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Understanding Optimal Progress from an Autism Spectrum Disorder: Cognitive, Language, Adaptive and Social Functioning

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Understanding Optimal Progress from an Autism Spectrum Disorder:
Cognitive, Language, Adaptive and Social Functioning

Emily Moulton, PhD

University of Connecticut, 2018

ASDs are generally considered lifelong disorders; however, emerging literature indicates that a subset of children with a documented ASD lose their symptoms and function in the average range of cognition and behavior. Several studies have provided in-depth descriptions of school-aged children who have demonstrated an “Optimal Outcome” from an early ASD diagnosis. The current study aims to extend this work to an earlier developmental time point, and to understand the clinical significance of this type of outcome during the preschool years. The current study comprehensively describes and compares children who demonstrate an Optimal Outcome by age four years (termed “Optimal Progress,” OP), to age and gender-matched peers with High Functioning Autism (HFA) and Typical Development (TD) in three critical domains (cognitive, adaptive, ASD symptomatology). Results indicate that by age four, the OP group is functioning comparably to TD peers cognitively and adaptively, except for parent-reported daily living skills, which are in the moderately low range. ASD symptoms are largely absent; however, children in the OP group are rated as having more pronounced motor atypicalities than TD peers, and more atypical social communication, which may be driven by differences in listening behaviors. We expect that these children will continue to display strong skills and abilities across domains, and will, over time, become increasingly indistinguishable from their typically developing peers. Future research should seek to continue to expand our understanding of the numerous developmental trajectories possible for children diagnosed with an ASD, with the goal of increasing the likelihood of highly positive outcomes.

Understanding Optimal Progress from an Autism Spectrum Disorder:
Cognitive, Language, Adaptive and Social Functioning

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B.A., Hamilton College, 2012

M.A., University of Connecticut, 2014

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APPROVAL PAGE

Doctor of Philosophy Dissertation

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Cognitive, Language, Adaptive and Social Functioning

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Understanding Optimal Progress from an Autism Spectrum Disorder: Cognitive, Language, Adaptive and Social Functioning

Autism Spectrum Disorders (ASDs) are a group of neurodevelopmental disorders characterized by deficits in social communication accompanied by repetitive behaviors and/or restricted interests, which may include sensory sensitivities. The Center for Disease Control (CDC, 2014) reports an overall prevalence rate for ASDs of one in 68, with boys affected at greater rates than girls (4.5:1). ASDs occur within all racial/ethnic and socioeconomic groups (CDC, 2014; Fombonne, 2003); however, evidence indicates that disparities in access to health care may contribute to decreased reported prevalence and later age of diagnosis for children in minority groups, and children of families with lower socioeconomic status (Fombonne, 2003; Herlihy et al., 2014; Mandell, Listerud, Levy, & Pinto-Martin, 2001).

Diagnostic Stability of ASDs

ASDs are generally considered lifelong disorders by clinicians and parents (Levy & Perry, 2011; Seltzer, Shattuck, Abbeduto, & Greenberg, 2004). Follow-up studies of individuals diagnosed in childhood indicate that approximately 80 to 90% of individuals continue to meet diagnostic criteria in adolescence or adulthood (Anderson, Liang & Lord, 2014; Charman et al., 2005; Seltzer et al., 2004; Woolfenden et al., 2012). Increases in the understanding of the early behavioral profiles of individuals with ASD have allowed reliable diagnoses to be given in early childhood, often around 24 months (Chawarska, Klin, Paul, Macari, & Volkmar, 2009; Eaves & Ho, 2004; Kleinman et al., 2008; Steiner, Goldsmith, Snow, & Chawarska, 2012; Turner & Stone, 2007). Diagnostic stability is high following diagnoses given as early as 18 to 24 months. Studies have reported between 68 and 100% stability of ASD diagnoses made at approximately age two to follow-up at age three or four (Chawarska, Klin, Paul, & Volkmar, 2007; Eaves &

Ho, 2004; Kleinman et al., 2008; Moulton, Barton, Robins, Abrams, & Fein, 2016; Ozonoff et al., 2015; Turner & Stone, 2007; Woolfenden et al., 2012). A subset of children initially diagnosed with an ASD at approximately age two appear to lose their ASD diagnosis by age four. The majority of studies investigating diagnostic stability in toddlers have found that this occurs for between 6 and 18% of children (Eaves & Ho, 2004; Kim, Macari, Koller, & Chawarska, 2015; Kleinman et al., 2008; Moulton, Barton, Robins, Abrams & Fein, 2016; Sutera et al., 2007).

