variable responses from healthcare providers on their perspectives of the role of genetic counseling, the clinical utility of genetic testing for Autistic individuals, and the current published professional guidelines. Of all participants (n=58), 44.1% were developmental and behavioral pediatricians (DBPs), 32.2% were psychologists, and 13.6% were pediatricians. Other fields represented include pediatric/child psychiatry and social work.

Overall, more than half of the healthcare providers indicated that they were comfortable (32.8%) or very comfortable (27.6%) with the professional guidelines about genetic testing for Autistic individuals. Additionally, only 57.1% of providers selected the correct first-tier genetic testing recommended by the American College of Medical Genetics (ACMG) and American Academy of Pediatrics (AAP) guidelines. Most providers believe genetic counselors are an available resource (74.1%); however, not all are familiar with the full scope of genetic counselors.

Due to the gaps identified, there is a need to increase support for healthcare providers routinely seeing Autistic individuals. Maximizing efficient communication between these healthcare providers and genetic counselors can improve ordering appropriate tests and referral rates. Utilizing society/professional organizations and seminars that provide CME credits to communicate practice guidelines will hopefully improve levels of comfort and familiarity. To sustainably provide this support to healthcare providers, the field of genetic counseling must continue to grow. If genetic counselors are an increasingly available resource and communication and interpretation of practice guidelines is improved, then healthcare providers may feel more equipped to provide their patients with increased access to genetic evaluations.

2.2 Introduction

Autism Spectrum Disorder (ASD) is a neurodevelopmental disorder with significant variability in presentation and is defined by deficits in social and communication skills and repetitive and restricted behaviors (American Psychological Association, n.d.; Schaefer et al., 2013). In the United States, the prevalence continues to increase and is now reported to be 1 in 44 (Maenner et al., 2021). Although an ASD diagnosis can be established as early as 18 to 24 months of age, the current median age of diagnosis in the United States is 50 months of age (Council on Children With Disabilities et al., 2006; Lipkin et al., 2020; Maenner et al., 2021). An early diagnosis is beneficial to allow for evidence-based early intervention (Hyman et al., 2020).

ASD has a high heritability of 0.7 to 0.9 providing evidence that genetics plays an essential role. Several genetic syndromes that increase the risk for ASD have been identified, including *FMR1* repeat disorder, *MECP2*-related disorders, *PTEN*- related

disorders, and Angelman syndrome (Schaefer et al., 2013). Establishing an underlying genetic etiology can inform patients and families regarding associated medical concerns and recurrence risks. Additionally, further gratuitous genetic testing can be prevented and management and surveillance recommendations can be made (Schaefer, 2016; Schaefer et al., 2013; Shafqat et al., 2022). For example, *PTEN*-related disorders can be associated with benign and malignant tumors. For individuals with pathogenic *PTEN* variants, specific surveillance recommendations can be offered in childhood for early identification and treatment of tumors (Yehia, 2021).

The American College of Medical Genetics (ACMG) recommends that every Autistic individual be offered a genetic evaluation. A genetic evaluation includes a review of family history, a physical examination, offering first-tier and second tier-testing as indicated, and genetic counseling. The estimated diagnostic yield for a genetics evaluation for Autistic individuals is reported to be 30-40% (Schaefer et al., 2013).

Several professional organizations have published guidelines on the recommended genetic testing for Autistic individuals. ACMG published guidelines in 2013 recommending chromosomal microarray (CMA), replacing karyotype, and *FMR1* repeat testing for males as first-tier testing. If an individual has clinical features specific to a genetic syndrome associated with ASD, targeted testing may be recommended (Schaefer et al., 2013). The AAP published recommendations in 2020 stating that all Autistic individuals should be offered genetic evaluations including a detailed family history and physical examination, with CMA and *FMR1* repeat testing being the first-tier genetic tests. Furthermore, the AAP states that whole exome sequencing (WES) can be considered if initial testing is negative (Hyman et al., 2020). The *FMR1* repeat disorder

guidelines published by the National Society of Genetic Counselors (NSGC) in 2012 recommend that both Autistic males and females be offered *FMR1* repeat testing (Finucane et al., 2012). In 2014, the American Academy of Child and Adolescent Psychiatry (AACAP) stated that a medical evaluation, which includes genetic testing, should be offered to all Autistic individuals and also lists CMA as a first-tier test (Volkmar et al., 2014). Each professional organization has differences in the phrasing and specificities of recommendations. Standard guidelines that all healthcare providers reference for offering genetic testing to Autistic individuals do not exist.

Although there are published guidelines, studies have shown that not all Autistic individuals are offered genetic evaluations and the overall utilization of testing is low (Barton et al., 2018; Rutz et al., 2019; Shafqat et al., 2022; Tchaconas & Adesman, 2017). Only some healthcare providers who see Autistic individuals discuss genetics with families and believe all Autistic individuals should be offered genetic testing (Rutz et al., 2019). Healthcare providers have also expressed that the published guidelines are variable and discordant (Barton et al., 2018). In Tchaconas & Adesman (2017), developmental and behavioral pediatricians and child neurologists were given two scenarios of Autistic individuals. For both scenarios, most healthcare providers chose to order genetic tests that did not align with the guidelines. In addition, some healthcare providers do not entirely agree with the clinical utility of genetic testing for Autistic individuals (Barton et al., 2018). Therefore, a clear gap exists between healthcare providers' practice and the published guidelines for Autistic individuals.

Parents of Autistic individuals are open to learning more about genetic testing and are interested in access to genetic testing for their Autistic children (Chen et al., 2013;

Zhao et al., 2019; Zhao et al., 2021). However, not all parents are familiar with genetic testing as an option (Chen et al., 2013; Zhao et al., 2019). Furthermore, some parents express that they do not receive a referral for a genetics evaluation and do not learn about genetic testing from their Autistic children's healthcare providers (Zhao et al., 2019). To improve access to genetic testing for patients and families, healthcare providers must be well-informed regarding genetic testing practice guidelines.

A more recent national study assessing healthcare providers' understanding and level of comfort with genetic evaluations for Autistic individuals and how to potentially bridge the previously identified gaps is warranted. This study had the following objectives: (1) Evaluate the practice gap of offering genetic evaluations for healthcare providers seeing Autistic individuals, (2) Assess healthcare providers' implementation of genetic testing practice guidelines, (3) Investigate healthcare providers' perspectives on the role of genetic counseling, (4) Identify healthcare providers' perspectives of the clinical utility of genetic testing for Autistic individuals, and (5) Explore tools to improve level of comfort and familiarity with offering genetic testing for Autistic individuals.

2.3 Methods

The current study utilized a questionnaire to directly examine responses from healthcare providers across the United States. Items of the questionnaire were developed to address each objective of this study. Additionally, this study was approved by the University of South Carolina Institutional Review Board (#Pro00122804).

Healthcare providers have been reported to prefer person-first language; however, it is reported that most individuals of the Autistic community prefer identity-first

language (Botha et al., 2023; Taboas et al., 2023). To be most respectful and inclusive of the Autistic community, identity-first language will be used in this paper.

2.3.1 Survey

The questionnaire was designed through Qualtrics.com. It included qualitative and quantitative questions in the form of Likert scales, text-entry, ranking, multiple-choice, matrix, and selection of all which apply. A total of 35 questions were included in the questionnaire (see Appendix D). The items assessed the knowledge and usage of professional guidelines, the understanding of genetic counselors' roles, the clinical utility of genetic testing, and preferences for tools to improve the present gaps. In addition, there were five scenario-based questions that simulated patient indications to identify how the healthcare providers would approach genetic testing. Demographic questions were also included to elucidate the professional background and experience of the respondents such as their title as a healthcare provider, the type of certification and licensure they hold, the years of experience as a licensed or certified provider, the state or territory of the United States they practice in, the types of communities they routinely practice in, and if they care for an Autistic child at home. One item assessed the participants' involvement in specific programs and organizations. Two common programs/organizations were listed as possible selections in this question: Leadership Education in Neurodevelopmental and Related Disabilities (LEND) and the research study, SPARK. The questionnaire did not include personal identifying questions. The items were developed and approved by the principal investigator, two genetic counselors, a psychologist, and a developmental and behavioral pediatrician.

At the end of the questionnaire, a message appeared to the respondents thanking them for participating. This message included details for participants to opt-in to a raffle to win a gift card, including a separate link to a Qualtrics.com form to enter their email address if they chose to participate. Five participants that opted-in for the raffle were randomly selected via a random number generator. After the questionnaire closed, five Amazon gift cards of $25 each were sent to the selected participants (see Appendix E). The raffle was funded by a $125 grant awarded to the principal investigator by the National Society of Genetic Counselors Pediatric Special Interest Group.

2.3.2 Participants and Procedures

Participants were included if they currently see Autistic individuals, have certification or licensure as a healthcare provider in the United States and are a healthcare provider that practices within the United States. Participants were excluded if they identified as a genetics professional.

An invitation letter that summarized the study, consented the participants, and included a link to the survey was posted on the Society for Developmental and Behavioral Pediatrics' discussion board (see Appendix A). Additionally, clinics and providers across the United States were contacted via email with the invitation letter (see Appendix B). A flyer that advertised the study and included a QR code for the invitation letter was also emailed to various clinics and providers across the United States (see Appendix C).

