Symptoms of Autism Spectrum Disorder in Individuals with Down Syndrome or Williams Syndrome

THESIS

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Abstract

Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by persistent deficits in social communication, and restricted, repetitive patterns of behavior (American Psychiatric Association, 2013). Despite past research demonstrating that individuals with Down syndrome (DS) are not impaired in the social domain, and that Williams syndrome (WS) is a phenotypic opposite of autism, individuals with these conditions display increased prevalence of ASD.

The primary aim of this study was to examine characteristics of ASD in a group of children with DS and WS. Parents or primary caregivers of children with ASD ($n=39$), DS ($n=76$), or WS ($n=45$) completed demographic questions, an autism screener, a dimensional measure of autism symptoms, and an assessment of adaptive behavior. A total of 5 of the 76 respondents in the DS group (6.6%), and 4 of the 45 respondents in the WS group (8.9%) noted that their child had a comorbid ASD diagnosis. In regard to screening, 22.4% of individuals in the DS group scored above the cut off score on the Social Communication Questionnaire (SCQ), thus screening positive for ASD, and 43.5% of individuals with WS screened positive. Both of these percentages were significantly different than the 4.4% reported in previous research (Chandler et al., 2007). Individuals who screened positive on the SCQ had significantly higher Autism Spectrum Rating Scales (ASRS) total scores in comparison to those who screened negative. Additionally, both the DS and WS group ASRS total scores were different than the normative sample mean. These elevations were not driven solely by adaptive behavior
deficits. When controlling for sex, age, and adaptive behavior, individuals with ASD had significantly higher ASRS total scores than individuals with DS or WS. Exploratory analyses revealed that within the DS group, the Unusual Behaviors ASRS subscale was more elevated than the Social Communication and Self-Regulation subscales. Within the WS group, Unusual Behaviors were rated significantly higher than Social Communication.

Results suggest that there are elevations of ASD symptoms among individuals with DS and WS. There are many possible explanations for these elevations, such as issues with measurement, etiological overlap, or similar behavioral phenotypes among individuals with DS, WS and ASD. More research is needed to further our understanding of overlap of ASD symptoms in DS and WS populations. Future research can lead to improvements in areas of screening, diagnosis, and interventions for ASD among children with DS or WS.
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**Chapter 1: Introduction**

Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by persistent deficits in social communication and restricted, repetitive patterns of behavior (American Psychiatric Association, 2013). Recent studies suggest that the prevalence of ASD is about 1 in 68 (Centers for Disease Control and Prevention, 2010). There is considerable heterogeneity within the ASD phenotype. For example, estimates of the proportion of individuals diagnosed with autism without intellectual impairment range from 0 to 60% across 21 studies with variable sample sizes (Fombonne, 2005). This heterogeneity is also evident in language acquisition, as some children with ASD reach language milestones at the same time as typically developing peers, yet up to 25% remain non-verbal (Kjelgaard & Tager-Flusberg, 2001; Tager-Flusberg, Paul, & Lord, 2005).

Approximately 10-20% of cases of ASD can be linked to a variety of identifiable genetic variants, and the remaining 80-90% of cases are considered idiopathic. However, even among cases of idiopathic ASD, high heritability indicates a genetic component (Deng et al., 2015; Lichtenstein, Carlström, Råstam, Gillberg, & Anckarsäter, 2010; Ronald & Hoekstra, 2010; Rosenberg et al., 2009; Taniai, Mishiyama, Miyachi, Imaeda, & Sumi, 2008). In twin studies, higher concordance rates are observed among monozygotic twins (39-96%) than among dizygotic twins (13-31%) (Deng et al., 2015; Lichtenstien et al., 2010; Rosenberg et al., 2009; Taniai, et al., 2008). Molecular genetic studies indicate that ASD is usually inherited multifactorially, with a substantial number
of genes involved (Abrahams & Geschwind, 2008). Array chromosomal genomic hybridization studies suggest specific genetic targets in approximately 20-25% of individuals with the disorder (Miles, 2011). These can be classified into three groups: chromosomal abnormalities, which are observed in about 5% of cases; copy number variants (CNVs), including deletions and duplications, which are observed in about 10-20% of cases; and single genetic variants, which are observed in about 5% of cases (Miles, 2011). Of course, none of these mechanisms rule out contributions from variants at additional genetic loci.

**Genetics of ASD**

As research demonstrates a genetic component in ASD, a large focus of research lies in investigating specific genetic mechanisms of the disorder. Much of this research uses genetic linkage, association, or genome-wide association studies to identify candidate genes that confer a risk for ASD. Results of these studies implicate specific chromosome regions as contributors to ASD (Szatmari et al., 2007), and suggest that a combination of rare genetic mutations of larger effects and common variants of a small effect are linked to many cases of ASD (Freitag et al., 2010). As Freitag and colleagues note, the next step in determining causality of these CNVs lies in investigating genetics of large samples of individuals with ASD and healthy controls (Freitag et al., 2010).

Another method of investigating genetic underpinnings of ASD lies in examining disorders that are associated with increased risk of ASD, including those with distinct genetic causes. Due to its etiological heterogeneity, efforts to discover distinct genetic causes of ASD proves challenging, and research looking at genetic disorders with a high
comorbidity of ASD demonstrates potential for discovering biological targets for intervention, as well as insight into the pathophysiology of the disorder. One example of this approach examines fragile X syndrome (FXS), a monogenetic disorder in which the prevalence of ASD is estimated to be between 25-50%, depending on criteria used (Clifford et al., 2007; Garcia-Nonell et al., 2008; Hatton et al., 2006; Kauffman et al., 2004). Research in FXS demonstrates similarities between this disorder and idiopathic ASD, such as early brain overgrowth (Hazlett et al., 2012), and evidence from studies of both monogenetic and idiopathic ASD supports a role of dysregulation of a specific protein that may lead to brain overgrowth (Erickson et al., 2014a). Additionally, comparisons of those with FXS associated with idiopathic ASD suggests a potential for a common specific pathway processing bias in the two groups (Erickson et al., 2014a). In part due to research supporting the relevance of FXS to idiopathic cases of ASD, a recent study also investigated effectiveness of a drug associated with improvements in social avoidance behaviors in the FXS population in the idiopathic ASD population (Erickson et al., 2014b). This research is promising as in the open-label study, the drug showed beneficial effects on measures of social functioning, communication, and irritability in individuals with idiopathic ASD (Erickson et al., 2014b).

Taken together, this research demonstrates the merit of gathering both genetic data in large samples of individuals with ASD to identify candidate genes, and in investigating overlap of ASD in idiopathic and syndromic cases. In the current study, I focus on children with Down syndrome and Williams syndrome, two disorders with distinct genetic causes that display increased prevalence of ASD, despite seeming being
dissimilar phenotypically.

**Down Syndrome and Williams Syndrome**

Down syndrome (DS) and Williams syndrome (WS) are disorders with distinct genetic etiologies. Down syndrome is caused by partial or full duplication of Chromosome 21 material, and Williams syndrome is caused by a deletion of 26-28 genes on the seventh chromosome. In the past, sociability and friendliness associated with DS led researchers to believe that individuals with the disorder were not impaired socially (Gibbs & Thorpe, 1983), and due in part to the hypersociability associated with Williams syndrome, this syndrome was once described as a polar opposite of autism (Jones et al., 2000). These statements suggest that autism should be uncommon in individuals with these genetic conditions. However, more recent investigations of ASD in individuals with DS and WS show increased prevalence (Klein-Tasman, Mervis, Lord, & Phillips, 2007; Lincoln, Searcy, Jones, & Lord, 2007; Reilly, 2010). Therefore, reexamination of the ASD phenotype in persons with DS and WS is necessary, to improve our knowledge regarding overlap of these disorders.

**Down syndrome.** Down syndrome is the most common genetic cause of intellectual disability (Sheets et al., 2011). The prevalence of DS in the United States is approximately 8.27 per 10,000 (Presson et al., 2013). Individuals with DS tend to have a relative strength in social functioning, and frequently communicate positive affect via emotional displays including smiles (Fidler, 2005). However, current research indicates social impairments and related behavior challenges, albeit of a subtler presentation compared to other developmental disabilities (Cebula, Moore, & Wishart, 2010). For
example, children with DS may have slower acquisition of joint attention (Legerstee & Fisher, 2008), use less spontaneous requesting gestures (Fidler, Philofsky, Hepburn, & Rodgers, 2005), have poorer problem solving strategies (Fidler et al., 2005), and have more difficulties recognizing the emotions of fear, surprise, and anger than mental-aged matched peers (Kasari, Freeman, & Hughes, 2001). Studies also show that children with DS have difficulties with theory of mind and emotion processing, yet these difficulties are less apparent than in other developmental disabilities such as ASD (Cebula et al., 2010). Individuals with DS also exhibit language deficits (Cleland, Wood, Hardcastle, Wishart, & Timmins, 2010), with more pronounced impairments in expressive language compared to receptive language (Chapman, 1997). It is important to note that although individuals with DS experience impairments in social behaviors, they are often used as control participants in studies of developmental disabilities, as many assume that DS is not characterized by social dysfunction (Cebula et al., 2010).

**Down Syndrome and ASD.** As mentioned above, there is a high rate of ASD among individuals with DS, with prevalence estimates ranging from 5% to 39% (Reilly, 2010). Within the DS population, individuals with a comorbid diagnosis of ASD have lower IQs, poorer receptive and expressive language, and poorer adaptive behavior (Molloy et al., 2009). To investigate overlap of these disorders more closely, Channell and colleagues (2015) used the Social Responsiveness Scale (SRS; Constantino & Gruber, 2005) to examine characteristics of individuals, ages 10-21, with Down syndrome but without comorbid ASD (Channell et al., 2015). The SRS is a 65-item questionnaire filled out by the children’s primary caregivers, and is used to assess abilities and deficits in
social reciprocity, (Constantino et al., 2003). Each item is coded on a scale from 0-3, and scores are generated across the following five subscales: social awareness, social cognition, social communication, social motivation, and autistic mannerisms. Overall, DS participants show elevated mean scores on the SRS, which puts them within the clinically significant “mild to moderate” range for ASD symptoms (Channell et al., 2015). Within subscales, social cognition and autistic mannerisms are beyond the normal cutoff, whereas the social communication, social motivation, and social awareness subscales are just below the normal range cutoff (Channell et al., 2015). However, it is important to note that factor analysis of SRS yields only one factor (Bölte, Poustka, and Constantino, 2008). Thus, although there are five subscales, they assess only one underlying construct.

In another study, Kent and colleagues (1999) used International Statistical Classification of Diseases and Related Health Problems, 10th ed. (ICD-10; World Health Organization, 1992) criteria to determine if any among 33 individuals, ages 2-16 years, in their DS sample met criteria for autism (Kent, Evans, Paul, & Sharp, 1999). Four did, yet of the remaining 29 individuals, 11 had obsessive-compulsive behaviors which raised the question of an ASD diagnosis in the past (Kent et al., 1999).