Outcomes Following the Loss of an ASD Diagnosis

Many outcomes are possible for children who lose their ASD diagnosis in the toddler years or later in childhood. The large majority of children who lose their ASD diagnosis are subsequently diagnosed with another developmental disorder (60 to 100%), such as Developmental Delay or Developmental Language Disorder (Eaves & Ho, 2004; Kleinman et al., 2008; Turner & Stone, 2007). Of particular interest to the present study are the remaining children who lose their ASD diagnosis and appear to demonstrate more or less typical functioning across domains. In a review of literature reporting on outcomes, Helt and colleagues (2008) determined that between three and 25% of children appear to lose their ASD diagnosis sometime in development, and demonstrate functioning in the average range cognitively, adaptively and socially. Previous work by the current author has found that approximately nine percent of children show this outcome during the toddler years (Moulton et al., 2016).

Early predictors of the loss of an ASD diagnosis accompanied by average-range functioning include lesser early symptom severity, fewer early restricted, repetitive behaviors or interests (RRBIs), stronger early adaptive skills, particularly in the domain of motor skills, and an initial diagnosis of Pervasive Developmental Disorder, Not Otherwise Specific (PDD-NOS)

rather than Autistic Disorder (AD) (Anderson et al., 2014; Moulton et al., 2016; Sautera et al., 2007). Additionally, there is evidence that receiving earlier, and more intensive intervention is predictive of highly positive outcomes (Orinstein et al., 2014; Turner & Stone, 2007).

Optimal Outcomes

Several studies have characterized children who lose their ASD diagnosis sometime during childhood or early adolescence and appear to demonstrate an “optimal” or “very positive” outcome from an early ASD diagnosis. Anderson and colleagues (2014) followed a group of children diagnosed with an ASD at approximately age two to follow-up at age 19. Within a broader longitudinal project, at age 19 they identified eight children (9%) with a “very positive outcome” (VPO), which was defined as no longer meeting clinical criteria for an ASD, and verbal IQ (VIQ) of 70 or greater. When compared to peers with equivalent VIQ who retained an ASD diagnosis, in addition to expected significant differences in ASD symptoms, children in the VPO group displayed fewer parent-reported behavioral and mood difficulties (hyperactivity, depression, irritability), none of which were clinically significant. Additionally, they displayed stronger overall adaptive skills and greater independence (e.g., a higher percentage were living away from their families). Academic abilities were similar in the VPO and ASD groups (Anderson et al., 2014).

Studies by Fein and colleagues have compared the functioning of a group of approximately 30 children with “Optimal Outcome” (OO; age eight to 21 years) to peers with High Functioning Autism (HFA) and peers with Typical Development (TD). “Optimal Outcome” is defined similarly to VPO: the child must have previously met diagnostic criteria for an ASD following a gold standard diagnostic assessment, must no longer meet criteria for any ASD based on gold standard diagnostic assessment, must be participating in mainstream

classrooms without the help of an aid, and must demonstrate a full scale IQ greater than 70 (Kelley, Naigles, & Fein 2010) or greater than 77 (Fein et al., 2013; Orinstein et al., 2014; Troyb, Orinstein, Tyson, & Fein, 2014, and others). Additionally, children were required to display Vineland Adaptive Behavior Scale (VABS; Sparrow, Balla, & Cicchetti, 1984) *Socialization* and *Communication* standard scores greater than 77. Studies have focused on a broad range of areas including cognitive and adaptive functioning, language abilities, DSM-IV-TR ASD symptom domains, and other psychiatric and behavioral difficulties.

ASD symptom domains. Investigations of ASD symptom domains (social and communication abilities, restricted, repetitive behaviors and interests [RRBIs]) have utilized both parent-report (e.g., VABS) and observation-based measures (Autism Diagnostic Observation Schedule [ADOS]). Utilizing the VABS and ADOS, studies indicate that the OO group demonstrates no current social or communication impairments, and no current RRBIs (Fein et al., 2013; Kelley et al., 2010; Orinstein, Suh et al., 2015; Troyb et al., 2014), which is consistent with the findings for children with “very positive outcomes” (Anderson et al., 2014). Comparisons of children with OO, TD and HFA indicate that OO and TD groups show comparable scores across all ASD symptom domains, with the HFA group displaying more severe symptomatology as would be expected (Fein et al., 2013; Kelley et al., 2010; Orinstein, Suh et al., 2015; Troyb et al., 2014).