Data were collected from August to December 2022. The survey initially had 76 responses. Out of the 76 responses, 18 were excluded based on the exclusion criterion (n=2), trial responses (n=8), and completion rate (n=8). A survey was deemed incomplete

if participants completed less than 66% of the survey, excluding the demographic questions. After exclusion, the final participant sample was 58. To continue the survey, all participants had to select that they currently see or diagnose Autistic individuals.

2.3.3 Data Analysis

The data from Qualtrics.com were exported into Microsoft Excel and all responses were anonymous with no personal identifying information. Microsoft Excel and manual calculations were used to analyze quantitative data through frequencies, percentages, mean, median, mode, and range. Microsoft Excel and Microsoft Word were also used to create figures and tables. Statistical Package for Social Sciences (SPSS) was used for a Wilcoxon signed rank test to determine statistical significance for item 25. For each scenario-based question, responses were classified as either appropriate or not appropriate responses based on the clinical guidelines (Hyman et al., 2020; Manickam et al., 2021; Schaefer et al., 2013). If participants chose to refer to genetics professionals for each scenario and either chose not to order any diagnostic tests or chose to order diagnostic tests that would be appropriate based on the guidelines, the responses were classified as appropriate. If participants chose not to refer to genetics professionals, the response was classified as not appropriate. In addition, if participants chose diagnostic tests that were not warranted based on the clinical guidelines, they were classified as not appropriate. For item 17, if participants selected the correct recommended first-tier testing according to clinical guidelines and also chose ‘up to the clinician’ it was counted as correct. ‘Up to the clinician’ can be interpreted as additional targeted testing as indicated, which can align with the guidelines (Hyman et al., 2020; Schaefer et al., 2013). However, the variety of interpretation of ‘up to the clinician’ is a limitation of the study.

Themes were developed by the principal investigator and two genetic counselors for survey question nineteen, asking participants what the role of a genetic counselor is. If a topic or category was identified three or more times among the responses, it was counted as a theme. For standardization, certain categories were defined in Table 2.1.

Table 2.1 *Definitions used for selecting themes*

Education	1. Resources 2. Providing information 3. Explaining/counseling on genetic diagnosis
Pre-test counseling	1. Education about tests 2. Risks and benefits of testing 3. Possible outcomes 4. Consent
Post-test counseling	1. Interpreting results 2. Reviewing results
Care coordination	1. Next steps 2. Posttest decisions and recommendations

2.4 Results

2.4.1 Demographics

As seen in Table 2.2, of all the non-mutually exclusive provider titles identified by the participants, DBPs (44.1%) and psychologists (32.2%) were represented the most. While most participants practice in South Carolina (32.1%), 20 other states were represented (Figure 2.1). The average number of Autistic patients seen by the participants was 6.77 patients per week. Furthermore, the range of experience since becoming licensed or certified was 1 year to 35 years, while the average was 12.2 years. More than half of participants are not ordering providers of genetic testing (51.9%), while 48.1% are ordering providers (Table 2.2).

Table 2.2 *Demographics* [a]Due to rounding of values, the total percentage values for provider type is equivalent to 100.1%, [b]The total for license/certification type is 99.9%, [c]The total for years of experience is 100.1%, [d]Participants could identify more than one provider type and license/certification type

Demographic	Responses	Total (n)	Percent
Provider type[a,d] (n=59)	Developmental and Behavioral Pediatrician	26	44.1%
	Psychologist	19	32.2%
	Pediatrician	8	13.6%
	Pediatric/Child Psychiatrist	4	6.8%
	Social Worker	2	3.4%
License/Certification type[b,d] (n=65)	MD/DO	32	49.2%
	PhD/PsyD/LP/NCSP	23	35.4%
	CPNP/PNP/ARNP	5	7.7%
	LISW-CP/MSW	3	4.6%
	BCBA	1	1.5%
	MA	1	1.5%
Years of experience[c] (n=54)	0-5 years experience	16	29.6%
	6-10 years experience	12	22.2%
	11-15 years experience	11	20.4%
	16-20 years experience	5	9.3%
	21-25 years experience	4	7.4%
	26-30 years experience	3	5.6%
	31-35 years experience	3	5.6%
ASD patients seen weekly (n=53)	0-5 patients weekly	29	54.7%
	6-10 patients weekly	18	34.0%
	11-15 patients weekly	2	3.8%
	16-20 patients weekly	4	7.5%
Genetic testing ordering ability (n=54)	Ordering provider	26	48.1%
	Not an ordering provider	28	51.9%
Care for child with ASD at home (n=55)	Yes	1	1.8%
	No	54	98.2%

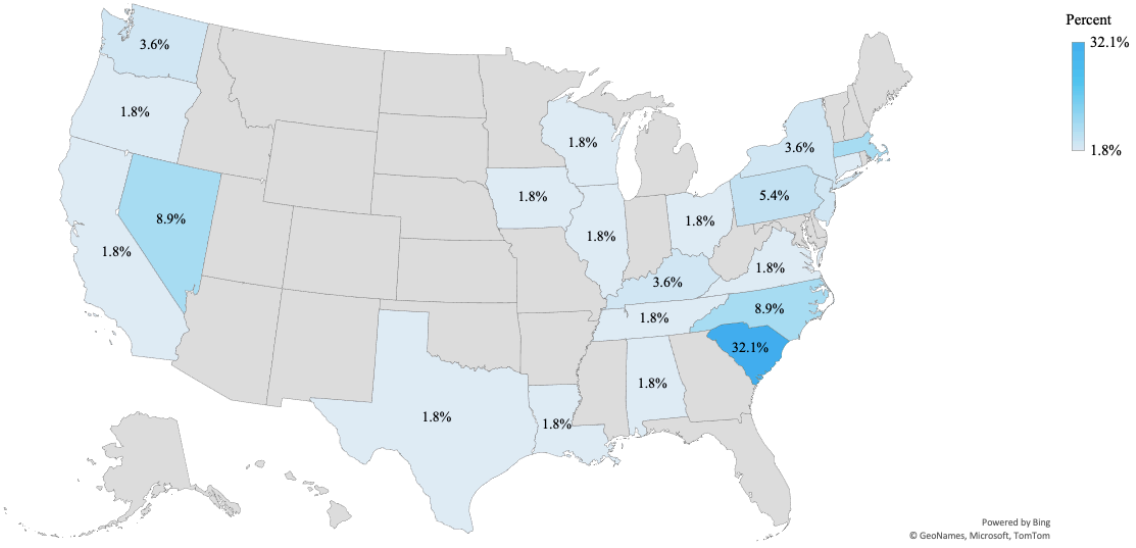

Figure 2.1 *States where participants practice* Due to rounding of values, the total percentage value is equivalent to 100.2%. Furthermore, participants could identify more than one state where they practice in (n=56).

In a select all that apply question, most participants identified that they either did or do participate in LEND and SPARK (32.7%); 23.6% participate in LEND alone, 5.5% participate in SPARK alone, and 29.1% do not participate in any program or organization. Participants that selected other programs or organizations (5.5%) listed SDBP, University Centers for Excellence in Developmental Disabilities (UCEDD), and ECHO Autism.

2.4.2 Professional organizations

Of all participants (n=57), most follow American Academy of Neurology (AAN) and AAP for clinical practice guidelines (Figure 2.2). For those that selected 'other', several listed SDBP and American Psychological Association (APA). One participant indicated that they know these organizations exist, but they do not closely follow one. Four participants follow ACMG, AACAP, AAP, and AAN, one of which also listed

'other'. Three participants follow ACMG and AAP for clinical practice guidelines. Two participants selected that they follow ACMG, AAP, and AACAP.

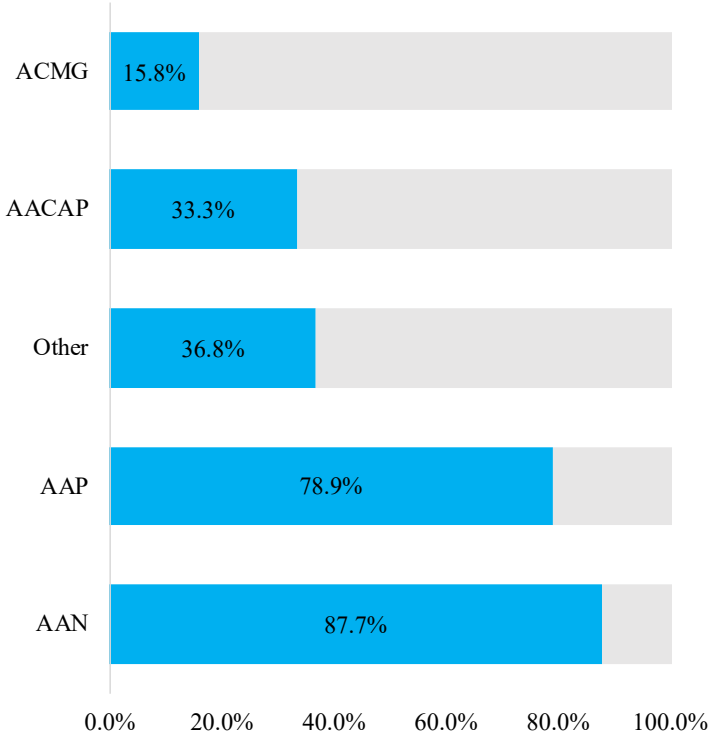

Figure 2.2 *Professional organizations participants follow* Participants could select all that apply (n=57)

2.4.3 Clinical guidelines

Most participants were familiar (56.9%) or very familiar (20.7%) with the clinical guidelines for which genetic tests to offer Autistic patients; however, 22.4% were either unfamiliar or very unfamiliar (Figure 2.3). More than half of the participants were either comfortable (32.8%) or very comfortable (27.6%) with the guidelines; however, 39.7% were either uncomfortable or very uncomfortable (Figure 2.4). All but three participants agree or strongly agree that there is clinical utility for genetic tests for Autistic individuals (Figure 2.5).