In another study, Hepburn et al. (2008) used two common autism diagnostic assessments, the Autism Diagnostic Observation Schedule-Generic (ADOS-G; Lord, Rutter, DiLavore, & Risi, 1999) and the Autism Diagnostic Interview-Revised (ADI-R; Lord, Rutter, & LeCouteur, 1994), along with clinical judgment, to investigate co-occurrence of autism among 20 individuals with DS within the 2-3-year-old age range, and then again when they were 4-5 (Hepburn, Philofsky, Fidler, & Rogers, 2008). The
ADOS is a semi-structured play-based assessment, whereas the ADI-R is a semi-structured interview with the parent or caregiver. At the first time point, 15% of children exceeded the autism cutoff on ADOS-G, but none met criteria for ASD based on the ADI-R results. However, each child who exceeded the cutoff on the ADOS-G also exceeded the cutoff on the communication subscale of the ADI-R. Clinical judgment placed 10% of the sample on the autism spectrum; however, an additional 45% met partial criteria. Although all of the children who met partial criteria demonstrated repetitive motor behaviors such as hand-flapping and limited play, they did not present with deficits in social relatedness (Hepburn et al., 2007). At follow up, no additional children received an ASD diagnosis, although the two who were placed on the spectrum based on clinical judgment had higher scores on the ADOS-G and the ADI-R, suggesting worsening of symptoms (Hepburn et al., 2007).

Although the aforementioned studies examined all ASD symptoms among DS samples, other studies investigated specific behaviors more closely. For example, Evans and Great (2000) compared restricted and repetitive behaviors in children with DS to a typically developing group. Although individuals with DS exhibited a similar number of compulsive behaviors as typically developing peers, they used these behaviors with greater frequency/intensity (Evans & Gray, 2000). Another study assessed a skill that is usually deficient in those with ASD, self-regulation, among individuals with DS, as well as in children with ASD (Bieberich & Morgan, 2004). Self-regulation can be defined as the set of processes through which individuals attempt to alter the way they think, feel, or behave in response to a person or situation (Muraven & Baumeister, 2000). Although
there are components of self-regulation that are subcortical and independent of executive functioning (Beauchaine, 2015), most aspects of self-regulation are related to cortical executive functions (Carlson & Moses, 2001). Perhaps unsurprisingly, individuals with autism typically demonstrate difficulties with executive function tasks such as theory of mind, and exhibit weaknesses in self-regulation (Fonagy & Target, 2002). Bieberich and Morgan examined self-regulation among children with DS or ASD at two different time points, the first at an average of 8.3 years, and then at 10.3 years. Consistent with their hypothesis, they found that children with ASD were more symptomatic than children with DS on the self-regulation factor of the Minnesota Preschool Affect Rating Scales (MN-PARS; Shapiro, McPhee, Abbott, & Sulzbacher, 1994). The MN-PARS is a measure of affective expression and self-regulation (McPhee & Shapiro, 1993). This assessment uses videotaped play sessions with the child, which are scored on positive affect, negative affect, self-regulation, and activity level. A deficit in self-regulation was found at both time points.

Overall, research demonstrates that more individuals with DS have a comorbid diagnosis of ASD compared to the reported Centers for Disease Control and Prevention (CDC) prevalence rate of ASD, and that many children with DS who are not diagnosed with ASD still exhibit ASD symptoms. Past research demonstrates that children with DS show elevated SRS scores (Channell et al., 2015), often exhibit obsessive-compulsive behaviors that are salient enough to raise questions about an ASD diagnosis (Kent et al., 1999), and demonstrate a high frequency of restricted/repetitive behaviors (Evans & Gray, 2000). Children with DS may also meet partial criteria for ASD due to repetitive
behaviors and limited play, but may not meet full criteria due to a lack of deficits in social relatedness (Hepburn et al., 2007). More research into the overlap of these conditions is warranted.

**Williams Syndrome. Cognitive and language profiles.** Williams syndrome is caused by a deletion of 26-28 genes on Chromosome 7, and similar to DS, is not inherited (Peoples et al., 2000). The syndrome is rare, affecting approximately 1 in 7,500 to 1 in 20,000 individuals (Strømme, Bjørnstad, & Ramstad, 2002). Seventy-five percent (75%) of children with WS demonstrate IQ and adaptive behavior scores consistent with developmental delay (Mervis & Klein-Tasman, 2000). Similar to DS, individuals with WS typically demonstrate language delays. However, in WS receptive language abilities are usually stronger than expressive language abilities (Udwin & Yule, 1990, Brock, 2007). Joint attention, a typical precursor to language, is also impaired among individuals with WS (Laing et al., 2002). Research shows that individuals with WS can engage in dyadic interaction. However, triadic interaction and both comprehension and production of referential and instrumental pointing are impaired (Laing et al., 2002). In fact, individuals with WS commonly produce referential language before they begin referential pointing, which differentiates them from both typically developing individuals and individuals with DS (Laing et al., 2002; Mervis, Morris, Bertrand, & Robinson, 1999). Children with autism often also produce referential language before exhibiting joint attention behaviors (Carpenter, Pennington, & Rogers, 2002). As pointing is considered an early milestone of social cognitive development, this similar pattern for ASD and WS suggests that the pathway of social communication development across
disorders may be similar (Asada & Itakura, 2012). In turn, this could suggest that individuals with ASD and WS may exhibit similar shortcomings in verbal communication skills which involve social cognitive abilities (Asada & Itakura, 2012). However, it is important to note that no known studies compare this reverse WS and ASD developmental pattern directly.

**Social profiles.** Individuals with Williams syndrome also display a social profile characterized by high levels of empathy, strength of communication, and sociability (Jones et al., 2000; Klein-Tasman & Mervis, 2003; Mervis, Klein-Tasman, & Mastin, 2001). This social profile led researchers in the past to consider Williams syndrome as an extreme opposite of ASD (Jones et al., 2000). High empathy distinguishes individuals with WS from those with other developmental disabilities (Klein-Tasman & Mervis, 2003). Klein-Tasman and Mervis (2003) compared behaviors of 8 to 10-year-old children with WS to those of children with developmental disabilities of other etiologies, using parent reports from the Children’s Behavior Questionnaire (CBQ; Rothbart & Ahadi, 1994). The CBQ uses a 7 point Likert scale to indicate how typical listed behaviors are. The WS group’s empathy scores were significantly higher than those of the mixed etiology group (Klein-Tasman & Mervis, 2003).

As mentioned above, communication is typically a strength of individuals with WS, with socialization being the greatest strength (Mervis et al., 2001). Extreme sociability exhibited by individuals with WS is a characteristic feature of the disability, as manifested in overfriendliness and lack of fear of strangers (Jones et al., 2000). Such overfriendliness can be a liability (Gosch & Pankau, 1994), and many parents are
concerned that their children are unable to resist temptations to approach unfamiliar people (Doyle, Bellugi, Korenberg, & Graham, 2004). Social deficits in individuals with WS can also manifest as trouble establishing friendships, social isolation (Davies, Udwin, & Howlin, 1998), and low levels of social well-adjustment (Gosch & Pankau, 1994).

**Williams syndrome and ASD.** Although no population-based studies of ASD prevalence among individuals with WS exist, several studies suggest that the rate of ASD among individuals with WS is higher than the population prevalence listed by the CDC (CDC, 2010; Klein-Tasman et al., 2007; Lincoln et al., 2007). Using the Autism Diagnostic Observation Schedule, Klein-Tasman and colleagues (2007) found that approximately 50% of 29 participants with WS, ages 2.5 to 5.5 years, met the cutoff score for ASD (Klein-Tasman et al., 2007). A majority of participants also showed abnormal communicative abilities, with 21 of the 29 meeting or exceeding the ASD cutoff on the communication scale of the ADOS (Klein-Tasman et al., 2007). Abnormalities in play, and restricted and repetitive behaviors and interests were also seen (Klein-Tasman et al., 2007). Children with WS who met the cutoff score for ASD on the ADOS directed fewer vocalizations and facial expressions toward others, had less modulated eye contact, and did not initiate joint attention as effectively as the non-spectrum group (Klein-Tasman et al., 2007). However, the authors did note that both the ASD and non-spectrum groups displayed difficulties with pointing, giving, and showing. Deficits in these areas may therefore not be useful indicators of comorbid ASD in children with WS (Klein-Tasman et al., 2007).

In another study Lincoln et al. (2007) used the ADOS to examine ASD symptoms in a
small sample of individuals with WS, and found 5-10% co-occurring ASD. Similar to the findings of Klein-Tasman and colleagues (2007), a majority (11 of 20) individuals met or exceeded the cutoff score for ASD on the communication problems scale of the ADOS. On the social scale of the ADOS, two children met the cutoff score for ASD. However, when examining the children’s ADOS total scores, which are a combination of social, communication, and restricted and repetitive interest scales, only two were placed on the spectrum. Many children with WS also had difficulties with gestures, pointing, showing, and spontaneous initiation of joint attention, similar to findings reported previously. In another, smaller scale study of nine individuals with comorbid diagnoses of ASD and WS, ages 4-27 years (Tordjman et al., 2012), all participants displayed severe deficits in communication, reciprocal social interaction, and repetitive behaviors and stereotyped patterns, as measured by the ADI-R. All also showed a severe lack of shared enjoyment while between 4-and 5-years-old, according to the ADI-R. However, the eight participants who were over age six showed substantial improvement on ADI-R social interaction scores. All nine individuals displayed stereotyped behaviors, such as hand flapping and rocking.

Although these studies inform us about ASD symptoms among individuals with WS, none directly compared individuals with ASD vs. WS on an ASD measure. In fact, few studies investigate symptom overlap between these two disabilities (Järvinen et al., 2015; Klein-Tasman, Phillips, Lord, Mervis, & Gallo, 2009; Lough et al., 2015). Lough and colleagues (2015) investigated overlap between ASD and WS in the context of personal space violations (Lough et al., 2015), using the Social Responsiveness Scale (SRS). This
study included a large, multisite sample of 101 individuals with ASD and 77 individuals with WS, who ranged from 4 to 37 years of age. Mean total SRS T-scores were in the severely abnormal range for both the WS and ASD groups. However, the mean total SRS score for the ASD group was higher, which is indicative of more severe ASD symptoms. The authors also noted that within the ASD group, only 1% of children had SRS total T-scores within the normal range of social functioning, compared 18% in the WS group and 92% in a typically developing sample. Significant differences were found between the ASD and WS groups on communication, motivation, and mannerisms sub-domains.

Järvinin and colleagues (2015) also used the Social Responsiveness Scale as part of a larger study in which they investigated differences between ASD and WS groups on behavioral responses to social and non-social stimuli (Järvinin et al., 2015). This study included only 12 individuals with WS and 17 individuals with ASD, ages 7.5-13.5 years. The only significant difference between groups was in social motivation. Importantly, all children with ASD were classified as high functioning, which may account for few differences between groups.