A more in-depth investigation of social and communication abilities revealed mild weaknesses in OO children’s insight into and ability to describe typical social relationships when compared to TD peers (Orinstein, Suh, et al., 2015). Additionally, OO children demonstrated a tendency toward greater social immaturity (e.g., acted young for age, giggled too much; Orinstein, Suh et al., 2015). Despite these findings, children in the OO group were described as

being warmer, friendlier, and more approachable than their TD peers by a naïve rater based on a short video clip (Orinstein, Suh, et al., 2015).

Psychiatric and behavioral difficulties. Investigations of other current psychiatric and behavioral difficulties have also been conducted. Based on caregiver report on the BASC (Behavioral Assessment Scale for Children; Kelley et al., 2010) and on the Schedule for Affective Disorders and Schizophrenia for School-Aged Children Present and Lifetime version (K-SADS-PL; Orinstein, Tyson, et al., 2015), children in the OO group displayed a greater likelihood of having current attention regulation difficulties than TD peers. Rates of attention regulation difficulties were similar in the OO and HFA groups (Orinstein, Tyson, et al., 2015). These findings are consistent with observation-based findings indicating greater attention regulation weaknesses, and greater difficulties with self-control in children with OO than peers with TD (Orinstein, Suh, et al., 2015).

Further, parents of children with OO and HFA report similar rates of current specific phobias, which are higher than those reported by parents of TD children (Orinstein, Tyson, et al., 2015). Specific phobias reported by parents of OO children were commonly related to sound (e.g., loud noises, crying babies), and appear to be consistent with the sensory sensitivities commonly seen in ASD (Orinstein, Tyson, et al., 2015). Parents of children with OO did not report greater difficulties than parents of TD children on any other domain of the BASC (Kelley et al., 2010), or the K-SADS-PL (Orinstein, Tyson, et al., 2015). Additionally, no differences were found between OO and TD children in clinician-observed anxiety or withdrawal/depression during the ADOS (Orinstein, Suh, et al., 2015). Children with HFA were reported as having higher rates of current tic disorders, and clinician observed withdrawal/depression than both the OO and TD groups (Orinstein, Suh, et al., 2015; Orinstein, Tyson, et al., 2015).

Cognitive and adaptive functioning. As noted above, to meet criteria for OO, children were required to demonstrate a full scale IQ greater than 70 (Kelley et al., 2010) or greater than 77 (Fein et al., 2013), and additionally had to display VABS Socialization and Communication scores greater than 77 (Fein et al., 2013). Comparisons of performance on the Wechsler Abbreviated Scale of Intelligence (WASI; Wechsler, 1999) indicate no significant differences between OO and TD groups in verbal IQ (VIQ) or nonverbal IQ (NVIQ; Fein et al., 2013). Children with HFA displayed lower VIQ than OO and TD peers, although still in the average range, and comparable NVIQ. Investigations of scores on three domains of the VABS (*Socialization, Communication, Daily Living Skills*) also indicated no significant group differences between the OO and TD groups, with weaker performance across all domains for the HFA group (Fein et al., 2013). VABS *Motor Skills* were not compared.

Language abilities. In-depth investigations of language abilities consistently reveal average abilities for children with OO across domains, with some mixed findings when children are compared to TD peers. Several studies indicate comparable vocabulary, pragmatic, semantic and syntactic knowledge and abilities between children with OO and TD peers (Fein et al., 2013; Kelley et al., 2010; Kelley, Paul, Fein, & Naigles, 2006; Tyson et al., 2014), with a few exceptions on specific subtests. Specifically, a somewhat younger sample of children with OO have demonstrated mild residual weaknesses in their categorical induction abilities (Naigles, Kelley, Troyb, & Fein, 2013), and in their understanding of mental state verbs (Kelley et al., 2006). Additional weakness have been found in aspects of narrative quality (e.g., higher rate of self-corrections, greater likelihood of using idiosyncratic language, fewer causal explanations; Kelley et al., 2006; Suh et al., 2014). A recent study of narrative quality, however, found no significant differences between OO and TD adolescent's narratives, with the exception of lower

qualitative ratings by naïve raters of “story goodness” and “cohesiveness” (Canfield, Eigsti, de Marchena, & Fein, 2016). Additional differences between OO and TD children have been found in a few areas (e.g., receptive vocabulary, ability to formulate sentences from a prompt); however, these differences are likely attributable to the above average scores of the TD groups in these studies (Fein et al., 2013; Tyson et al., 2014).