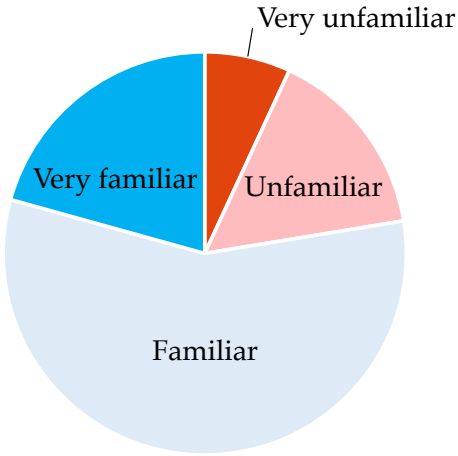

Figure 2.3 *Familiarity with clinical guidelines*

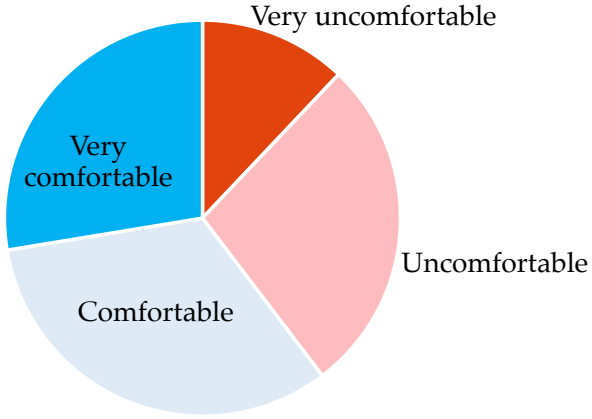

Figure 2.4 *Comfort level with clinical guidelines*

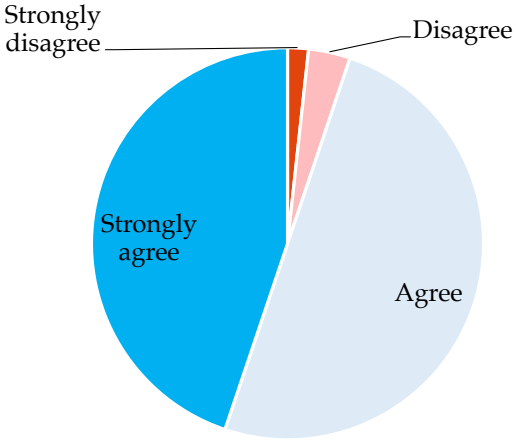

Figure 2.5 *Level of agreement with the following statement: Genetic tests have clinical utility*

Participants (n=56) selected which test(s) they believe is the recommended first-tier test for Autistic patients (Figure 2.6). Most participants selected CMA and Fragile X testing (FGX) (51.8%). Three participants chose CMA, FGX, and up to the clinician. Therefore, 57.1% of participants correctly selected the first-tier genetic testing recommended by ACMG and AAP, when including CMA, FGX, +/- 'up to the clinician'. Other participants also chose CMA and FGX with either WES or karyotype.

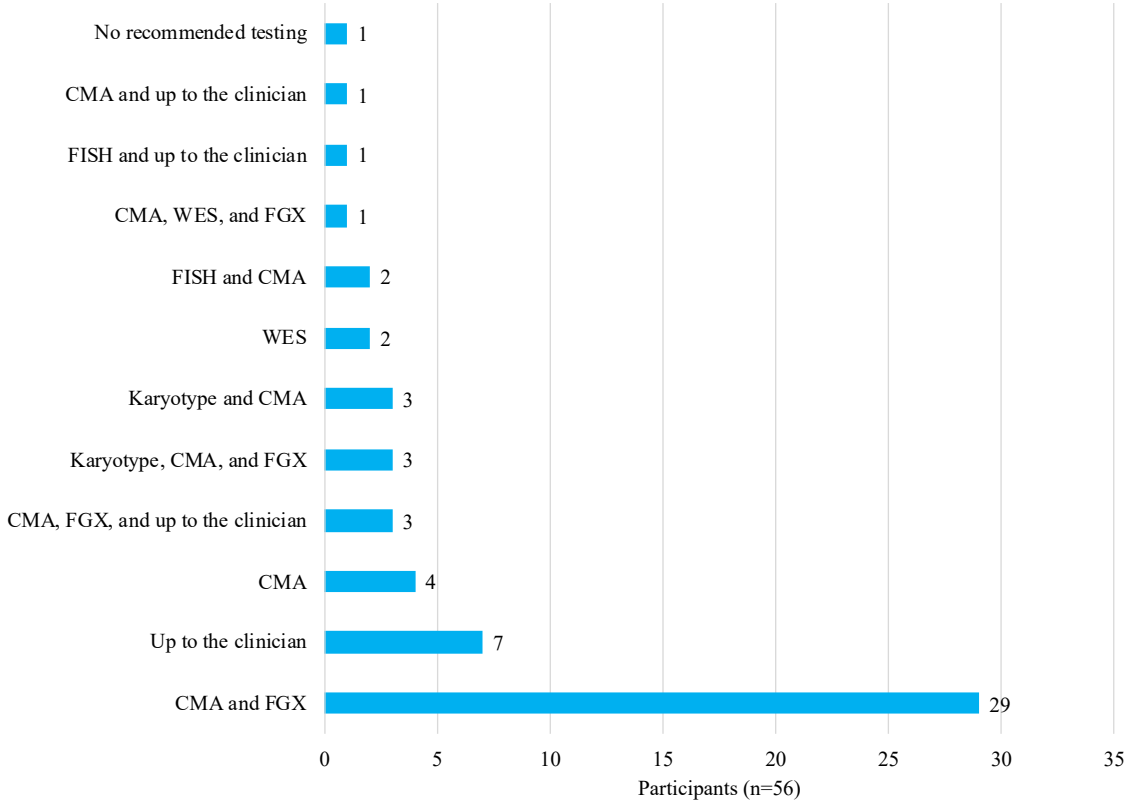

Figure 2.6 *Participants' selection of first-tier testing*

However, when participants (n=58) were asked if they discuss or offer genetic testing to all Autistic individuals, only 70.7% selected 'yes'. Participants who selected that they do not discuss or offer genetic testing to all Autistic individuals were asked to provide reasons when they would choose to discuss or offer genetic testing. Of those 17 participants, eight stated additional medical concerns, six listed family history, three

listed if the presentation is more severe, two listed if the family/patient requests it, two listed if there is a suspected syndrome, and two listed if a specialist/provider recommends it. One participant listed history of genetic testing as a reason to offer or discuss genetic testing. Three shared they would discuss genetic testing if the presentation were more severe, including one participant who also stated that they would discuss or offer genetic testing if the onset of developmental delay was before age five. One participant shared that they "do not find genetic testing very useful" because it does not yield management changes and they have had patients without ASD who have also been found to have genetic changes in the same genes as their Autistic patients. A different participant noted that they hope to discuss genetic testing with all patients, however lack of time and overwhelmed families are reasons that they are not able to. The same provider indicated that they try to discuss genetic testing at follow-up visits. Another participant indicated that after an ASD diagnosis is made, they refer to genetics. However, they did not indicate that they discuss or offer genetic testing to all Autistic patients.

Of all participants, 12.1% never consult the clinical guidelines for Autistic individuals (ex. ACMG, AAP, AACAP guidelines), while 36.2% always consult the clinical guidelines (Figure 2.7). Participants (n=56) shared how they find out about practice guidelines and could select all that apply. Most participants selected independently through society, professional organization websites and/or clinical reports (85.7%) and/or through institutions and/or clinics (67.9%). Less than half of participants chose seminars (44.6%). In the open text entry to identify other methods, some participants mentioned psychiatry grand rounds, colleagues, a geneticist, AAP daily digests, national conferences, and regular reviews of literature.

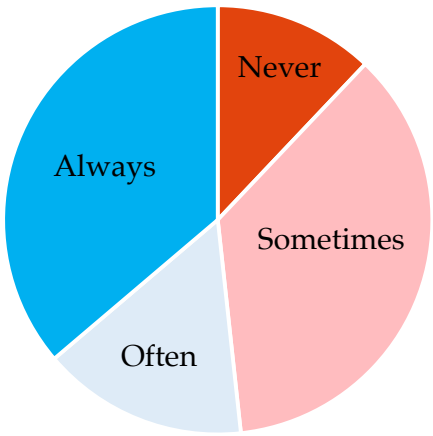

Figure 2.7 *Participant clinical guideline consultation*

2.4.4 Understanding of genetic counselors and accessibility

Participants (n=55) identified who they would contact if they had an inquiry about genetic testing. Most identified a genetics department/institution or a specific geneticist/genetic counselor (84.5%). Some participants identified pediatricians (6.9%), DBPs (3.4%), and a neurologist (1.7%). One participant expressed that they do not have a contact.