Only one study included autism symptoms in WS and ASD as a main outcome (Klein-Tasman et al., 2009). Klein-Tasman and colleagues used the ADOS module one, designed for children who have no language or limited language, among 2.5-5.5-year-old participants. The authors calculated mean algorithm scores for social skills, communication, restricted repetitive interests, and play, as well as a total score. The ADOS classified approximately half of children with WS as on the autism spectrum, and results displayed significant differences between the ASD and WS groups on
communication, social, and total algorithm scores. There were no differences on the restricted and repetitive interest or play areas. The authors came to the conclusion that developmental delay alone does not account for deficits seen in social and communication among individuals with WS, as the differences persisted even when controlling for developmental level by the using Mullen Scales of Early Learning scores (Mullen, 1995) as a covariate.

Not only is there less research comparing individuals with WS and ASD than research comparing DS and ASD on ASD symptoms, there is a paucity of research comparing WS and ASD using measures of ASD symptoms, and no known studies that examine the prevalence of ASD among individuals with WS. Thus, more research regarding this overlap is needed to verify any increased prevalence of ASD among individuals with WS, in order to inform screening, diagnosis, and interventions (Klein-Tasman et al., 2007; Lincoln et al., 2007).
Screening for ASD

As demonstrated in the research reviewed above, young children with other developmental disabilities often share many behavioral symptoms with young children with ASD (Lord & Storoschuk, 1993). In fact, previous research demonstrates that a misdiagnosis of autism can occur in individuals with other disabilities due to delayed development (Bishop, Luyster, Richler & Lord, 2008). Therefore, a valid and reliable screening measure that differentiates ASD from other developmental disabilities is crucial, so individuals who meet criteria for ASD in addition to another developmental disability can receive specific services that they need, starting from a young age.

Research demonstrates that autism usually manifests no later than age three years (Lord, Cook, Leventhal, & Amaral, 2000), and that early, intensive behavioral intervention is imperative to prevent worsening of symptoms. Accordingly, much research on the clinical utility of screening measures has focused on early childhood.

Many diagnostic and screening instruments for ASD exist. These instruments range from "gold standard" diagnostic assessments, such as the Autism Diagnostic Observation Schedule (ADOS) and the Autism Diagnostic Interview-Revised (ADI-R), which are lengthy tests administered by trained professionals, to quicker parent-report screening assessments such as the Modified Checklist for Autism in Toddlers (M-CHAT; Robins et al., 2001) and the Social Communication Questionnaire (SCQ; Berument, Rutter, Lord, Pickles, & Bailey, 1999). Screening instruments have many benefits, such as being more time and cost efficient. Thus, it often makes sense to screen children for autism, then use
longer, more detailed assessments for children who fail screening. However, screening measures should not be used for diagnosis, since there is a high risk of false positives (Eaves, Wingert, Ho, & Mickelson, 2006; Witwer & Lecavalier, 2007).

Much research has addressed how useful screening assessments are in distinguishing individuals with ASD from typically developing controls, and from individuals with other developmental disabilities. Ventola and colleagues (2006) investigated differences between young individuals with ASD and individuals with global developmental delay or developmental language disorder. All participants were between 16-32 months of age, and although not all had an ASD diagnosis, all failed the M-CHAT autism screen. Failure on the M-CHAT is defined as any three of 23 total items failed, or any two critical items (e.g. “does your child respond to his/her name when you call,” or “does your child ever use his/her index finger to point, to indicate interest in something”) failed. The ASD group, compared with the global developmental delay and developmental language disorder groups, had lower standard scores on all four subtests of the Vineland Adaptive Behavior Scales (communication, daily living, socialization, and motor function), and many areas assessed by the ADOS and ADI-R differentiated the ASD group from the other groups. These assessments found deficits in reciprocal social interaction, pointing, and frequency of vocalizations toward others (Ventola et al., 2006). Thus, during early childhood, differences between individuals with ASD and individuals with other disabilities may be subtle enough for both groups to screen positive for ASD; however, the groups can be differentiated when more stringent diagnostic tests are administrated.
An additional study by Eaves and colleagues investigated the validity of a different screening assessment that is based on the ADI-R, called the Social Communication Questionnaire, or SCQ (Eaves et al., 2006). The SCQ is a 40 item yes/no assessment, with a cutoff score of 15 being recommended to differentiate individuals with ASD from individuals with other diagnoses (Berument et al., 1999). This study included 151 participants ranging from 36-82 months (Eaves et al., 2006). All participants were referred to an autism clinic for suspected autism diagnoses, but following a lengthy assessment including a parent interview, a play observation, and standardized assessments, as well as diagnostic clinical judgment. Among these 151 participants, 102 were classified as nonautistic, and 49 were classified as on the autism spectrum. Overall, the sensitivity score (individuals with autism correctly screening positive) was .71, and specificity scores (individuals without autism correctly screening negative) ranged from .53-.76, depending on the cutoff score used, as well as the clinic the sample was taken from (Eaves et al., 2006). Also, it is important to note that across all groups, there was a significant negative correlation (-.30) between the individual’s score on the SCQ and their Vineland Adaptive Behavior composite. Overall, this study supports the SCQ as a valuable screening tool, although the authors note that the differences are more difficult to distinguish when a child is either a high-functioning individual with autism, or a low-functioning individual with another disability (Eaves et al., 2006).

As screening is typically used for younger children, few studies investigate screening in older populations. Witwer and Lecavalier (2007) investigated the Developmental Behaviour Checklist-Autism Screening Algorithm (DBC-ASA; Brereton, Tonge,
Mackinnon, & Einfeld, 2002), a screening measure developed from the Developmental Behavior Checklist, as well as the SCQ (Witwer & Lecavalier, 2007). This study included 49 total participants, 36 with ID as well as pervasive developmental disorder (now categorized as part of the autism spectrum), and 13 with ID only (Witwer & Lecavalier, 2007). Individuals in the PDD group had a mean age of 8.3 years, and the individuals in the ID only group had a mean age of 10.2 years. The authors also note that the SCQ contains two versions, a current version which focuses on behaviors within the past three months, and a lifetime version, which encompasses behaviors throughout the child’s lifetime (Berument et al., 1999). The authors used the lifetime version in this study. The mean SCQ Total Score, and the mean DBC-ASA Total Score, were higher in the PDD group than in the ID only group (Witwer & Lecavalier, 2007). Within this older age range, both the SCQ and the DBC-ASA to be effective at identifying individuals with PDD, with the sensitivities/specificities being .92/.62 and .94/.46, respectively. Again, adaptive behavior, as measured by the Scales of Independent Behavior-Revised, was correlated negatively with SCQ Total Scores. These authors note that in the initial study for the SCQ, Berument and colleagues (1999) cautioned that lower mental ages can lead to higher rates of false positives (Berument et al., 1999).

As the above reviewed research demonstrates, screening instruments, although not as precise as “gold standard” diagnostic assessments, are useful in differentiating individuals with ASD from individuals with other/no disabilities, especially when a “gold standard” assessment is not feasible. However, few studies focus on screening for autism in the Down syndrome and Williams syndrome populations (DiGuiseppi et al., 2010;
Magyar, Pandolfi, Dill, 2012; Osório et al., 2015). This is a concern, as children with DS and WS have delays in adaptive behavior and overall development, which could increase the risk of false positives (Berument et al. 1999). However, the few studies that examine these populations suggest that autism screening is still feasible within these populations.

DiGuiseppi et al. (2010) screened 123 children with DS, age 2-11 using either the Social Communication Questionnaire or the Modified Checklist for Autism in Toddlers, depending on the child’s age and level of communication (DiGuiseppi et al., 2010). DiGuiseppi and colleagues assessed each child for autism with both the ADOS and the ADI-R, and used a measure of adaptive behavior. The combined sensitivity and specificity for both screeners was 87.5% and 49.9%, respectively. A false positive test was more likely if the child had a known hearing problem, a persistent vision problem even with the addition of glasses, or was born premature (DiGuiseppi et al., 2010).

Another study investigating the SCQ in individuals with comorbid DS/ASD or DS alone found that overall, the SCQ demonstrated strong sensitivity and specificity, and discriminated between the ASD/DS and the DS alone groups (Magyar et al., 2012).

A different study used SCQ to investigate autism symptoms in individuals with WS, to compare them with individuals with another genetic condition called Smith-Magenis syndrome (Osório et al., 2015). Every individual in the study (including 14 individuals with WS ages 4-38) was administered both the Current and the Lifetime versions of the SCQ. On the Lifetime and Current forms, the WS average mean was below cutoff for ASD. There were no significant sex differences on either of the SCQ forms.
Unfortunately, as the main goal of this study was to compare autism symptoms in individuals with Williams syndrome and Smith-Magenis syndrome, the researchers did not follow up the screener with a diagnostic assessment. Therefore, they made no claims regarding sensitivity and specificity.

Overall, screeners such as the SCQ are feasible in the DS and WS population. However, positive screen results must be interpreted with caution, and additional, more stringent diagnostic tests are needed, especially when children have significant adaptive behavior impairments, since there can be a higher rate of false positives. However, more research is needed, as no known studies examined the sensitivity/specificity of screeners among individuals with WS, and few studies investigate screening in individuals with DS. As both of these disorders have a higher prevalence of autism than in the overall population, more research into the overall profile of children with DS and WS who screen positive/negative is warranted.

**Adaptive Behavior**

The construct of adaptive behavior has been tied closely to intellectual disabilities for the last 100 years (Greenspan, 1999; Tassé et al., 2012), and as demonstrated in the aforementioned research, may play a critical role in correctly screening individuals with ID for autism. Adaptive behavior is used in the American Association on Intellectual and Developmental Disabilities (AAIDD) criteria for ID, which is two standard deviations below the mean on either a conceptual, social, or practical measure of adaptive behavior, or an overall score two standard deviations below the mean on a standardized measure of adaptive behavior (Schalock et al., 2010). According to the DSM-V, levels of adaptive
behavior should be used to determine severity of ID (American Psychiatric Association, 2013). According to Tassé and colleagues (2012), there are currently four psychometrically sound assessments of adaptive behavior developed for ruling in or out a diagnosis of ID (Tassé et al., 2012). These assessments include the Adaptive Behavior Scale—School (ABS-S; Lambert, Nihira, & Leland, 1993), the Vineland Adaptive Behavior Scales (Sparrow, Cicchetti, & Balla, 2005), the Scales of Independent Behavior-Revised (SIB-R; Bruininks, Woodcock, Weatherman, & Hill, 1996), and the Adaptive Behavior Assessment System (ABAS; Harrison & Oakland, 2003). It is important to note that among these assessments, only one, the Adaptive Behavior Assessment System, has three domains which correspond with the three areas of adaptive behavior listed by AAIDD.