The Present Study

A number of studies have provided in-depth descriptions of the functioning of school-aged children (ages eight to 21 years) with optimal outcomes from an early ASD diagnosis. To our knowledge, no previous study has thoroughly investigated this outcome in younger children. Given the state of the research on highly positive outcomes from ASDs, the current study seeks to comprehensively assess and describe the age-four functioning of children who demonstrate an optimal outcome during the preschool years. To differentiate the current research from previous work with older children, we employ the term “Optimal Progress” to describe preschool-aged children who have lost their ASD diagnosis and are functioning within 1.5 standard deviations of the mean across domains. In the current study, we seek to formally compare children who demonstrate Optimal Progress to same-aged peers with High Functioning Autism and Typical Development (note: specific group criteria are outlined below).

We believe that this work is an important extension of existing work with older children with optimal outcomes. By conducting similar analyses with preschool-aged children, we seek to better understand the clinical significance of this outcome at an earlier developmental time point. Specifically, through comparisons with HFA and TD peers, we hope to better understand the ways in which the OP group’s development has already diverged from HFA peers, and the ways in which it has not, at this early developmental time point. The current work will explore this

outcome in a new, non-overlapping group of children, and thus, will additionally help to assess the replicability of previous findings. Clinically, we hope that this work helps to identify areas that may require continued monitoring or intervention for children who demonstrate Optimal Progress. More broadly, we hope that this work contributes to the growing literature on the numerous possible developmental trajectories following an early ASD diagnosis.

To achieve these aims, in the current study, we formally compare the current (age four) profiles of children who demonstrate Optimal Progress (OP) to peers with High Functioning Autism (HFA) and to children with a history of typical development (TD) in three critical domains (cognitive, adaptive, ASD symptomatology). Using gold standard assessment measures, we will compare the three groups' score profiles to determine whether unique skill/ability patterns exist at age four years. Three profile analyses will be conducted (repeated measures analysis of variances [RM ANOVAs]) with the between-subjects factor of group (OP, HFA, TD) and within-subjects factors of measure domains for the Mullen Scales of Early Learning (Mullen), VABS(-II), and Childhood Autism Rating Scale (CARS). When significant differences in group profiles are identified, additional comparisons will be conducted to determine the source and direction of the effects (e.g., pairwise RM ANOVAs, domain-level one-way ANOVAs).

Additionally, to better understand the clinical significance of Optimal Progress at age four, including identifying any remaining intervention or monitoring needs, we will thoroughly describe each group's age-four profile of cognitive (Mullen) and adaptive (VABS[-II]) abilities. We will determine whether a group demonstrates a flat profile, with no significant differences between measure domains, or demonstrates an uneven profile. Following the methodology of Oliveras-Rentas et al. (2012), for each group (OP, HFA, TD), repeated measures ANOVAs will be conducted to investigate within-group differences in Mullen and VABS(-II) domain scores.

Based on previous research with older children who demonstrate optimal outcomes, we hypothesize that by age four, the OP group will be largely indistinguishable from their TD peers in the domains of ASD symptomatology, cognitive abilities, and language functioning. We expect that these children may display mild residual weaknesses in their expressive language skills. We hypothesize that the OP and TD groups will show similar adaptive abilities in the domains of socialization, communication and daily living skills. Based on the absence of previous research, no specific hypothesis is presented regarding the motor skills of the OP group. We hypothesize that children in the OP group may display more difficulties with emotion regulation than TD peers (as assessed by the CARS), based on previous findings of difficulties with attention regulation and self-control. We hypothesize that the HFA group will display weaker overall cognitive and adaptive abilities, and greater ASD symptomatology than both the OP and TD groups.