Participants were asked how they define the role of a genetic counselor in an open text entry question (Figure 2.8). Forty-one responses were included; some participants did not complete this item and two responses were excluded. A total of nine themes were identified. Most participants listed posttest counseling, followed by pretest counseling, counseling families, and education. None of the participants identified all nine themes in their response. One participant identified consenting the family within the role of genetic counselors. One participant indicated that their understanding of a genetic counselors' role is that it differs depending on different states and institutions they are in and on their level of independence and autonomy. Two participants only knew of genetic counselors'

role in a prenatal or preconception setting. Furthermore, one participant said that they were “unsure” and another had “minimal to some understanding”. Other roles identified that were not considered themes include insurance, ordering/facilitating tests, knowing guidelines, deciding tests to order, gathering information, advising other professionals, and facilitating patient decisions.

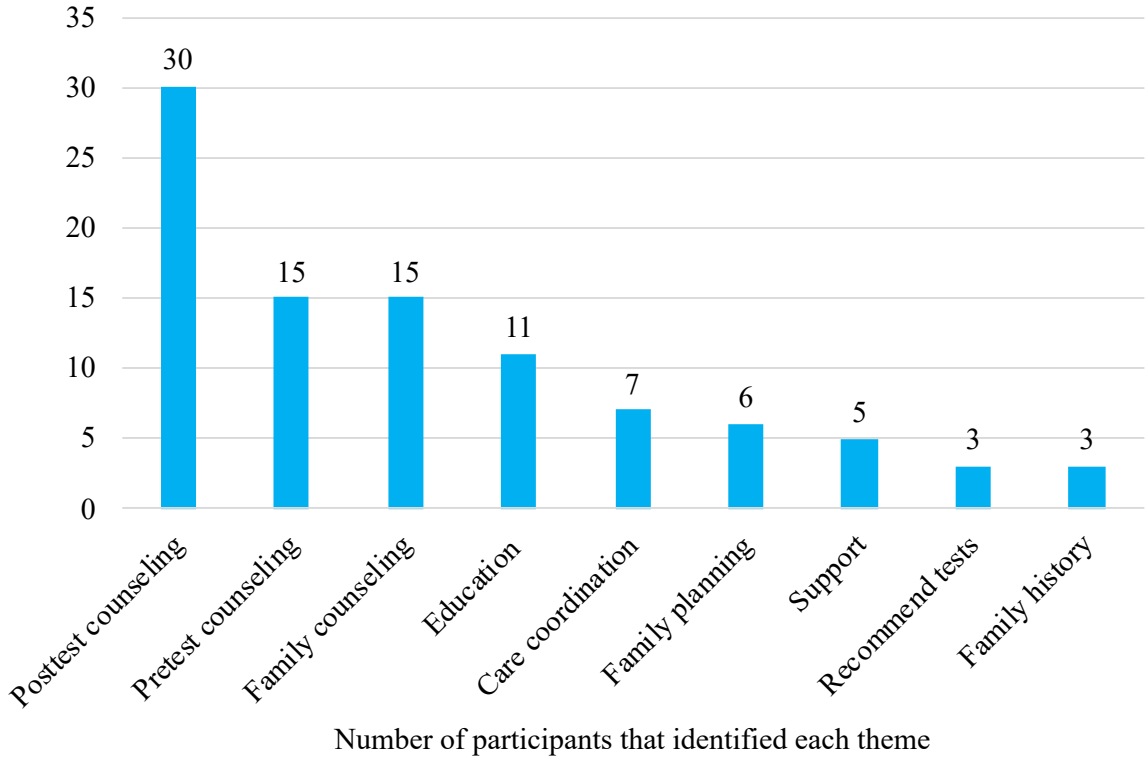

Figure 2.8 *Role of genetic counselors*

Most participants (n=58) agree (43.1%) or strongly agree (31.0%) that genetic counselors are an available resource. However, 25.8% of participants either strongly disagree or disagree that genetic counselors are an available resource. Due to rounding, the total percentage is equal to 99.9%. Furthermore, out of all participants (n=58), 77.6% of participants have access to a genetic counselor or genetics team within or near their practice but 25.9% of all participants never interact with genetic counselors. All

participants (n=58) agreed or strongly agreed that genetic counselors add value to their profession.

2.4.5 Scenarios

Participants were given five scenarios of patients with different indications that warrant specific testing plans and/or referrals in selecting all that apply questions. Each scenario varied in severity and ranged from isolated ASD to ASD with specific medical concerns. Participants were also allowed to identify other responses to the scenarios through open text entry. Participants selected what they would offer their patients for each scenario (Figure 2.9).

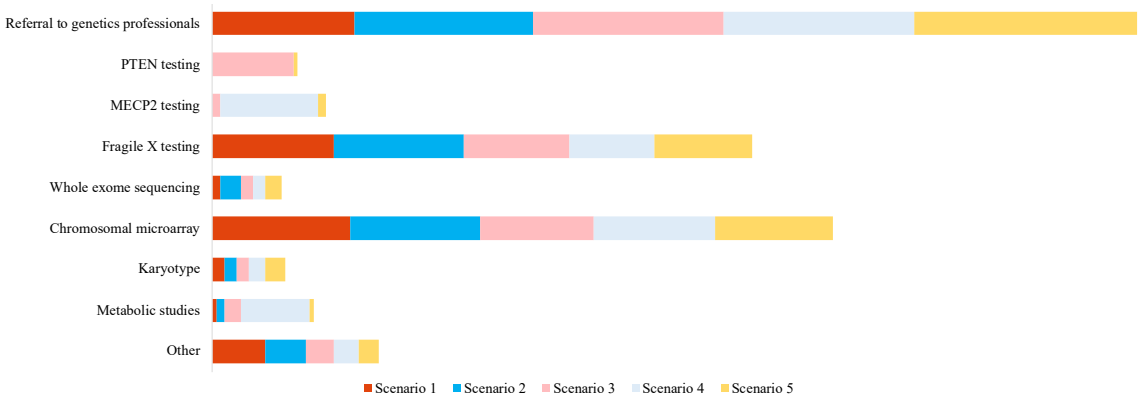

Figure 2.9 *Responses to scenarios* Participants could select all that apply

Scenario 1 described a 4-year-old male recently diagnosed with ASD with difficulties socially and engaging in daily activities. For the first scenario, selections including referral to genetics professional with or without a combination of recommended 1st tier genetic testing and 'other' were considered appropriate based on the clinical guidelines. In this scenario, 29.3% only selected referral to genetics professionals, 13.8% selected CMA, FGX, and referral to genetics professionals, 3.4% selected CMA and referral to genetics professionals, 5.2% selected CMA, FGX, referral

to genetics professionals and 'other', and 1.7% selected referral to genetics professional and 'other'. Selections including referral to genetics professionals and genetic tests not aligning with clinical guidelines, or no selection of referral to genetics professionals, were not appropriate based on clinical guidelines. Out of all participants, 20.7% of participants selected CMA and FGX, without a referral to genetics professionals, 3.4% selected CMA, WES, FGX, and referral to genetics professionals, 1.7% selected karyotype, CMA, and referral to genetics professionals, 1.7% selected karyotype and CMA, 1.7% selected karyotype, CMA, FGX, and referral to genetics professionals, 5.2% selected CMA, FGX and 'other', and 10.3% only selected 'other'.

Overall, only 53.4% of all responses for scenario 1 were appropriate based on the clinical guidelines. Out of all participants, 60.3% included referral to genetics professionals. Due to rounding, total percentages were equivalent to 99.8%. The participants that chose 'other' listed DBP referrals, ABA referrals, behavioral and intervention services referrals, refer to genetics if requested by family, and refer to genetics if primary genetic testing is negative. One participant indicated that they would pursue targeted testing if there are specific indicators in medical history and listed this as a response in all five scenarios. Furthermore, this participant explained that if initial testing is negative and the family is interested in a genetics referral, they will do so.

Scenario 2 described a 4-year-old male recently diagnosed with ASD with global developmental delay, minimal words, and difficulty focusing and transitioning. The selections considered appropriate based on clinical guidelines were the same for scenario 2 as scenario 1. In this scenario, 34.5% participants only selected referral to genetics professionals, 22.4% chose to order CMA, FGX, and referral to genetics professionals,

1.7% chose CMA and referral to genetics professionals, 3.4% selected CMA, FGX, referral to genetics professionals and 'other', and 1.7% selected referral to genetics professionals and 'other'. The selections considered not appropriate based on clinical guidelines were the same for scenario 2 as scenario 1. Out of all responses, 5.2% selected CMA, WES, FGX, and referral to genetics professionals, 1.7% selected metabolic studies, karyotype, CMA, FGX, and referral to genetics professionals, 1.7% selected WES, FGX, and referral to genetics professionals, 1.7% selected metabolic studies, karyotype, WES, FGX, and referral to genetics professionals, 1.7% selected karyotype, CMA, FGX, and referral to genetics professionals, and 10.3% selected CMA and FGX.