Diagnosis of ASD, WS and DS all correspond with deficits in adaptive behavior; however, each condition has its own unique adaptive behavior profile (Bölte & Poustka, 2002; Daunhauer, 2011; Greer, Brown, Pai, Choudry, & Klein, 1997). The adaptive behavior profile for individuals with ASD typically includes a relative strength in daily living skills, fewer delays in communication, and greatest delays in socialization (Bölte & Poustka, 2002). In contrast individuals with WS typically demonstrate the largest relative strength in socialization, with communication being a strength as well, and typically have lower daily living domain scores (Greer et al., 1997). Although most studies of individuals with DS display socialization to be a relative strength in comparison to communication, research on the daily living skills abilities of individuals with DS has been mixed (Dolva, Coster, & Lilja, 2004; Dykens, Hodapp, & Evans, 2006:}
Leonard, Msall, Bower, Tremont, & Leonard, 2002). Daily living skills are a relative strength in comparison to communication based on a study using the VABS (Dykens et al., 2006); however, studies using other measures to investigate daily living skills show these skills to be a challenge for individuals with DS (Dolva et al., 2004; Leonard, Msall, Bower, Tremont, & Leonard, 2002). However, when Daunhauer (2011) synthesized all of the adaptive behavior profiles into one summative report, she concluded that daily living skills should be listed as an overall weakness in the DS adaptive behavior profile (Daunhauer, 2011). As demonstrated above, all three groups have unique adaptive behavior profiles, which includes both overlaps and disparities between groups.

Only one known study has compared the adaptive behavior profiles of DS individuals with and without comorbid ASD, and no known studies investigate the aforementioned comparison among individuals with WS (Molloy et al., 2009). Molloy and colleagues compared scores on the Vineland Adaptive Behavior Scales within 19 pairs of children, one child having DS and ASD, and the other having only DS, matched on chronologic age, race and sex.

Results displayed significant differences between the groups on the Adaptive Behavior Composite Score and the Daily Living Skills, Communication, and Social domains, with the DS only group having higher scores in each area. There was also a significant difference between groups one Adaptive Behavior Composite Scores. Those with comorbid autism and Down syndrome had lower adaptive behavior levels than those with DS alone.

**Research Needs**
Previous research demonstrates the utility of investigating overlap between ASD and genetic conditions which display a higher prevalence, as this can lead to new understandings as to potential etiologies of autism in those conditions. Additionally, research into overlap between ASD and genetic conditions can improve autism screening, diagnosis, and interventions in these populations. Previous research on ASD and DS shows that not only does ASD occur more frequently among these individuals than in the population, but many children with DS who do not receive an ASD diagnosis still exhibit elevated ASD symptoms. More research is warranted to determine how autism symptoms manifest in individuals with DS, using an assessment which can give meaningful score differences in different deficit areas common to autism. With regard to Williams syndrome, less is known about overlap between individuals with WS and ASD, as limited research exists. There are no known large-scale studies of the prevalence of ASD in individuals with WS, and relatively few studies investigate overlap between these two disorders on the basis of autism symptoms. However, research studies demonstrate that individuals with WS do seem to exhibit higher rates of autism than reported in the overall population. Again, more research is needed to further understand this overlap. Further research is also warranted regarding the role of adaptive behavior in autism symptom testing results, as although ASD, DS, and WS exhibit their own unique adaptive behavior profiles, research demonstrates that children with a genetic condition and a comorbid ASD diagnosis (in this case DS) have significantly lower adaptive behavior scores than individuals with DS alone (Molloy et al., 2008). Therefore, additional research regarding ASD overlap in individuals with DS and WS is warranted.
Current Study

In the current study I aimed to investigate overlap of autism symptoms in school-aged children with two genetic conditions known to have increased prevalence of autism, Down syndrome and Williams syndrome. I used an online survey platform to compare groups of individuals with ASD, DS, and WS. Parents of children completed a dimensional measure of autism symptoms (Autism Spectrum Rating Scales; ASRS) to examine symptom profiles in more detail, and a screening measure (Social Communication Questionnaire; SCQ) to examine how many children in these groups screen positive for autism. We also investigated adaptive behavior profiles using the Adaptive Behavior Assessment System, Third Edition (ABAS-3; Harrison & Oakland, 2015a). This is the first known study to directly compare these three conditions, and the first known study of children with DS or WS to use the Autism Spectrum Rating Scales (ASRS; Goldstein & Naglieri, 2009).

The SCQ is the best available screening instrument for differentiating between children with ASD and children with other developmental disabilities (Charman et al., 2007; Magyar et al., 2012), and was therefore used to investigate the number of individuals at-risk for ASD in each group, and to separate WS and DS groups into screen-positive versus screen-negative subgroups. The ASRS is a measure designed to assess the presence of autism symptoms, and has three factors in individuals ages 6-18 years: social/communication, unusual behaviors, and self-regulation (Goldstein & Naglieri, 2010). We used ASRS as a dimensional measure of ASD symptoms in these groups. Using a dimensional measure of ASD symptoms with this three-factor structure allowed
me to examine potential differences between ASD symptom clusters. Finally, we used the ABAS-3 to explore adaptive behavior profiles in each subgroup to examine the relation between ASD symptoms and adaptive behavior profiles. As previous research shows that a misdiagnosis of autism can occur in individuals with other disabilities due to delayed development (Bishop, Luyster, Richler & Lord, 2008), we used an older sample (individuals ages 6-18) in order to reduce the chances of delayed development as a confound. It is my hope that this research will shed light on phenotypic overlap between autism and these known genetic conditions, and the profile of autism symptoms displayed on the ASRS within each group. This, in turn, could lead to new insights on how autism manifests in both Down syndrome and Williams syndrome, and will develop future directions for new research in how to best screen, diagnose, and create interventions for these groups of individuals.
Chapter 2: Methods

Participants

Recruitment. Participants were contacted via email from research databases, national conferences, Nisonger Center distribution lists and contacts, and through Qualtrics. Primary caregivers of individuals with Down syndrome were contacted via DS-Connect®, primary caregivers of individuals with WS were contacted via the Williams Syndrome Association research registry (www.williams-syndrome.org/registry); owned by the WSA, as well as at the Williams Syndrome National Conference in Columbus, Ohio, July 4-8, 2016 and primary caregivers of individuals with autism were contacted via the Nisonger Center research registry, and through a Qualtrics recruitment pool. DS-Connect® is a resource created by the National Institutes of Health and is designed to foster connections between researchers and individuals with DS and their families who are interested in participating in research. At the time of the study, DS-Connect® listed 1264 individuals with DS within our age range. The WS Association research registry is a resource created by the Williams Syndrome Association to promote research in WS. At the time of this study, the registry listed over 300 individuals within our age range. Both registries have a specific process in receiving permission to recruit through their database, DS-Connect® utilizing a Research Review Committee, and the WS Association registry utilizing an approval process. We recruited primary caregivers of
individuals with autism via the Nisonger Center Research Registry and distribution lists, as well as through the Qualtrics recruitment pool. As an incentive to participate, survey respondents received the option to enter an email address to be placed in a drawing to receive one of four $25 Amazon gift cards. The exception to this was the group recruited through Qualtrics, as they had a prearranged compensation agreement.

**Inclusion Criteria.** To be eligible for the study, primary caregivers had to have a child, ages 6-18 years, with a diagnosis of autism, Down syndrome, or Williams syndrome. Primary caregivers also had to be able to complete the survey in English, as the survey was only offered in English. As this study is solely survey based, confirmation of diagnosis relied on parental report.

**Exclusion Criteria.** For participants with a child with ASD, the individuals with ASD were required to screen positive for autism on the SCQ to be eligible for the study. Additionally, parents or primary caregivers of individuals with DS or WS must note that their child has a genetic confirmation of his/her diagnosis.

A total of 167 participants (ASD= 44, DS= 78, WS=46) participated in the survey. We excluded a total of 8 cases excluded from the analyses, due to being in the ASD group and not screening positive on the SCQ (n=5), or being in the DS or WS group and not having genetic confirmation (DS=2, WS=1). A flowchart of subject participation is displayed in Figure 1.

A majority of the survey respondents in all groups were mothers (ASD=64.1%, DS=92.1%, WS=80.0%), identified their race as White (ASD=89.7%, DS=93.4% WS=93.3%), and their ethnicity as not Hispanic or Latino (ASD=82.1%, DS=96.1%
English was the primary language spoken in the home for all groups (ASD=100.0%, DS=97.4% WS=91.1%). The groups varied with regards to level of education, with the percentage noting that they had at least a college level of education being 56.4%, 73.3%, and 90.8%, in the ASD, WS, and DS groups, respectively. Groups also varied in household income, with more individuals in the DS (64.5%) and WS (40%) groups reporting a household income of $90,000 or greater in comparison to the ASD group (23.1%).

Visual inspection of outliers revealed three outliers in the parent age variable. Inspection of the data led us to believe that parents had mistakenly entered the age of their child, as the outliers consisted of ages between the ages of 6-18 years. Therefore, we excluded three parent ages from the demographics. The average age of participants varied across groups, with the respondents in the DS group ($M=47.91$ years, $SD=5.31$) being significantly older than the individuals in both the ASD ($M=42.97$ years, $SD=10.04$ years) and WS groups ($M=42.82$ years, $SD=7.12$ years), $F(2,156)=9.49$, $p<.001$. A summary of respondent demographics is displayed in Table 1.

In regards to the target children, there was a significant different in sex, with a higher percentage of males in the ASD group (74.4%) than in the DS (38.2%) and WS groups (60.0%), $F(2,159)=8.10$, $p<.001$. This difference was expected due to the known increased prevalence of ASD in boys compared to girls. Similar to respondent characteristics, a majority of participants noted their child’s race as white (ASD=84.6%, DS=93.4%, WS=93.3%), and their ethnicity as not Hispanic or Latino (ASD=87.2%, DS=96.1%, WS=88.9%). Although children in the WS group had a younger average age
(M=10.60 years, SD=3.62 years) than children in the DS (M=11.88 years, SD=3.28 years) and ASD (M=11.96 years SD=3.61 years) groups, child age was not different across groups. In regard to percent of day spend with typically developing peers in the school setting, more children with ASD spent their entire day in a classroom with typically developing peers (35.9%), in comparison to children in the DS (7.9%) or WS (8.9%), although the difference was not statistically significant. A summary of child demographics can be found in Table 2.

**Power Analysis.** As no known studies used the Autism Spectrum Rating Scales in comparing two of the groups, let alone all three groups, we computed a power analysis with studies that used the Social Responsiveness Scale, another parent report measure of autism symptoms studies (Channell et al., 2015, Lough et al., 2015). Additionally, as no known studies compare ASD, DS, and WS across a measure of autism symptoms, we combined data from two different studies to create the three groups that this study will be comparing. We used the means, standard deviations, and sample sizes from Lough and colleagues for the ASD and WS groups, as we found the large, multi-site nature of the study and the participant ages to most closely mirror the methods for this study (Lough et al., 2015). The third comparison group in this study was a typically developing group, so we replaced data with DS data from Channell and colleagues (Channell et al., 2015). We chose this study as it used children from a similar age group, and also used a larger, multi-site data collection method. Cohen’s $d$ for these three comparisons ranged from 0.89 to 2.3. As three comparisons will be made for the primary hypothesis (ASD vs. DS, ASD vs. WS, and DS vs WS), the alpha level of .05 was divided by three for a new alpha
of .017. Based on a power of .8, the calculated required sample size was 28 per group, or 84 total participants.