Regarding skill and ability profiles, we hypothesize that the TD group will display a relatively flat profile of cognitive and adaptive abilities (i.e., no significant differences between domains), whereas the OP and HFA groups may display more varied profiles. Based on previous studies of children with HFA, we hypothesize that the HFA group will show within group cognitive strengths in nonverbal abilities (i.e., Mullen *Visual Reception*), with relatively weaker language abilities (i.e., Mullen *Expressive* and *Receptive Language*) (Fein et al., 2013; Planche & Lemonnier, 2012) and motor skills (i.e., Mullen *Fine Motor*) (Planche & Lemonnier, 2012). Adaptively, we hypothesize the HFA group will show a relatively flat profile, with possible greater weaknesses in VABS *Socialization* abilities (Fein et al., 2013; Kjellmer, Hedvall, Fernell, Gillberg, & Norrelgen, 2012). Given limited literature investigating the cognitive and adaptive profiles of children similar to our OP group, we refrain from specific hypotheses.

Methods

Participants

Participants include a subset of individuals participating in an ongoing study to evaluate the psychometric properties of an autism-specific screening questionnaire, the Modified Checklist for Autism in Toddlers (M-CHAT; Robins, Fein & Barton 1999) and its revision (M-CHAT-R/F; Robins, Fein & Barton 2009). This research was approved by the University of Connecticut IRB and the Georgia State University IRB. The current study includes three groups of children: Optimal Progress (OP), High Functioning Autism (HFA) and Typical Development (TD). Groups were defined based on information obtained in two developmental and diagnostic evaluations, conducted at approximately ages two and four years (see Table 1). Optimal progress (OP) was defined as follows: a child must have met criteria for a DSM-IV-TR Pervasive Developmental Disorder (Autistic Disorder [AD], Pervasive Developmental Disorder Not Otherwise Specified [PDD-NOS] or Asperger's Disorder) using gold standard diagnostic procedures at age two, must no longer have met criteria for any DSM-IV-TR Pervasive Developmental Disorder at follow up at age four, and must demonstrate functioning in the average range (within 1.5 SD of the mean) on standardized measures of cognition, language, communication and social skills at age four. High Functioning Autism (HFA) was defined as follows: a child must have met criteria for DSM-IV-TR AD, PDD-NOS or Asperger's Disorder at ages two and four, and must score in the average range cognitively at age four. Typical development (TD) was defined as follows: children must have never met criteria for any clinical diagnosis, must never have had any clinically significant concerns at any study evaluation, must score in the average range cognitively and adaptively at age four, and must have no known

siblings with a diagnosis of ASD. Additional details regarding group inclusion criteria can be found in Table 1.

Children in the OP group were selected from a larger sample of children in the MCHAT(-R/F) study if they met OP criteria as defined above, and if they had sufficiently complete data. Of the 20 children who met OP criteria, one child was excluded due to incomplete age four evaluation data, and one child was excluded due to the use of unique evaluation measures that precluded meaningful comparisons to other children. As a result, 18 children were retained in the OP group. Children in the HFA and TD groups were selected from the larger sample of individuals in the MCHAT(-R/F) study based on the age and gender characteristics of the OP group. Gender (exact match) and age-matched (closest match within 6 months) TD and HFA peers were selected at random for each OP child, resulting in a final sample of 54 children, with 18 children in each of the three groups.

Children included in the current analyses were recruited for the MCHAT(-R/F) study through three sources: receiving the screener at their 18 or 24-month pediatric well-child visit ($N = 26$), receiving the screener from an early intervention provider or psychologist ($N = 23$), or receiving the screener following caregiver self-referral ($N = 5$). Informed consent was obtained from all parents/caregivers of children included in the study. Following positive screening on the M-CHAT or M-CHAT-R/F, children attended developmental and diagnostic evaluations. All children in the OP and HFA groups were evaluated at age two years and at age four years. Ten children in the TD group were evaluated at both age two years and age four years; eight children in the TD group were evaluated only at age four years.

The sample is 66.7% male ($N = 36$) and 33.3% female ($N = 18$). Each group (OP, HFA, TD) includes 6 females and 12 males. The three groups are matched on race/ethnicity (Fisher's

Exact Test = 6.88, $p = .565$), as well as age at their 48-month evaluation ($F(2,51) = 0.015$, $p = .985$). At this evaluation, on average, the OP group was 50.72 months of age ($SD = 5.82$), the HFA group was 50.44 months ($SD = 4.40$) and the TD group was 50.49 months ($SD = 5.07$) (see Table 2).