Overall, 63.7% of the responses for scenario 2 were appropriate based on clinical guidelines. Of all participants, 75.9% selected referral to genetics professionals. Due to rounding, total percentages were equivalent to 99.8%. Participants that identified 'other' listed behavioral/developmental interventions, refer to genetics if primary tests are negative, refer to genetics if requested by family, referral to DBP, and referral to ABA. One participant indicated that if the initial testing is negative and if the family wishes, they would refer to genetics.

Scenario 3 described an Autistic 6-year-old male with macrocephaly, bumps around his mouth, and family history of breast and thyroid cancer. For scenario 3, selections including referral to genetics professionals with or without a combination of recommended 1st tier genetic testing, 'other' and *PTEN* were considered appropriate selections based on the clinical guidelines. In this scenario, 41.4% only selected to referral to genetics professionals, while 15.5% selected CMA, FGX, *PTEN*, and referral to genetics professionals, 3.4% selected CMA, FGX, and referral to genetics

professionals, 1.7% selected *PTEN* and referral to genetics professionals, 1.7% selected CMA, FGX, *PTEN*, referral to genetics professionals and 'other', and 3.4% selected referral to genetics professionals and 'other'. For scenario 3, selections including referral to genetics professionals with genetic tests not aligning with clinical guidelines, or no selection of referral to genetics professionals, were not appropriate based on clinical guidelines. Of all participants, 13.6% selected referral to genetics professionals with a combination of diagnostic tests including tests that are not recommended based on clinical guidelines such as karyotype, *MECP2*, and WES. Although 10.3% selected appropriate diagnostic testing based on clinical guidelines such as *PTEN*, CMA, and FGX, they did not select referral to genetics professionals.

Overall, 67.1% of all responses in scenario 3 were appropriate based on clinical guidelines. Of all participants, 6.9% chose to order metabolic studies, 5.2% chose to order karyotype, 3.4% chose to order *MECP2* testing, 34.5% chose to order *PTEN* testing, and 81% chose referral to genetics professionals. Due to rounding, total percentages were equivalent to 99.5%. Participants who chose 'other' listed behavioral/educational interventions, referral to DBP, head/cranial imaging, and referral to genetics if primary testing is negative. One participant noted the importance of further medical history and referring to the tuberous sclerosis diagnostic guidelines. This participant said they would then consider a referral to genetics professionals.

Scenario 4 described a 3-year-old female recently diagnosed with ASD and losing previously acquired skills around age 2. For scenario 4, selections that included referral to genetics professionals with or without a combination of *MECP2*, recommended 1st tier testing, metabolic testing and 'other' were considered appropriate based on the clinical

guidelines. In this scenario, 36.2% only selected referral to genetics professionals, 3.4% selected *MECP2* and referral to genetics professionals, 1.7% selected CMA and referral to genetics professionals, and 12.1% selected metabolic studies, CMA, FGX, and referral to genetics professionals. Furthermore, 6.9% chose to order CMA, FGX, *MECP2*, and referral to genetics professionals, 1.7% selected metabolic studies, CMA, *MECP2*, and referral to genetics professionals, 3.4% selected metabolic studies, CMA, FGX, and referral to genetics professionals, 1.7% selected metabolic studies, CMA, and referral to genetics professionals, 1.7% selected metabolic studies, *MECP2*, and referral to genetics professionals, and 1.7% selected referral to genetics professionals and 'other'. In addition, 1.7% selected CMA, *MECP2*, referral to genetics professionals and 'other' and 1.7% selected metabolic studies, CMA, *MECP2*, referral to genetics professionals and 'other'. Selections including referral to genetics professionals and genetic tests not aligning with clinical guidelines, or no selection of referral to genetics professionals, were not appropriate based on clinical guidelines. Of all participants, 5.1% selected referral to genetics professionals with a combination of diagnostic tests including tests that are not recommended based on clinical guidelines such as karyotype and WES. In addition, 5.1% selected a combination of diagnostic tests including tests that are not recommended based on clinical guidelines such as karyotype and WES and did not select referral to genetics professionals. Although 8.5% selected appropriate testing such as *MECP2*, metabolic testing, CMA, and FGX, they did not select referral to genetics professionals.

Overall, 73.9% of the responses for scenario 4 were appropriate based on clinical guidelines and out of all participants, 29.3% chose to include metabolic studies, and

41.4% chose *MECP2* testing. In addition, of all participants, 81% selected referral to genetics. Due to rounding, total percentages were equivalent to 99.4%. Participants that chose 'other' listed a neurology evaluation and developmental/behavioral intervention. One participant indicated that they would rule out other causes of regression and provided environmental toxins as an example.

Scenario 5 described an Autistic 8-year-old male who is nonverbal, has an intellectual disability and epilepsy, and has a history of congenital atrial septal defect and cleft palate. For scenario 5, selections that included referral to genetics professionals with or without a combination of recommended 1st tier testing and 'other' were considered appropriate based on clinical guidelines. In this scenario, 44.8% only referred to genetics, 3.4% selected CMA and referral to genetics, 3.4% selected FGX and referral to genetics professionals, 20.7% selected CMA, FGX, and referral to genetics professionals, 3.4% selected CMA, WES, FGX, and referral to genetics professionals, 1.7% selected referral to genetics professionals and 'other', and 3.4% selected CMA, FGX, referral to genetics professionals, and 'other'. Selections including referral to genetics professionals and genetic tests not aligning with clinical guidelines, or no selection of referral to genetics professionals, were not appropriate based on clinical guidelines. Of all participants, 18.7% selected referral to genetics professionals with a combination of diagnostic tests including tests that are not recommended based on clinical guidelines such as karyotype, *MECP2*, and *PTEN*. Of the 18.7%, one participant selected CMA, referral to genetics professionals, and 'other', which was considered inappropriate as it was noted in 'other' that the participant would order "FISH for Di George".

Overall, 80.8% of the responses for scenario 5 were appropriate based on clinical guidelines and out of all responses 94.8% selected referral to genetics professionals. Of all participants, 8.6% chose to order karyotype, 6.9% chose WES, 3.4% chose *MECP2* testing, 1.7% chose *PTEN* testing. Due to rounding, total percentages were equivalent to 99.5%. One participant that chose 'other' listed that they would FISH for Di George. A different participant that chose 'other' listed that if CMA and FGX are negative, then they may select WES. Another participant explained that their institutional policy is only to order WES after CMA and FGX testing.

2.4.6 Preferred methods to receive updates

Participants (n=51) ranked their preferred methods for ways to receive updates about practice guidelines including society/professional organization websites, regular meetings with genetics professionals, seminars that provide CME credits, virtual service helpline to consult with genetics professionals when needed, and an optional identification of other methods (Figure 2.10). The fifth option was 'other', where participants could provide a different method. Rank one was considered the highest rank, while rank five was considered the lowest. Society/professional organizations were statistically significant ($p < 0.001$) as the highest ranked method among participants (n=51). Regular meetings with genetics professionals and seminars that provide CME credits were not statistically significant ($p = 0.230$) in their ranking as 2 and 3 respectively. A virtual service helpline to consult with genetics professionals was statistically significant ($p = 0.006$) as the lowest ranked method. In the optional identification of other methods, one individual indicated research articles.