**Procedures**

The Institutional Review Board at Ohio State University approved this study. Potential study participants were contacted via email. If a participant chose to take part in the study, the email directed the participant to click on a secure, password protected link, which took him/her to the Qualtrics survey. This email also made respondents aware that the survey could be completed in more than one setting. The survey began with demographic questions (see Appendix A). However, the survey did not ask for identifying information, such as names or birthdays.

After the demographic survey, the caregiver then filled out the three assessments, in the following order: Autism Spectrum Rating Scales, Social Communication Questionnaire, Adaptive Behavior Assessment System, Third Edition. The survey did not force respondents to answer any questions; however, it did ask one additional time for a respondent to complete all questions if a question is left blank. The reminder message was as follows: *There are __ unanswered questions on this page. Would you like to continue?* Respondents may then continue without answering, or answer the question. The survey also displayed a progress bar so respondents were aware of their progress. At the conclusion of the survey, a message thanked respondents, and gave them the option to enter their email address to receive a gift card (with the exception of the Qualtrics recruitment group). To further protect participant confidentiality, we did not link this
survey to the study survey. The study survey took approximately 20-35 minutes to complete, and we collected data from June 2016-March 2017.

It is important to note that although two of the assessments (ASRS and ABAS-3) are currently available in online formats, we converted all three assessments to one Qualtrics survey to minimize participant dropout due to excessive links and instructions. We obtained permission to convert all three assessments from their respective publishing companies (MHS for the ASRS and WPS for the SCQ and the ABAS-3).
Measures

Social Communication Questionnaire (SCQ; Rutter, Bailey, & Lord, 2003a). The SCQ is a 40-item yes/no autism screening questionnaire that is filled out by the child’s parent or primary caregiver. This test can be used in children over the age of four, with a mental age over 2 years, and assesses the symptoms corresponding with autism spectrum disorder. Items are scored as either a 0 or a 1, with a score of 1 endorsing a higher risk for autism, leading to the potential highest score being a 39 as the first question is a measure of the child’s language level. The SCQ was developed from a current diagnostic interview, the Autism Diagnostic Interview-Revised (ADI-R; Lord et al., 2005). There are two versions of the SCQ, the Current form and the Lifetime form. As the Lifetime form is better suited for diagnostic purposes, and the Current form is best utilized for younger children and to assess change (Rutter et al., 2003b), we used the Lifetime form in this study. When assessed for validity, 85% of the SCQ items significantly differentiated autism from other diagnoses (Berument et al., 1999). Correlations between the SCQ and the ADI-R total scores, as well as the ADI-R domain scores, were statistically significant as well, suggesting strong construct validity. The creators of the SCQ determined a cut off score of 15 to be the best score to differentiate ASD from other intellectual disabilities, with a sensitivity of .96, and a specificity of .67. Although lowering the cutoff score to 11 improves sensitivity and specificity in some studies (Corsello et al., 2007; Snow & Lecavalier, 2008), this study used the recommended cut
off score of 15, as the previously mentioned studies had samples with individuals under the age of 6.

**Autism Spectrum Rating Scales** (ASRS; Goldstein & Naglieri, 2009). The ASRS are designed to assess behaviors associated with ASD in children aged 2-18. This assessment is available in both a short and full-length format, and can be filled out by either an individual’s primary caregiver or teacher. This study used the full length parent/primary caregiver form for individuals aged 6-18 years, which contains 71 items. The full length scale for ages 6-18 yields a total score, which is comprised of the three ASRS scales (Social/Communication, Unusual Behaviors, and Self-Regulation), as well as a DSM-IV-TR scale, and eight treatment scales. As research has demonstrated a three factor solution being the best fit for the ASRS (Goldstein & Naglieri, 2009) corresponding with the three ASRS scales, only these scales, as well as the total score, will be used for analyses in this study. This specific form has exhibited strong reliability, with Total Score weighted average internal consistency being .97, and ASRS scales reliability ranging from .92-.95. When ratings of children with ASD were compared with individuals with other diagnoses, the ASD group scored significantly higher on all scales which will be utilized in this study, indicative of good criterion-related (Goldstein & Naglieri, 2009). Strong construct validity for this assessment is also evidenced by the three factor structure found, corresponding to the three ASRS scales.

**Adaptive Behavior Assessment System, third edition** (ABAS; Harrison & Oakland, 2015a). We used the ABAS-3 parent/primary caregiver form (ages 5-21) in this study. The ABAS-3 gives a General Adaptive Composite score, comprised of conceptual,
social, and practical domain scores. These domains are further broken down into a total of 9 skill sets, which are as follows: communication, community use, functional academics, home-living, health and safety, leisure, self-care, self-direction, and social. Additionally, there is a work skill set that can be administered; however, this study did not utilize the work skill set. Each skill set consists of 20-25 questions, and respondents answer each question as either ‘is not able’, ‘never (or almost never) when needed’, ‘sometimes when needed’, or ‘always (or almost always) when needed’. Each item also gives respondents the opportunity to check a box if they guessed on a question.

Reliability of the ABAS-3 is strong, with coefficient alphas for the GAC ranging from .96-.99 (Harrison & Oakland, 2015b). Skill sets comprise three factors, representing the Social, Conceptual, and Practical Domains, or the ABAS-3 can fit into a one-factor model represented by the GAC. Although the one-factor model provided the best fit, both the one- and three-factor models showed improved fit over the null model. The ABAS-3 also demonstrates good construct validity, evidenced by its moderate to strong correlations (average of .66) with the Vineland Adaptive Behavior Rating Scales, Second Edition. The current validity studies reported for the ABAS-3 are identical to the studies reported for the ABAS-II, as the two editions are extremely similar on item content (Harrison & Oakland, 2015b)

**Hypotheses and Analyses**

Primary study hypotheses were as follows:

1. More individuals with DS and WS will screen positive on the SCQ than the population prevalence reported in previous research (Chandler et al., 2007)
a. A Fisher exact test of independence comparing the proportion of individuals
the DS and WS group who score above the cutoff score of 15 on the SCQ was
compared against the 4.4% reported by Chandler and colleagues in a general
population sample.

2. The ASD group will have a Total Score on the ASRS significantly higher than both
the DS and WS group.
   a. To test this hypothesis, we used a one-way ANOVA with the three groups

3. The ASD group, the WS group and the DS group will have significantly higher
ASRS total scores in comparison to the normative sample mean.
   a. To test this hypothesis, we used three one-sample t-tests to compare each
group to the normative sample mean of 50 and standard deviation of 10.

4. There will be an overall negative correlation between ABAS-3 General Adaptive
Composite scores and ASRS Total Scores.
   a. We used a Pearson correlation between ABAS-3 General Adaptive Composite
Scores and ASRS Total Scores to test this hypothesis.

5. When controlling for adaptive behavior, sex, and age, group membership (DS, WS,
ASD) will predict a child’s ASRS total score.
   a. To test this, we used a multiple regression analysis with ASRS total score as
the dependent variable, and group membership, sex, age, and ABAS-3
General Adaptive Composite Scores as the predictor variables

The secondary hypothesis of the study was as follows:
1. The screen negative groups for each syndrome will have significantly lower ASRS Total Scores than their corresponding screen positive group.

   a. We tested this hypothesis using a 2x2 ANOVA, comparing screen positive and screen negative individuals with DS and WS.

   One reason that we chose to utilize the ASRS as a measure of autistic symptoms was so we could examine the ASD “profiles” of individuals with DS and WS, by comparing their scores on the Self-Regulation, Social/Communication, and Unusual Behavior scales both within groups and between groups. However, as no known study has used the ASRS within the DS or WS population, we cannot generate specific hypotheses by subscale based on previous research. Therefore, examinations of group differences in ASRS subscales was considered exploratory.
Chapter 3: Results

ASD Diagnosis and Screening in DS and WS

A total of five of the seventy-six included respondents in the DS group (6.6%), and four of the forty-five included respondents in the WS group (8.9%) indicated that their child had a comorbid ASD diagnosis. Of respondents who did not state that their child had a comorbid ASD diagnosis, three (3.9%) in the DS group and five (11.1%) in the WS group stated that a professional has suggested their child be referred for an autism spectrum disorder diagnosis. Seventeen out of the seventy-six individuals (22.4%) in the DS group scored above the cut off score of 15 on the Social Communication Questionnaire (SCQ), thus screening positive, and twenty out of the forty-five individuals with WS (43.5%) screened positive. A Fisher exact test of independence revealed both of these proportions to be significantly different from the 4.4% general population screen positive rate reported in previous research (ps<.001).

On average, scores on the SCQ fell below the cutoff of 15 in the DS group (M=9.64, SD=6.91) and approximately at the cutoff in the WS group (M=14.68, SD=7.14). A one-way ANOVA indicated that the ASD, DS, and WS groups differed, on average, in their SCQ total scores, F(2,149)=44.24, p<.001. All pairwise comparisons using the Games-Howell method to correct for multiple tests revealed that the ASD group had a higher mean SCQ total score than both the DS group (p<.001) and the WS group.
Additionally, the WS group had a higher mean SCQ total score than the DS group \((p<.001)\). Frequency distributions of SCQ total scores for the DS and WS group are displayed in Figure 2.

**ASRS Total Scores**

Results of a Shapiro-Wilk test of normality revealed ASRS total scores to be normally distributed in the DS, WS, and ASD groups. Therefore, we used a one-sample \(t\)-test to compare the mean score of each group to the sample mean of 50. One-sample \(t\)-tests indicated that the average total score on the ASRS was significantly different from the mean ASRS score of 50 in the DS group \((M=58.96, SD=7.79), t=10.03, p<.001\), the WS group \((M=65.24, SD=6.03), t=15.57, p<.001\), and the ASD group \((M=71.74, SD=5.04), t=26.97, p<.001\). A one-way ANOVA revealed that the ASD, DS, and WS groups differed, on average, in their ASRS total scores, \(F(2,150)=47.21, p<.001\).

Pairwise comparisons using the Games-Howell method to correct for multiple tests revealed that the ASD group had a higher mean ASRS total score than both the DS group \((p<.001)\) and the WS group \((p<.001)\). Additionally, the WS group had a higher mean ASRS total score than the DS group \((p<.001)\).

To determine if there were significant differences on ASRS total scores between screen-positive versus screen-negative groups on the SCQ, we performed an ANOVA. Results of a two-way ANOVA revealed a significant main effect of screening positive on the SCQ on mean ASRS total scores, \(F(1,110)=44.5, p<.001\). Those who screened positive on the SCQ had a higher mean ASRS total score \((M=67.86, SD=6.17)\) than those who screened negative \((M=57.91, SD=6.37)\). In the DS group, results indicated that
individuals who screened negative on the SCQ ($M = 56.72, SD = 6.33$) and those who screened positive ($M = 66.76, SD = 7.43$) differed, on average, on their ASRS total scores, $F(1,75)=31.18, p<.001$. Similarly, those with WS who screened negative on the SCQ ($M = 61.63, SD = 4.97$ and those who screened positive ($M = 68.84, SD = 4.77$) also differed, on average, on their ASRS total scores [$F(1,36)=20.85, p<.001$]. Descriptive statistics of ASRS scales are displayed in Table 3.