Estimated median household incomes were determined based on the United States Census Bureau census tract associated with the address each family provided at their child's age four evaluation. Groups (OP, HFA, TD) did not differ in median household income ($F(2,51) = 0.211$, $p = .811$). The average estimated median income (in 2014 inflation-adjusted United States Dollars) of each group was as follows: OP ($M = \$85,855.25$, $SD = \$31,909.05$), HFA ($M = \$92,300.85$, $SD = \$28,144.35$), TD ($M = \$86,814.97$, $SD = \$35,929.29$). Based on these estimates, on average, families in the current study had annual household incomes \$18,425 higher than the median for the state of Connecticut in 2014 (\$69,899, United States Census Bureau, 2014). Please see Appendix C for additional information regarding census tract estimated median income methodology.

At age four, the total number of clinician-reported DSM-IV-TR Pervasive Developmental Disorder (PDD) symptoms differed significantly across groups ($F(2,49) = 111.84$, $p < .001$, $\eta^2 = .820$), as would be expected based on group inclusion criteria. Games-Howell post-hoc comparisons indicated that the HFA group displayed significantly more PDD symptoms ($M = 4.61$, $SD = 1.15$) than the OP group ($M = 1.44$, $SD = 1.09$), who had more symptoms than the TD group ($M = 0.11$, $SD = .33$). Clinician-rated Childhood Autism Rating Scale (CARS) *Total* scores also significantly differed across groups ($F(2,51) = 79.33$, $p < .001$, $\eta^2 = .757$), with Games-Howell post-hoc comparisons indicating that all groups differed from each other (HFA > OP > TD). ADOS Calibrated Severity Score (CSS) *Total* scores also varied significantly across

groups ($F(2,51) = 82.08, p < .001, \eta^2 = .762$). Games-Howell post-hoc comparisons indicated that the HFA group had significantly more severe ADOS CSS *Total* scores ($M = 4.94, SD = 1.43$) than the OP ($M = 1.56, SD = .86$) and TD ($M = 1.11, SD = .32$) groups, who did not differ from each other. ADOS *Social-Affect* CSS followed the same pattern (see Table 3). ADOS *Restricted Repetitive Behavior (RRB)* CSS also differed significantly across groups such that the HFA group displayed significantly more severe ADOS *RRB* scores than the TD group ($M = 1.67, SD = 1.53$), and displayed a strong trend ($p = .058$) toward more severe scores than the OP group ($M = 3.28, SD = 2.37$). The OP group displayed a strong trend ($p = .056$) toward more severe *RRB* scores than the TD group. See Table 3 for additional sample PDD diagnostic and symptom severity information.

Procedure

Children's caregivers were provided the M-CHAT (Robins et al., 1999; $N = 40$) or M-CHAT-R/F (Robins et al., 2009; $N = 14$) screeners to complete at their pediatrician's office during their child's 18 or 24-month well-child visit, or at an early intervention site or psychologist's office. Once the questionnaire was completed, it was sent to the University of Connecticut Early Detection laboratory to be scored. Two children were screened in Georgia through a collaborating site, Georgia State University. All of the following procedures were followed for these two children at Georgia State University. If a caregiver's responses indicated that a child screened positive, they were contacted via telephone to complete the relevant structured follow-up items (Follow-Up Phone Interview). If a child continued to screen positive after the Follow-Up Phone Interview, he or she was invited to attend a free developmental and diagnostic evaluation conducted at the University of Connecticut or Georgia State University.

As noted above, all children in the OP and HFA groups (N = 36) and 10 children in the TD group attended evaluations following positive screening at 18 or 24 months. The remaining eight children in the TD group screened negative at 18 or 24 months, and therefore were not evaluated at this time point. All children who were screened at 18 or 24 months were re-screened at approximately 48 months with the M-CHAT(-R/F) and the Social Communication Questionnaire (SCQ). All children who screened positive at the 48-month screening were invited for an evaluation. In addition, all children who had previously been evaluated through the study were invited for a 48-month re-evaluation regardless of their 48-month screening result. Eight children in the TD group screened positive for the first time at 48 months and were invited for a developmental and diagnostic evaluation. At this evaluation, they were determined to meet criteria for TD (as defined above). Based on the positive predictive value of the MCHAT (.98; Chlebowski, Robins, Barton, & Fein, 2013) and MCHATR (.95; Robins et al., 2014) for any developmental delay or concern, we would expect that a small subset of children who screened positive would be typically developing.