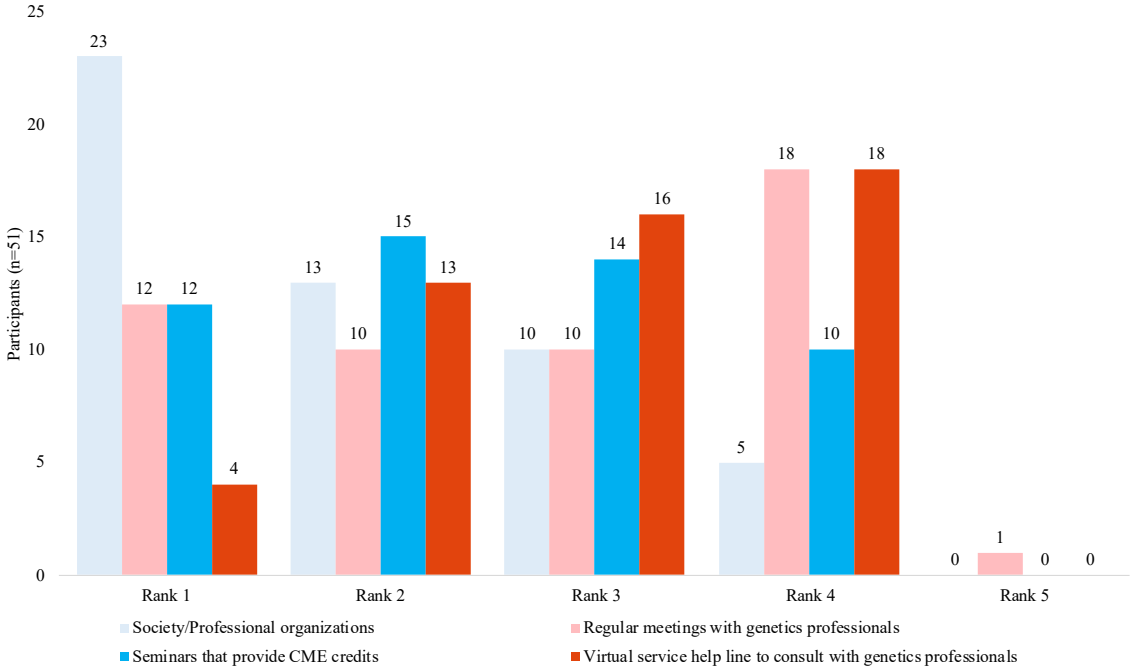

Figure 2.10 *Ranking of preferred methods*

2.5 Discussion

2.5.1 Tools for healthcare providers to receive updates regarding clinical guidelines

Several professional organizations have published clinical guidelines for the recommended first-tier genetic testing for Autistic individuals. ACMG, AAP, and AACAP recommend that genetic testing be offered to all Autistic individuals (Hyman et al., 2020; Schaefer et al., 2013; Volkmar et al., 2014). Our study showed that healthcare providers typically learn of updates to clinical guidelines through society, professional organization websites and/or clinical reports and through an institution and/or clinic. Other methods selected and/or identified by providers included seminars, grand rounds, AAP daily digests, national conferences, and regular review of literature. This provides evidence that there is not a standard way that all healthcare providers find out about updates to clinical guidelines.

Healthcare providers do not consistently follow one professional organization. In our study, healthcare providers primarily indicated they follow the AAN and/or AAP. Since the AAP guidelines were recently updated in 2020, it is reassuring that most providers follow the AAP guidelines (Hyman et al., 2020). In 2000, the AAN published now retired guidelines that recommended karyotype and *FMR1* repeat testing for certain patients (American Academy of Neurology, n.d.; Filipek et al., 2000). Some participants indicated they only follow the AAN; therefore, they may not be referencing updated guidelines that are available through other professional organizations. On another note, one participant indicated that they do not follow a specific organization. With no standard protocol available for all healthcare providers to follow, differences in the phrasing of guidelines, and differences in the publication dates, an environment is created in which healthcare providers practice differently when it comes to their Autistic patients and options for genetic testing or evaluation.

Our results demonstrated that most providers prefer to receive updates through society/professional organizations compared to other methods of receiving updates. Some also prefer regular meetings with genetics professionals and seminars that provide CME credits. The least preferred method was a virtual service helpline to consult with genetics professionals. It is valuable to know that healthcare providers are less interested in more unique methods that involve direct communication with genetics professions. It is possible that lack of time for healthcare providers is hindering the implementation of other methods that may not be as convenient. It is important to note that our results showed that receiving updates through society/professional organizations was a method in which most healthcare providers identified that they currently receive updates.

However, since healthcare providers follow different professional organizations, standardization of these guidelines may help to ensure different specialties are receiving similar updates at similar times.

Since most providers prefer to receive updates through society/professional organizations, it is important that the organizations develop avenues for improving the communication of updates and how to interpret clinical guidelines. Since some providers ranked regular meetings with genetics professionals and seminars that provide CME credits next, it would be beneficial to create those opportunities for providers. Genetic counselors are equipped to host meetings and seminars with referring providers; however, there are less than 6,000 genetic counselors in the United States as of 2021 (National Society of Genetic Counselors, n.d.). Notably, one provider in this study stated that more genetic counselors are needed.

Although the least preferred method to receive updates was a service helpline to consult with genetics professionals, a similar delivery model has been found beneficial in primary care in a study by Carroll et al. (2022). This study assessed if electronic consultations, or eConsults, between primary care providers and geneticists was an effective method of communication. EConsults allowed primary care providers to have their questions answered by geneticists. Additionally, it improved efficiency since referrals could be triaged with geneticists, and advice from geneticists could be implemented into practice by the primary care providers (Carroll et al., 2022). This could be a potential solution between referring providers of Autistic patients and genetic counselors if there is interest and access to such a collaboration.

2.5.2 Discrepancy between the self-reported level of familiarity, understanding of, and utilization of clinical guidelines

In our study, 13 out of 58 participants indicated they were either 'unfamiliar' or 'very unfamiliar' with the clinical guidelines, and 23 out of 58 participants indicated they were either 'uncomfortable' or 'very uncomfortable' with the clinical guidelines. Therefore, some healthcare providers are aware of these guidelines but likely have difficulty interpreting or implementing them. In addition, almost all participants 'agreed' or 'strongly agreed' that genetic tests have clinical utility for Autistic individuals. Since most healthcare providers agree that there is clinical utility, it is salient to equip them with the tools to provide their patients with accurate information and resources within their scope. However, since a few participants did not agree with the clinical utility of genetic testing, and there was difficulty interpreting and/or implementing the guidelines, there may be benefits in providing genetics education. For example, in Carroll et al. (2022), several primary care providers decided to alter their initial plans after their eConsult with a geneticist, such as whether a referral is warranted. Therefore, it could be valuable to consult with genetics professionals regarding the purpose of genetic testing and why specific patients should be offered a referral to genetics.

Although 77.6% of healthcare providers in this study selected that they were 'familiar' or 'very familiar' with the clinical guidelines, fewer participants correctly chose CMA and FGX testing as the recommended first-tier genetic testing for Autistic individuals. Three participants chose CMA, FGX, and 'up to the clinician', which was categorized as an appropriate answer, even though the answer choice 'up to the clinician' has limitations given possible different interpretations. Several participants (n=7) believe

it is up to the clinician to decide on first-tier testing, and one participant indicated no recommended testing. Prior to the updated clinical guidelines that state CMA and FGX are recommended first-tier tests, karyotype was the first-tier test (Manning et al., 2010). Karyotype was selected by six participants as the recommended first-tier testing; therefore, it is possible that some providers are not familiar with the updated guidelines. In summary, there is discordance between participants self-reporting familiarity with the clinical guidelines and their identification of the up-to-date clinical guidelines. In addition, the responses to the scenarios in our study highlight the potentially unnecessary diagnostic tests that are likely being ordered for Autistic individuals.

The participants were provided with scenarios of varying complexities that all warrant genetic evaluations and specific types of genetic tests. Not all healthcare providers chose the recommended tests based on professional guidelines. Both guideline compliance and referral rates increased as the complexity of each scenario increased. The referral rate was the lowest for the isolated ASD indication (60.3%), increased some for the isolated ASD case with global developmental delay (75.9%), increased further for the *PTEN*-related indication (81%) and *MECP2*-related indication (81%), and was the highest for the indication with ASD, intellectual disability, epilepsy, and birth defects (94.8%). Since the complexity increased with each scenario, with the exception of the *PTEN* and *MECP2*- related scenarios being more targeted, it is possible that the participants believed it is more likely to be genetic if there are additional medical concerns and were more likely to defer testing decisions to genetics professionals. However, the referral rate has yet to reach 100%.

For the first scenario, half of the participants followed the guidelines and selected the appropriate genetic testing and referral. In scenario 2, two-thirds of the participants were compliant with the guidelines. For scenarios 3 and 4, the compliance rate further increased. Furthermore, it is important to note that for scenario 3, which was a *PTEN*-related indication, only one-third of participants selected *PTEN* genetic testing. Similarly, for scenario 4, which was a *MECP2*- related indication, less than half of healthcare providers chose *MECP2* genetic testing. Finally, for scenario 5, the compliance rate was at its highest, 80.8%.

Our findings are consistent with previous studies that exhibit a lack of guideline compliance and limited access to genetic evaluations for Autistic individuals (Barton et al., 2018; Rutz et al., 2019; Tchaconas & Adesman, 2017). Furthermore, Rutz et al. (2019) also reported discordance between self-reports of familiarity with clinical guidelines and adherence to them. Our results confirmed that there is a gap in knowledge and utilization of clinical guidelines. This suggests that diagnostic tests are being ordered that are not recommended by the updated clinical guidelines. All Autistic individuals do not have access to genetic evaluations. For example, in each scenario, some participants selected karyotype, which is no longer recommended in clinical guidelines (Hyman et al., 2020; Manickam et al., 2021; Manning et al., 2010; Schaefer et al., 2013). Tchaconas & Adesman (2017) had a significantly lower guideline compliance rate for each of their scenarios compared to our study. It is promising that after several years the results of this study show an improved guideline compliance rate. However, there is still room for growth.

2.5.3 Barriers to offering genetic testing to Autistic individuals

Most participants indicated that they discuss or offer genetic testing to all Autistic patients. However, some did express that whether they discuss or offer genetic testing is dependent on additional factors, including the presence of additional medical concerns, family history, and severity. Two participants shared that they would discuss or offer genetic testing if the family or patient requests it or if a specialist or provider recommends it. However, the family or patient may not be aware of genetic testing as an option, as seen in the studies by Chen et al. (2013) and Zhao et al. (2019), and therefore would not know to request it.