**Role of Adaptive Behavior**

Descriptive statistics of ABAS-3 scales are displayed in Table 3. Results of a Pearson correlation revealed a significant weak negative correlation between General Adaptive Composite Scores (GAC) and ASRS total scores, $r(144) = -0.30, p < 0.005$. At the group level, there was a significant moderate negative correlation between GAC and ASRS total scores in the DS group, $r(73) = -0.49, p < 0.005$, but there were no significant correlations in the WS or ASD group. To test the hypothesis that group membership would predict ASRS total scores, when controlling for age, sex, and adaptive behavior (as measured by the General Adaptive Composite on the ABAS-3), we performed a multiple regression analysis. Results of the analysis revealed that when controlling for sex, age, and GAC total scores, individuals with ASD had significantly higher ASRS total scores, on average, than individuals with DS, $R = 0.705, b_{2x}=-12.82 \ p < 0.001$, or WS, $R = 0.705, b_{2x}=-6.8 \ p < 0.001$. These results are displayed in Table 4.

**ASRS Exploratory Analyses**

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1 This remained significant even after removing individuals that had comorbid diagnoses of ASD and DS/WS
As one of the secondary aims of this study was to use results of the ASRS to examine the ASD “profiles” both the WS and DS group, we used a repeated measures ANOVA to investigate differences both between and within groups on the three ASRS subscales (Self-Regulation, Social/Communication, and Unusual Behaviors). After applying a Greenhouse-Geisser correction for a violation for the assumption of sphericity, results indicated a significant main effect among the subscale on the ASRS both within the DS, $F(1.73)=25.64; \ p<.001; \ \eta p^2=.26$, and WS, $F(1.47)=5.28; \ p<.05; \ \eta p^2=.13$, groups. Following a Bonferroni correction, pairwise comparisons for the DS group revealed a significant difference between the Unusual Behaviors subscale ($M = 61.79, \ SD = 8.23$), and the Social Communication ($M = 55.93, \ SD = 9.26$) and Self-Regulation ($M = 54.88, \ SD = 7.57$) subscales ($p<.001$). Within the WS group, pairwise comparisons indicated a significant difference between the Unusual Behaviors ($M = 65.53, \ SD = 6.42$) and Social Communication ($M = 60.84, \ SD = 8.69$) subscales ($p<.05$).
Chapter 4: Discussion

The main goal of this study was to examine the presence of autism symptoms in individuals with Down syndrome and Williams syndrome. Overall, we found that children in both the DS and WS groups exhibited elevated ASD symptoms across two different measures of autism symptoms. These elevations were not solely accounted for by deficits in adaptive behavior.

Firstly, the percentage of individuals who entered the study with a comorbid diagnosis of ASD was higher than one would expect (DS=6.6%, WS=8.9%), based on the 1 in 68 (1.47%) prevalence reported by the CDC (CDC, 2010). This is in line with previous research, suggesting that the prevalence of ASD is higher in the DS and WS populations (Klein-Tasman et al., 2007; Lincoln et al., 2007; Reilly, 2010). Additionally, of the respondents who did not note that their child had a comorbid ASD diagnosis, three (3.9%) in the DS group and five (11.1%) in the WS group stated that a professional has suggested their child be referred for an autism spectrum disorder diagnosis in the past. This suggests that not only are children with DS or WS receiving ASD diagnoses at a higher rate than the general population, but they are also being flagged by professionals for ASD referrals. However, it is not known why professionals flagged these children as at-risk, and if these children had follow-up assessment. Results of this study do demonstrate that there seems to be an elevation in ASD diagnoses and referrals in the DS and WS population.
Along with this, more individuals with DS (22.4%) and WS (43.48%) screened positive on the SCQ than the 4.4% reported in previous research (Chandler et al., 2007), including all nine of the individuals noted to have a comorbid ASD diagnosis. Significantly more individuals in the WS group screened positive on the SCQ in comparison to the DS group, which suggests more pronounced symptoms of ASD in those with WS. Although we had a relatively large number of individuals screen positive, results of this study cannot determine how many individuals in our sample have a comorbid diagnosis of autism. Previous research demonstrates that for individuals with DS, the SCQ has excellent sensitivity (100.0%), but a specificity of 57.1%, suggesting the potential for false positives in the DS population (DiGuiseppi et al., 2010). However, as the creators of the SCQ adapted this screener from the Autism Diagnostic Interview-Revised, a gold standard autism diagnostic assessment (Berument et al., 1999; Lord et al., 1994), it is likely that the children who have SCQ scores above the cutoff are exhibiting symptoms associated with ASD. Additionally, children who screened positive on the SCQ had significantly higher total scores on a dimensional measure of autism symptoms, in comparison to those who screened negative.

The significantly higher scores in both the DS and WS groups in comparison to the normative sample mean on ASRS total scores also suggest elevated levels of ASD symptoms in these populations. Again, this is similar to previous research, which found elevated ASD symptoms in the DS and WS populations (Channell et al., 2015; Evans & Gray, 2003; Järvinen et al., 2015; Kent et al., 1999; Klein-Tasman et al., 2009; Lough et al., 2015). Additionally, the WS group had significantly higher scores than the DS
groups, which suggests more pronounced ASD symptoms in the WS group in comparison to the DS group. Both groups’ mean ASRS total scores were significantly lower than the ASD group. This suggests the most pronounced elevations of ASD symptoms in the ASD group, followed by the WS group, the DS group, and then the normative sample. Taken together, these findings regarding parent-reported rate of ASD diagnosis, elevated screen-positive rates on the SCQ, and elevated ASD symptom scores on the ASRS suggest an increase in ASD diagnoses in both the DS and WS group, as well as an increase in ASD symptoms in both groups, particularly in the WS group.

As mentioned previously, we chose to use the ASRS as its three-factor structure allowed us to make meaningful comparisons using the ASRS subscales as well. Looking across subscales on the ASRS, we saw that all three subscales (Social Communications, Self-Regulation, and Unusual Behaviors) were significantly higher than the mean score of 50 in both the DS and WS groups. This suggests that there is not only one type of symptom associated with ASD elevated for individuals with DS and WS, rather, there are elevations across all areas of ASD symptoms. Additionally, these elevations are not only present for those who screen positive for ASD.

Looking at each group individually, different subscale patterns emerged. In the DS group, the Unusual Behaviors subscale was significantly higher than both the Social Communication and Self-Regulation subscales. All of these subscales were significantly lower than the ASD group, suggesting that although significantly higher than the normative sample mean, the DS group overall had less ASD symptoms across all areas in comparison to the ASD group. However, this was not the case for the WS group. Within
the WS group, only a significant difference between unusual behaviors and social communication emerged, suggesting that for both the DS and WS groups, the most substantial ASD symptoms are in the area of unusual behaviors. However, in the WS group the only subscale that was significantly different from the ASD group was the Social Communication subscale. This suggests that based on the ASRS, behaviors associated with self-regulation abilities or the presence of unusual behaviors do not differentiate individuals with WS from individuals with ASD.

There are several potential explanations for the elevated ASD symptom scores observed in children with WS and DS in this study. One potential explanation for these findings could be false positives and ASRS elevations simply due to low developmental level, as seen in previous research (Bishop et al., 2008). Individuals with substantial developmental delays (especially in younger age groups) may show false positives on ASD measures due to not yet having attained important developmental milestones in the social area (e.g., using pointing gestures, engaging in reciprocal conversation). One way we attempted to alleviate this was by using an older sample, to hopefully reduce the effect of the confound of developmental delay. Additionally, results of this study suggest that developmental delay does not fully account for the elevations on measures of ASD symptoms, as group membership predicted ASRS total scores, even when controlling for adaptive behavior. If impairments in adaptive behavior fully explained the elevated ASRS scores, then group membership would not have been a significant predictor after adaptive behavior was added to the model. Therefore, we can assume that delayed development is not the reason for the elevated ASRS total scores.
A second potential explanation is that elevated scores on ASD measures are simply an artifact of measurement issues. Although the SCQ demonstrates good sensitivity/specificity, research does demonstrate a higher false positive rate for those with DS (DiGuiseppi et al., 2010), and although no known studies have investigated the sensitivity/specificity of the SCQ in the WS population, research demonstrates a higher false positive rate for those with ID (Witwer & Lecavalier, 2007). There is a possibility that certain questions on the SCQ may be misunderstood by parents or apply differently to the DS or WS population. For example, many individuals with WS display an affinity for music (Dykens, Rosner, Ly, & Sagun, 2005), which may lead a parent to noting that their child has had a “special interest that was unusual in its intensity, but otherwise appropriate for his/her age.” Interestingly, 59.5% of parents of children with WS noted the above statement as applying to his/her child. Additionally, 73.0% of parents of children with WS marked that their child has used socially inappropriate questions or statements, and 51.3% of parents of children with DS noted that their child has had things that he/she seemed to have to do in a particular way, or order or rituals they insisted others go through. Past research demonstrates extreme friendliness in children with WS (Jones et al., 2000), which may manifest as socially inappropriate questions, and individuals with DS are known to display obsessive compulsive behaviors (Kent et al., 1999). These results suggest that certain questions on the SCQ may not differentiate those with DS and WS who have a comorbid diagnosis from those who do not. Screening for ASD in the DS or WS populations could be improved upon by examining individual items on screeners such as the SCQ, to determine which items are most successful in
differentiating individuals with DS or WS who have a comorbid ASD diagnosis from those who do not. Interestingly, although parents of children with WS endorsed some questions asking about social-communicative behaviors at high rates, such as asking socially inappropriate questions or not engaging in imaginative play with others, results of the ASRS subscale analyses demonstrated that on the ASRS, questions about social communication were the only questions that differentiated the WS group from the ASD group. However, questions on the social-communication subscale of the ASRS are related to empathy, “understand how someone else felt,” and social interest, “share his/her enjoyment with others” or “show an interest in the ideas of others.” Therefore, it is possible that questions asking about social interest and empathy may better differentiate children with WS from those with WS and a comorbid ASD diagnosis.

Although children with DS were significantly different from those with ASD across all subscales of the ASRS, the significantly higher elevation on the Unusual Behaviors subscale combined with the fact that research demonstrates obsessive-compulsive behaviors in individuals with DS suggests that questions asking about social communication skills may be better at differentiating children with a comorbid ASD diagnosis in comparison to questions asking about unusual behaviors.

Although the measurement concerns discussed above may partially explain the high SCQ and ASRS scores, it is likely that this does not account for all of screen positives and elevated ASRS scores in this sample. Previous research using gold standard diagnostic assessments for ASD, such as the ADOS, has found an increased number of individuals in the DS and WS population receiving a comorbid diagnosis of ASD.
(Hepburn et al., 2007; Klein-Tasman et al., 2007; Lincoln et al., 2007). Based on this, it is likely that true elevations in ASD symptoms account for all or part of these findings. Therefore, one explanation may be a potential etiological overlap between DS/WS and ASD. The genetic etiology of DS and WS may be known, however; much still needs to be learned regarding the roles of the genetic material that is duplicated or deleted in these conditions. It is possible that there is a similar genetic etiology in these genetic conditions and idiopathic ASD. As we continue to learn more about the genetic causes of ASD, it is possible that genes in the WS region or on the twenty-first chromosome may be implicated. For example, the gene/or genes responsible for the hypersociability seen in WS is still not fully understood. Once we gain a deeper understanding, it is possible that these genes may be a target to investigate in large-scale genetic studies of individuals with idiopathic autism. Of course, research demonstrates that it is likely a combination of genes implicated in ASD, so it is highly unlikely that just one of these genes is driving the genetic etiology of autism.

Additionally, there is a possibility that although genetic etiology may differ, the neurological processes underlying each disorder may be similar. For example, although not all children with the genetic abnormalities found in fragile X have a comorbid diagnosis of ASD, a dysregulation in amyloid beta precursor protein is seen in individuals with fragile X and idiopathic ASD, which might be contributing to the brain overgrowth seen in ASD and FXS (Erickson et al., 2014a). In regards to Williams syndrome, one potential neurobiological pathway may be related to the amygdala, as abnormalities in amygdala functioning are seen in both individuals with WS (Haas, Mills, Yam, Hoeft,
Bellugi, & Reiss, 2009) and ASD (Kleinhans et al., 2008). In regards to DS, research demonstrates repetitive behaviors in mouse models with targeted CNS insults, such as in the amyloid precursor protein transgenic model of Alzheimer’s disease (Ambree et al., 2006). Given the relation between APP in ASD and FXS, and the relationship between Alzheimer and DS, this has the potential for shared neurobiological processes in DS and ASD in regards to restricted and repetitive behavior. More research is needed using functional brain imaging and mice models to further investigate the potential for shared neurobiological pathways in ASD and DS/WS.

As this study only used an autism screener and a dimensional measure of autism symptoms, we cannot make claims as to how many individuals in our sample would receive an autism diagnosis. However, our results do show elevations in ASD symptoms in the DS and WS population, and we did have more individuals entering the study with an ASD diagnosis than we would expect based on the reported population prevalence. Therefore, we can conclude that our sample does have an increase in ASD diagnosis and symptoms in comparison to the population prevalence. This raises the question as to what it means to have an autism spectrum disorder and the utility of giving an additional ASD diagnosis in individuals who already have a genetic diagnosis. ASD is a behaviorally defined disorder. Therefore, individuals with many different etiologies may show similar behavioral characteristics and receive ASD diagnoses.

There is a possibility that although etiologically different, individuals with DS and WS display behavioral characteristics synonymous with autism spectrum disorder. Based on the results of this study, we know that there is a higher number of screen positive
individuals on the SCQ than in a sample used in previous research, that there is an elevation across all subscales and total scores on the ASRS, and that there is a meaningful difference on ASRS total scores from those who screen positive and those who screen negative. However, we do not know how many of these individuals would receive a diagnosis of ASD. Along with this, we do not know if the characteristics displayed by these individuals are etiologically or functionally different from features of ASD in individuals with idiopathic ASD, and if this matters in terms of intervention. For example, if children with ASD and WS both have inappropriate social behavior, yet the mechanisms behind this behavior are different, how might that alter the effectiveness of intervention? Research demonstrates a decrease in fusiform face area (FFA) activation in individuals with ASD during facial recognition tasks (Corbett et al., 2009), with the potential of increasing FFA activation as a goal for social skills intervention. Yet, individuals with WS have enhanced FFA activation in response to faces, and a larger FFA volume (Golarai et al., 2010). It is not known whether this potential underlying etiological difference would diminish the effectiveness of ASD interventions for those with a comorbid diagnosis. More research is warranted as to the reasons behind the results of this study, as well as to whether or not targeted ASD interventions are beneficial for children with WS or DS and a comorbid ASD diagnosis, regardless of whether the symptoms are etiologically or functionally different.

Limitations

This study is not without limitations. Firstly, the sample size was small. However, the sample was large enough to provide sufficient power for analyses. Additionally,
diagnoses of the children in the study solely relied on parent report. However, we tried to minimize the effects of this by screening out children with ASD who did not screen positive on the SCQ, and those with DS or WS who did not have genetic confirmation of their diagnosis. Perhaps the largest limitation of this study was the reliance on parent report of autism symptoms and adaptive behavior. Previous research found that although teacher ratings of social deficits in children with ASD were associated with clinicians’ observations of ASD symptom severity, parent ratings were not (Azad, Reisinger, Xie, & Mandell, 2016). Additionally, research demonstrates only fair interrater reliability between parents reporting about the same child on the SCQ (Möricke, Buitelaar, & Rommelse, 2016). Without a direct assessment of these children’s behavior, we cannot determine whether or not these parent’s reports are an accurate depiction of their child’s behaviors.

**Future directions**

These findings highlight the importance of research in the areas of screening, diagnosis, and interventions for ASD in children with DS or WS. More research is needed to determine the sensitivity and specificity of screeners such as the SCQ in the DS and WS populations, so children with DS and WS can receive earlier and more accurate diagnoses. This is imperative so these children can receive access to interventions. Additionally, researchers should evaluate individual items on screeners such as the SCQ to determine which items best discriminate individuals with DS or WS from those who may have a comorbid ASD diagnosis. This also may inform diagnosis by providing information as to which behaviors clinicians should put more weight into when
determining if a child with DS or WS should receive a comorbid ASD diagnosis. Along with this, more research is needed to investigate if children with DS or WS who receive an ASD diagnosis are functionally different from those with autism without a comorbid genetic condition. Research is also needed in the area of intervention, to determine if empirically supported interventions for autism spectrum disorder, such as applied behavior analysis, would be effective for children with DS or WS and a comorbid ASD diagnosis. Finally, more research is needed to better understand the etiology of idiopathic autism. A better understanding of the etiology of autism could lead to a clearer understanding as to the areas of overlap between autism and genetic conditions such as DS or WS. More research using animal models and fMRI to example potential similarities and differences in the neural pathways underlying ASD, DS, & WS is needed to further our understanding in this area.

**Conclusion**

In a sample of children and adolescents with DS and WS, more children entered the study with an ASD diagnosis in comparison to the reported population prevalence. Additionally, we saw elevated ASD symptoms in DS and WS across multiple measures. More children screened positive on the SCQ than the percentage reported in previous research using a general population sample (Chandler et al., 2007). Additionally, both groups displayed elevations in regards to total ASRS scores, as well as across all subscales, in comparison to the normative sample mean. These elevations are not solely due to low developmental level, as group membership predicted ASRS total scores even when controlling for adaptive behavior. When comparing individuals who screened
positive on the SCQ to those who screened negative, there was a significant difference in ASRS total scores, suggesting that the SCQ is capturing symptoms associated with ASD. Within groups comparisons of ASRS subscales found Unusual Behavior scores to be significantly higher in comparison to Self-Regulation and Social Communication scores in individuals with DS, and Unusual Behaviors to be significantly higher compared to Social Communication scores in individuals with WS. As higher scores on the ASRS are indicative of more severe ASD symptoms, this may suggest that questions asking about unusual behaviors may not separate those with DS or WS from those who also have a comorbid ASD diagnosis. This seems to be more prevalent in the WS group, as there was not a significant difference between the ASD and WS group on Unusual Behavior scores. This suggests that in our sample, individuals with WS had similar levels of unusual behaviors as the individuals with ASD, regardless of whether or not they had a comorbid diagnosis. However, there was a significant difference between Social Communication scores between the ASD and WS groups. This suggests that problems in social communication may best differentiate those with WS who have a comorbid diagnosis from those who do not. Based on the results of this study, questions asking about social interest and empathy may best separate those with WS who do not have ASD diagnosis from those who do. Although significantly different from the ASD group, the significantly higher elevation in the Unusual Behaviors subscale in the DS group, combined with previous research demonstrating elevations in OCD-like symptoms in this populations, suggests that social communication questions may also better differentiate those with a comorbid ASD diagnosis from those without. More research is needed to
determine the types of questions needed to effectively screen for ASD in the DS/WS populations, to determine the accuracy of ASD diagnoses in these populations, and to investigate the utility of empirically supported interventions for those with DS/WS and a comorbid ASD diagnosis.
Appendix A: Tables
Table 1. Respondent characteristics by group

<table>
<thead>
<tr>
<th>Variables</th>
<th>Mean (SD)/Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ASD N=39</td>
</tr>
<tr>
<td>Respondent Age</td>
<td></td>
</tr>
<tr>
<td></td>
<td>42.97 (10.04)</td>
</tr>
<tr>
<td>Relationship to Child</td>
<td></td>
</tr>
<tr>
<td>Mother</td>
<td>64.1%</td>
</tr>
<tr>
<td>Father</td>
<td>30.8%</td>
</tr>
<tr>
<td>Other</td>
<td>5.1%</td>
</tr>
<tr>
<td>Respondent Race</td>
<td></td>
</tr>
<tr>
<td>American Indian or Alaska Native</td>
<td>2.6%</td>
</tr>
<tr>
<td>Asian</td>
<td>7.7%</td>
</tr>
<tr>
<td>Black or African American</td>
<td>0.0%</td>
</tr>
<tr>
<td>Native Hawaiian or Other Pacific Islander</td>
<td>0.0%</td>
</tr>
<tr>
<td>White</td>
<td>87.9%</td>
</tr>
<tr>
<td>Other</td>
<td>0.0%</td>
</tr>
<tr>
<td>Respondent Ethnicity</td>
<td></td>
</tr>
<tr>
<td>Hispanic or Latino</td>
<td>17.9%</td>
</tr>
<tr>
<td>Not Hispanic or Latino</td>
<td>82.1%</td>
</tr>
<tr>
<td>Respondent Education Level</td>
<td></td>
</tr>
<tr>
<td>Prefer Not to Answer</td>
<td>0.0%</td>
</tr>
<tr>
<td>Less than 7th Grade</td>
<td>0.0%</td>
</tr>
<tr>
<td>Junior High School, Including 9th Grade</td>
<td>0.0%</td>
</tr>
<tr>
<td>High School Graduate</td>
<td>25.6%</td>
</tr>
<tr>
<td>Partial College, at least one year of specialized training</td>
<td>17.9%</td>
</tr>
<tr>
<td>Standard College or University Graduation</td>
<td>38.5%</td>
</tr>
<tr>
<td>Graduate/Professional Training</td>
<td>17.9%</td>
</tr>
<tr>
<td>Household Income</td>
<td></td>
</tr>
<tr>
<td>Less than $20,000</td>
<td>20.5%</td>
</tr>
<tr>
<td>$20,000-$40,000</td>
<td>12.8%</td>
</tr>
<tr>
<td>$40,000-$60,000</td>
<td>17.9%</td>
</tr>
<tr>
<td>$60,000-$90,000</td>
<td>20.5%</td>
</tr>
<tr>
<td>More than $90,000</td>
<td>23.1%</td>
</tr>
<tr>
<td>Prefer Not to Answer</td>
<td>5.1%</td>
</tr>
<tr>
<td>Primary Language Spoken in Home</td>
<td></td>
</tr>
<tr>
<td>English</td>
<td>100.0%</td>
</tr>
<tr>
<td>Spanish</td>
<td>0.0%</td>
</tr>
<tr>
<td>Other</td>
<td>0.0%</td>
</tr>
</tbody>
</table>
Table 2. Child demographics by group