One participant expressed a desire to discuss genetic testing with all patients but explained that there are barriers, such as lack of time, that prevent them from being able to do so. This participant stated that these specific factors affect whether they discuss genetic testing at the initial visit or a follow-up visit. For example, ASD diagnostic evaluations involve significant information for the families; therefore, they may be overwhelmed and need time to process the clinical diagnosis. As a result, some providers may not feel that it is appropriate to discuss genetic testing at that time. Furthermore, due to the significant amount of information discussed during these visits and the time constraints, there may not be enough time to discuss genetic testing and properly consent families for testing. One participant stated in our study that, in their experience, referrals to genetics must be made by pediatricians to ensure insurance accepts the referrals. Therefore, this creates an additional step in the referral process. Another provider explained that according to their experience with insurance, genetic counselors must be on staff for genetic tests to be ordered. Furthermore, a DBP stated that insurance requires

geneticists or neurologists to order genetic testing. This provider believes efficiency will improve if they can order genetic testing. Similar barriers to ordering genetic testing and referrals to genetics were identified by Rutz et al. (2019), including wait time for genetics professionals and insurance.

Although the diagnostic yield can increase when there are additional medical concerns, family history, and increased severity, the clinical guidelines state that all individuals with an ASD diagnosis should be offered genetic evaluations and/or testing (Hyman et al., 2020; Schaefer et al., 2013; Volkmar et al., 2014). Our results show that there are gaps in knowledge and barriers that are preventing all Autistic individuals from accessing genetic evaluations.

2.5.4 Healthcare providers' understanding of genetic counseling and access to genetics resources

Most of the providers in this study stated having a genetics-related resource to contact if they have an inquiry about genetic testing. However, about 10% indicated contacting pediatricians or developmental and behavioral pediatricians about genetic testing inquiries. Some inquiries that healthcare providers have about genetics may be better suited for genetics professionals than providers of other specialties. Therefore, it is salient that all healthcare providers have access to genetics professionals. In addition, most providers believe genetic counselors are an available resource and have access to either a genetic counselor or genetics team within or near their practice. All participants believe genetic counselors add value to their profession; however, 15 out of 58 participants do not believe genetic counselors are an available resource, and 15 of 58 participants never interact with genetic counselors. Lack of communication with genetic

counselors has previously been reported as a barrier for physicians ordering genetic testing (Rutz et al., 2019). Therefore, there may be a benefit to increasing access and communication between referring healthcare providers and genetic counselors.

NSGC developed a definition of genetic counseling which includes obtaining medical and family histories, describing the chance of occurrence and the chance of recurrence, and education, as well as topics covered in pre-test counseling and post-test counseling (National Society of Genetic Counselors' Definition Task Force, 2006). In our study, healthcare providers identified the central roles of a genetic counselor. Post-test counseling, pre-test counseling, family counseling, and education were the most commonly identified themes. Family planning, care coordination, support, recommendations of tests, and family history were also identified. There was a wide variety of definitions that providers shared. Some indicated that they did not have a good understanding of the role of genetic counselors. There were not any providers that selected all themes, which indicates that most healthcare providers' understanding of the role of genetic counselors is limited. Due to the mixed understanding of the role of genetic counselors found in our study, it is important for healthcare providers to be provided with resources and education regarding genetic counselors, to promote access to genetic counselors and genetic evaluations for patients.

It is salient that healthcare providers understand the full scope of genetic counselors to utilize them as resources appropriately. For example, one provider noted that their clinic has the policy to refer all Autistic patients for genetic testing based on recommendations from a geneticist that works with the clinic. This is a clear example of how genetics professionals, as a resource, have improved access to genetic evaluations

for Autistic individuals. With an increased workforce of genetic counselors, there will be further support resources for referring healthcare providers when inquiries arise. Implementing these potential solutions will improve healthcare providers' level of comfort and familiarity with the clinical guidelines, increase referral rates for patients that meet guidelines, decrease barriers for healthcare providers, and reduce the ordering of genetic tests that are not recommended based on clinical guidelines. Ultimately, this will allow for improved access to genetics evaluations for Autistic individuals.

2.5.5 Limitations and future directions

Some limitations of this study were in the design of the survey. Several of the questions were optional for participants; therefore, the completion rate was not 100% for each question. Furthermore, there needed to be a clear distinction between discussing genetic testing, offering genetic testing, and offering genetic referrals in some questions. If some participants selected that they do not discuss genetic testing with all patients, they might still discuss a genetics referral. Additionally, categorizing how providers interact with patients newly diagnosed with ASD versus follow-up patients would have been valuable. Some providers may offer genetic evaluations at follow-up visits instead of the initial visit, so the lack of distinction between those interactions is a limitation of this study. Although several states were represented in this study, a larger sample size would be beneficial. Since potential solutions to the gaps identified in this study have been proposed, a future study investigating the implementation of these potential solutions into practice and measuring the effectiveness at bridging the identified gaps would be useful. Increasing awareness of the role of genetic counselors and the need for improved access to them will allow healthcare providers to feel equipped with the tools to be comfortable

with the clinical guidelines. It is important for healthcare providers that routinely see Autistic individuals, genetic counselors, and society/professional organizations to acknowledge the present gaps, form professional relationships, and develop effective avenues of communication.

CHAPTER 3: CONCLUSION

Healthcare providers that routinely see Autistic individuals do not unanimously feel comfortable with the genetic testing clinical guidelines for Autistic individuals. The gaps in comfort and familiarity with the clinical guidelines prevent guideline compliance and utilization. Many healthcare providers need to offer genetics referrals to patients that warrant them. Since the genetics referral rates are lower than expected, there is reduced access to genetic evaluations for Autistic individuals. Furthermore, many healthcare providers are offering genetic tests that may not be necessary, which can elongate the time for a patient to receive a genetic diagnosis. Societies and professional organizations can identify ways to communicate updates to guidelines more effectively, as that is the most preferred method to receive updates by healthcare providers. If there is either a set of standard guidelines or if the different professional organizations more closely align with their published guidelines, all healthcare providers can provide clearer recommendations for their Autistic patients. Additional methods can also be explored to improve the identified gaps. Moreover, there is a lack of understanding regarding the full scope of a genetic counselor's role. This prevents referring healthcare providers from identifying and utilizing them as accessible resources. A barrier to genetic counselors as accessible resources is also the small workforce. Therefore, a push for more genetic counselors in the United States is imperative to ensure that healthcare providers have trusted professionals to help improve their patients' care. If there is increased access to genetic counselors for healthcare providers and tools in place to improve communication

and interpretation of guidelines, healthcare providers may feel empowered to increase access to genetic evaluations for their patients.

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APPENDIX A: PARTICIPANT INVITATION LETTER

Dear Potential Participant,

I am a genetic counseling graduate student at the University of South Carolina School of Medicine. This letter is an invitation to participate in a research study that entails completing an online survey. The intent is for this survey to reach healthcare providers that care for patients with Autism Spectrum Disorder (ASD) and that identify as non-genetics professionals.

The goal of this study is to understand the patterns of healthcare providers with patients diagnosed with ASD, specifically related to genetics referrals, genetic testing, and professional guidelines. Participating in this study will provide data on how to improve accessibility and familiarity with genetic testing and associated resources. Additionally, it can help enhance the resources that are available to patients and families with ASD.

The survey will include three scattered general knowledge questions to differentiate between humans and robots. If any of the first three security questions are answered incorrectly or skipped, you will automatically exit the survey.

At the end of the survey, there will be an option to enter a raffle. There will be a link where participants can enter their email address. Five participants will be randomly selected, and a $25 gift card will be sent directly to their email address. Immediately after the winners have been chosen, the email addresses will be deleted from the survey software. Your email address will not be linked to your survey responses in any way.

Participation and completion of this survey is entirely voluntary. If you begin the survey and choose to continue, please answer each question to the best of your ability. You may choose to withdraw from the study at any time by exiting the survey. No personal identifying information will be used, and anonymity will be maintained. There is no anticipated risk to participants, aside from any potential emotional reactions or beliefs.

Thank you for taking this research study into consideration. If you are comfortable doing so, please share this invitation letter and survey with your colleagues and/or clinic.

Please reach out to myself or my faculty advisor, Crystal Hill-Chapman, if you have any questions concerning this research. For more specific questions or concerns about participating in research and your rights please communicate with the Office of Research Compliance at the University of South Carolina. Contact information for each party is below.

The link to the survey is below. It is not expected to take more than 10 minutes to complete.

Link to survey: https://uofsc.co1.qualtrics.com/jfe/form/SV_2htkbSKNDrUcCY6

Nisha Pandya, B.S.
Genetic Counseling Candidate
University of South Carolina School of Medicine USC Genetic Counseling Program
Two Medical Park, Suite 103
Columbia, SC 29203
npandya@uscmed.sc.edu

Crystal Hill-Chapman, PhD, LP, NCSP, ABPP Faculty Advisor
University of South Carolina School of Medicine USC Genetic Counseling Program
Two Medical Park, Suite 103 Columbia, SC 29203
Office of Research Compliance at the University of South Carolina (803) 777-7095

APPENDIX B: PARTICIPANT RECRUITMENT EMAIL

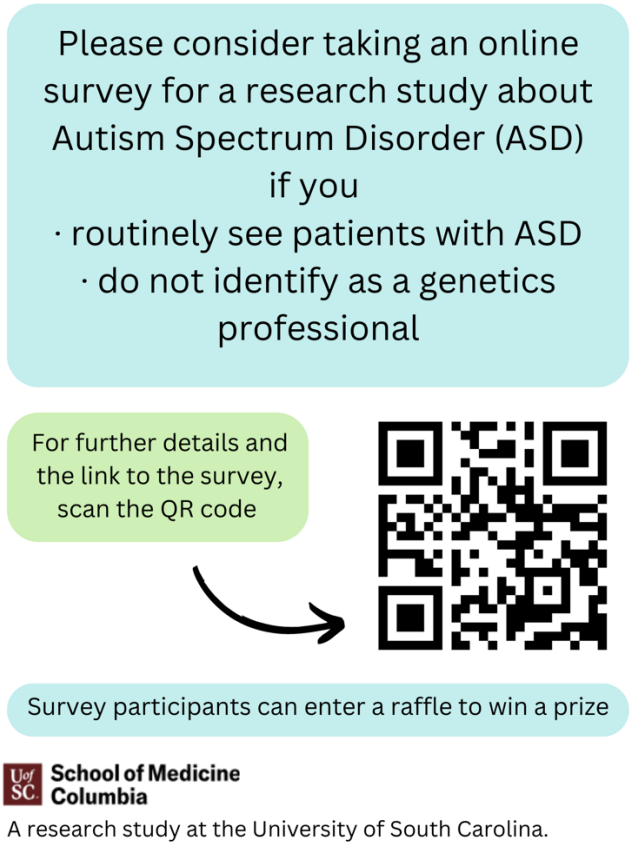
I am a genetic counseling graduate student at the University of South Carolina School of Medicine. If you identify as a healthcare provider that sees patients with Autism Spectrum Disorder (ASD) and do not identify as a genetics professional (geneticist, genetic counselor, etc.), I would appreciate if you consider participating in this survey.

Attached is a document that invites you to participate in this research study. Please read the invitation letter for more details and the link to the survey.

I would appreciate if you share this invitation letter with colleagues that will fit the participant criteria.

APPEDIX C: PARTICIPANT RECRUITMENT EMAIL WITH FLYER

I am a genetic counseling graduate student at the University of South Carolina School of Medicine. Below is a flyer with information on a research study about Autism Spectrum Disorder. Scanning the QR code on the flyer will take you to the invitation letter to participate. I would appreciate if you would consider participating and if you share this invitation letter with colleagues that will fit the participant criteria.



APPENDIX D: PARTICIPANT QUESTIONAIRRE

Default Question Block

4 + 5 = ____?

Do you currently see or diagnose patients with ASD?

- ◯ Yes
- ◯ No

What is your title as a healthcare provider? (e.g. developmental and behavioral pediatrician)

Identify the type of certification or licensure that you hold? (e.g. FNP, NP, DO, etc.)

Which professional organization do you follow for clinical practice guidelines? Select all that apply

- ☐ American Academy of Pediatrics
- ☐ American College of Medical Genetics
- ☐ American Academy of Neurology
- ☐ American Academy of Child and Adolescent Psychiatry
- ☐ Other

How familiar are you with the clinical guidelines for what genetic testing to offer patients with ASD?

- ◯ Very unfamiliar
- ◯ Unfamiliar
- ◯ Familiar
- ◯ Very familiar

How often do you consult or refer to genetic testing practice guidelines for patients with ASD?

- ◯ Never
- ◯ Sometimes
- ◯ Often
- ◯ Almost always

How comfortable are you with the clinical guidelines for what genetic testing to offer to patients with ASD?

- ◯ Very uncomfortable
- ◯ Uncomfortable
- ◯ Comfortable
- ◯ Very comfortable

Do you discuss or offer genetic testing to all patients with ASD?

- ◯ Yes
- ◯ No

When do you decide to discuss or offer genetic testing to patients with ASD?

A 4-yo male has recently been diagnosed with ASD. He has difficulty with interacting and communicating with classmates and other children socially and does not initiate social communication. His parents find it difficult to get him to

engage in daily activities such as eating when he is repeatedly lining his toy cars up. What would you offer to this patient? Select all that apply

- [ ] Metabolic studies
- [ ] Karyotype
- [ ] Chromosomal microarray
- [ ] Whole exome sequencing
- [ ] Fragile X testing
- [ ] MECP2 testing
- [ ] PTEN testing
- [ ] Referral to genetics professionals
- [ ] Other

A 4-yo male has recently been diagnosed with ASD. He has severe global developmental delay and uses less than 10 words to communicate. He has difficulty staying focused on one task. His parents express that they rarely leave the house because of their son's difficulty with transitions. What would you offer to this patient? Select all that apply

- [ ] Metabolic studies
- [ ] Karyotype
- [ ] Chromosomal microarray
- [ ] Whole exome sequencing
- [ ] Fragile X testing
- [ ] MECP2 testing
- [ ] PTEN testing
- [ ] Referral to genetics professionals
- [ ] Other

A 6-yo male has recently been diagnosed with ASD. His head measurement is above the 97th percentile and several bumps are found near and on his mouth. He also has a significant family history of breast cancer and one relative with thyroid cancer. What would you offer this patient? Select all that apply

- [ ] Metabolic studies
- [ ] Karyotype
- [ ] Chromosomal microarray
- [ ] Whole exome sequencing
- [ ] Fragile X testing
- [ ] MECP2 testing
- [ ] PTEN testing
- [ ] Referral to genetics professionals

☐ Other

2 + 3 = ____?

A 3-yo female has recently been diagnosed with ASD. She was developing typically until about 8 months, when her parents expressed that she seemed overly apathetic. By the time she was 2 years old, she had lost some previously acquired skills, including loss of words and walking. What would you offer this patient? Select all that apply

- ☐ Metabolic studies
- ☐ Karyotype
- ☐ Chromosomal microarray
- ☐ Whole exome sequencing
- ☐ Fragile X testing
- ☐ MECP2 testing
- ☐ PTEN testing
- ☐ Referral to genetics professionals
- ☐ Other

An 8-yo male with ASD is non-verbal and was recently diagnosed with intellectual disability. He has epilepsy and had surgeries for congenital atrial septal defect and cleft palate. What would you offer this patient? Select all that apply

- ☐ Metabolic studies
- ☐ Karyotype
- ☐ Chromosomal microarray
- ☐ Whole exome sequencing
- ☐ Fragile X testing
- ☐ MECP2 testing
- ☐ PTEN testing
- ☐ Referral to genetics professionals
- ☐ Other

What is the first-tier testing offered to patients diagnosed with ASD? Select all that apply

- [ ] Karyotype
- [ ] FISH
- [ ] Chromosomal Microarray
- [ ] Whole Exome Sequencing
- [ ] Fragile X testing
- [ ] There is no recommended testing
- [ ] It is up to the clinician to decide based on presentation

Who would you reach out to if you have a question about genetic testing?

What is your understanding of the role of genetic counselors?

Select your level of agreement with the following statements

	Strongly Disagree	Disagree	Agree	Strongly agree
There is clinical utility for genetic tests that are offered to patients with ASD	○	○	○	○
Genetic counselors are an accessible resource	○	○	○	○
Genetic counselors add value to my profession	○	○	○	○

How often do you interact with genetic counselors?

- ○ Never
- ○ Sometimes
- ○ Often
- ○ Almost always

Do you have access to a genetic counselor or genetics team within or near your practice?

- ○ Yes
- ○ No

What organizations did you or do you participate in? Select all that apply

- ☐ LEND
- ☐ SPARK
- ☐ Other
- ☐ None

In which way do you find out about updates to practice guidelines?

- ☐ Independently through society, professional organization websites and/or clinical reports
- ☐ Through institution and/or clinic
- ☐ Seminars
- ☐ Other

Rank the following below based on which method you would prefer to receive updates about practice guidelines

Society/Professional Organization Websites

Regular meetings with genetics professionals

Seminars that provide CME credits

Virtual service help line to consult with genetics professionals when needed

Other, please identify additional methods

How many years of experience do you have since you became licensed or certified as a healthcare provider?

On average, how many patients do you see that are diagnosed with ASD? (e.g. 5 per week)

Are you an ordering provider for genetic testing?

- ◯ Yes
- ◯ No

Which state or territory of the United States do you practice in?

6 + 7 = ____?

What state or territory of the United States do you practice in?

What communities do you routinely practice in? Select all that apply

- [ ] Urban
- [ ] Suburban
- [ ] Rural

Do you care for a child with ASD at home?

- ◯ Yes
- ◯ No

If you would like to add anything, please do so here

Type "I am not a bot" in the space below

APPENDIX E: RAFFLE INFORMATION AT END OF SURVEY

Thank you for participating in this research study. We appreciate the time you took to answer the questions on this survey. We invite you to share the invitation letter and survey with other non-genetics healthcare providers that see patients with ASD.

If you are interested in joining an optional raffle for a $25 gift card as a thank you for participating, please click on this
link: https://uofsc.co1.qualtrics.com/jfe/form/SV_0eSIXZZIMIoO1vM

Details on the raffle:
The linked page will ask you to enter your email address. We will randomly choose five participants and will send the gift card to the email address provided. The email addresses will be deleted from the survey software immediately after the raffle ends.