<table>
<thead>
<tr>
<th>Variables</th>
<th>Mean (SD)/Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ASD N=39</td>
</tr>
<tr>
<td>Child Age (Years)</td>
<td>11.96 (3.61)</td>
</tr>
<tr>
<td>Child Sex</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>74.4%</td>
</tr>
<tr>
<td>Female</td>
<td>25.6%</td>
</tr>
<tr>
<td>Comorbid ASD Diagnosis</td>
<td>N/A</td>
</tr>
<tr>
<td>Yes</td>
<td>N/A</td>
</tr>
<tr>
<td>No</td>
<td>N/A</td>
</tr>
<tr>
<td>Child Referred for ASD Diagnosis²</td>
<td>N/A</td>
</tr>
<tr>
<td>Yes</td>
<td>N/A</td>
</tr>
<tr>
<td>No</td>
<td>N/A</td>
</tr>
<tr>
<td>Child Race</td>
<td></td>
</tr>
<tr>
<td>American Indian or Alaska Native</td>
<td>2.6%</td>
</tr>
<tr>
<td>Asian</td>
<td>7.7%</td>
</tr>
<tr>
<td>Black or African American</td>
<td>0.0%</td>
</tr>
<tr>
<td>Native Hawaiian or Other Pacific Islander</td>
<td>0.0%</td>
</tr>
<tr>
<td>White</td>
<td>87.9%</td>
</tr>
<tr>
<td>Other</td>
<td>0.0%</td>
</tr>
<tr>
<td>Child Ethnicity</td>
<td></td>
</tr>
<tr>
<td>Hispanic or Latino</td>
<td>17.9%</td>
</tr>
<tr>
<td>Not Hispanic or Latino</td>
<td>82.1%</td>
</tr>
<tr>
<td>% of Time Spent in Classroom with TD Peers</td>
<td></td>
</tr>
<tr>
<td>School specifically for Children with DD</td>
<td>33.3%</td>
</tr>
<tr>
<td>Homeschooled/Other Alt. Learning Environment</td>
<td>2.6%</td>
</tr>
<tr>
<td>1-39%</td>
<td>17.9%</td>
</tr>
<tr>
<td>40-79%</td>
<td>5.1%</td>
</tr>
<tr>
<td>80-99%</td>
<td>5.1%</td>
</tr>
<tr>
<td>Entire Day</td>
<td>35.9%</td>
</tr>
<tr>
<td>Hearing Problems</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>7.7%</td>
</tr>
<tr>
<td>No</td>
<td>92.3%</td>
</tr>
<tr>
<td>Vision Problems</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>17.9%</td>
</tr>
<tr>
<td>No</td>
<td>82.2%</td>
</tr>
</tbody>
</table>

² This question was only displayed to respondents who did not note that their child had an ASD diagnosis
<table>
<thead>
<tr>
<th></th>
<th>ASD Mean (SD)</th>
<th>DS Mean (SD)</th>
<th>WS Mean (SD)</th>
<th>F Statistic</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ASRS Total Score</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Social Communication</td>
<td>68.74 (6.94)</td>
<td>65.93 (8.25)</td>
<td>60.84 (8.69)</td>
<td>28.78</td>
<td>&lt;.000**†‡</td>
</tr>
<tr>
<td>Unusual Behaviors</td>
<td>67.00 (8.96)</td>
<td>61.83 (8.30)</td>
<td>65.50 (6.43)</td>
<td>6.11</td>
<td>.003**‡</td>
</tr>
<tr>
<td>Self-Regulation</td>
<td>63.85 (5.45)</td>
<td>54.88 (7.62)</td>
<td>63.26 (5.83)</td>
<td>32.134</td>
<td>&lt;.000**‡</td>
</tr>
<tr>
<td><strong>ABAS-3 GAC</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Conceptual Domain</td>
<td>74.49 (15.16)</td>
<td>69.18 (12.04)</td>
<td>66.03 (10.77)</td>
<td>4.42</td>
<td>.018†</td>
</tr>
<tr>
<td>Social Domain</td>
<td>71.05 (11.32)</td>
<td>82.27 (14.09)</td>
<td>77.06 (11.97)</td>
<td>9.76</td>
<td>&lt;.000*‡</td>
</tr>
<tr>
<td>Practical Domain</td>
<td>75.13 (16.69)</td>
<td>70.86 (12.65)</td>
<td>63.76 (11.31)</td>
<td>6.36</td>
<td>.002†‡</td>
</tr>
</tbody>
</table>

*DS group significantly different from ASD group after using Games-Howell method to correct for multiple tests †WS group significantly different from ASD group after using Games-Howell method to correct for multiple tests ‡DS group significantly different from WS group after using Games-Howell method to correct for multiple tests; ASRS = Autism Spectrum Ratings Scale; ABAS-3 = Adaptive Behavior Assessment System, Third Edition; GAC = General Adaptive Composite
Table 4. Multiple regression using sex, age, adaptive behavior, & diagnosis, to predict ASRS total score

<table>
<thead>
<tr>
<th>Predictor Variable</th>
<th>R</th>
<th>R²</th>
<th>Beta</th>
<th>Sample Statistic&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Autism Spectrum Rating Scales Total Score</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall Model</td>
<td>.70</td>
<td>.50</td>
<td></td>
<td>27.18**</td>
</tr>
<tr>
<td>Sex</td>
<td>-.019</td>
<td></td>
<td>-.29</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>-.009</td>
<td></td>
<td>-.15</td>
<td></td>
</tr>
<tr>
<td>ABAS-3 General Adaptive Composite</td>
<td>-.296</td>
<td></td>
<td>-4.80**</td>
<td></td>
</tr>
<tr>
<td>Group (DS)†</td>
<td>-.750</td>
<td></td>
<td>-9.89</td>
<td></td>
</tr>
<tr>
<td>Group (WS)†</td>
<td>-.339</td>
<td></td>
<td>-4.46**</td>
<td></td>
</tr>
</tbody>
</table>

<sup>*p < .05; **p < .001</sup>

<sup>a</sup>Sample statistic = F for overall models, t for individual predictors; †Diagnosis was dummy coded, with ASD as the reference group; ABAS-3 = Adaptive Behavior Assessment System, Third Edition; DS = Down syndrome; WS = Williams syndrome
Appendix B: Figures
Survey Respondents
ASD=44, DS=78, WS=46

Excluded from study
Due to screen negative on the SCQ:
ASD=5
Due to no genetic confirmation:
DS=2, WS=1

Began Demographic Questions
ASD=39, DS=76, WS=45

Excluded from ASRS analyses
Due to dropout:
ASD=0, DS=0, WS=6
Due to incomplete data
ASD=0, DS=0, WS=1

Began Autism Spectrum Rating Scales
ASD=39, DS=76, WS=45

Excluded from SCQ analyses
Due to dropout:
ASD=0, DS=0, WS=2
Due to incomplete data
ASD=0, DS=0, WS=0

Began Social Communication Questionnaire
ASD=39, DS=76, WS=39

Excluded from ABAS analyses
Due to dropout:
ASD=0, DS=0, WS=4
Due to incomplete data:
ASD=0, DS=3, WS=1

Began Adaptive Behavior Assessment System
ASD=39, DS=76, WS=37

End of Survey

Figure 1. Flow chart of respondent dropout
Figure 2. Frequency distribution of SCQ Scores. Vertical line indicates screen positive cutoff.
Appendix C: Demographic Survey Questions

1). What is your relationship to the child?
   o Father
   o Mother
   o Other (please state)

2). What is your age (years)?
   ____________________

3). What is your race?
   o American Indian or Alaska Native
   o Asian
   o Black or African American
   o Native Hawaiian or Other Pacific Islander
   o White
   o Other

4). What is your ethnicity?
   Hispanic or Latino
   Not Hispanic or Latino

5). Which of the following best describes your highest grade completed?
   o Less than 7th grade
   o Junior high school, including 9th grade
   o Partial high school, 10th or 11th grade
   o High School Graduate
   o Partial College, at least one year of specialized training
   o Standard College or university graduation
   o Graduate/Professional Training
   o Prefer not to answer
6). Which of the following best describes your annual household income?
   - Less than $20,000
   - $20,001-$40,000
   - $40,001-$60,000
   - $60,001-$90,000
   - More than $90,000
   - Prefer not to answer

7). Which of the following has your child been diagnosed with? (check all that apply)
   - Autism spectrum disorder (autism, Asperger's, PDD-NOS)
   - Williams syndrome
   - Down syndrome
   - Other (please specify)

8). Does your child have a genetic confirmation of his/her diagnosis (for example a FISH test, microarray, or karyotype)? [Only displayed if ‘Williams syndrome’ Or ‘Down syndrome’ was selected in response to ‘Which of the following has your child been diagnosed with?’]
   - Yes
   - No

9). Has a professional ever suggested that your child be referred for an autism spectrum disorder diagnosis? [Only displayed if ‘No’ is selected in response to ‘Has your child completed an in person diagnostic test for an autism spectrum disorder?’]
   - Yes
   - No

10). How old is your child?
   Years____  Months _____

11). What is the sex of your child?
   - Male
   - Female
12). What is your child's race?
   o American Indian or Alaska Native
   o Asian
   o Black or African American
   o Native Hawaiian or Other Pacific Islander
   o White
   o Other

13). What is your child's ethnicity?
   o Hispanic or Latino
   o Not Hispanic or Latino

14). What is the primary language spoken in your home?
   o English
   o Spanish
   o Other (please state)

15). Does your child have significant hearing problems?
   o Yes (please explain)
   o No

16). Does your child have significant vision problems, even with the addition of glasses or contacts?
   o Yes (please explain)
   o No

17). On average, what percentage of the school day does your child spend with his/her typically developing peers?
   o My child is at a school specifically for children with developmental disabilities
   o My child is homeschooled, or participates in another alternative learning environment
   o My child does not spend any of his/her day in a classroom with typically developing peers
   o 1-39%
   o 40-79%
   o 80-99%
   o My child spends his/her entire day in a classroom with typically developing peers
References


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