A licensed clinical psychologist or a developmental pediatrician and a graduate student in the Clinical Psychology doctoral program at the University of Connecticut conducted evaluations. Evaluations consisted of measures of cognitive skills, adaptive skills, language abilities and ASD-related symptoms. At the conclusion of each evaluation, caregivers were provided with feedback regarding the assessment, which included any diagnoses the child might qualify for as well as recommendations for intervention and resources. Six to eight weeks after the evaluation, caregivers received a written report detailing the results of the assessment.

A diagnosis of an ASD was assigned based on clinical judgment of experienced clinicians (licensed psychologists or developmental pediatricians) utilizing scores from all

available information from direct testing and parent interviews, and in accordance with the clinicians' best estimate diagnosis using DSM-IV-TR diagnostic criteria (APA, 2000). ASD diagnoses included AD, PDD-NOS or Asperger's Disorder. Clinical judgment in the assignment of ASDs has been shown to have high inter-rater reliability and is considered best practice in the field of ASDs (Klin, Lang, Cicchetti, & Volkmar, 2000).

Measures

The following measures were utilized in the ongoing study: M-CHAT, M-CHAT-R/F, Autism Diagnostic Observation Schedule (ADOS), Autism Diagnostic Interview (-Revised) (ADI/ADI-R), Toddler Autism Symptom Interview (TASI), Mullen Scales of Early Learning (Mullen), Vineland Adaptive Behavior Scales (versions I and II; VABS[-II]), and the Childhood Autism Rating Scale (CARS). These measures have been determined to have excellent psychometric properties and are widely used in the field of ASDs, with the exception of the TASI, which is currently being validated. Age two and age four evaluation data was utilized to determine whether children met criteria for OP, HFA, or TD. The current study includes analyses using data from the measures described below, each of which was administered at approximately age four years.

Autism Diagnostic Observation Schedule - Generic (ADOS). The ADOS (Lord et al., 2000) is a semi-structured, standardized, play-based assessment of four areas: Reciprocal Social Interaction, Communication, Stereotyped Behaviors and Restricted Interests and Play, which is intended for use with children who are suspected to have an ASD. Higher scores indicate greater severity. Modules 1 and 2 were used in the current study. Gotham and colleagues (2007, 2014) developed the ADOS Calibrated Severity Score (CSS) to assess and compare symptom severity across ADOS modules. The CSS is a measure of autism severity that takes into account a child's

age and language abilities, allowing for a measure of symptom severity that is less influenced by age or verbal abilities (Gotham, Risi, Pickles, & Lord, 2007; Hus, Gotham, & Lord, 2014). *Total CSS*, *Social-Affect (SA) CSS* and *Restricted Repetitive Behavior (RRB) CSS* are included in the current analyses.

Vineland Adaptive Behavior Scales – Interview Edition (Versions I and II). The VABS (Sparrow et al., 1984) is a structured, parent-report interview measure of adaptive functioning across four domains: *Communication*, *Daily Living Skills*, *Socialization* and *Motor Skills*. Two or three subdomains comprise each domain (e.g., the *Motor* domain includes *Fine Motor* and *Gross Motor* subdomains). Scores are determined for each subdomain and domain, and then scores are combined to determine a total score, the *Adaptive Behavior Composite (ABC)*. In the current study, children’s caregivers were administered the VABS (Sparrow et al., 1984) or the Vineland Adaptive Behavior Scales – Second Edition (VABS-II), an updated version which was released in 2005 (Sparrow, Cicchetti & Balla, 2005). Due to the high degree of similarity between the two versions, VABS and VABS-II domain standard scores will be analyzed collectively.

Mullen Scales of Early Learning. The Mullen (Mullen, 1995) assesses five domains of cognitive development. These include *Visual Reception*, *Gross Motor*, *Fine Motor*, *Expressive Language* and *Receptive Language*. In addition, the measure provides a summative *Early Learning Composite (ELC)* score, which is computed from the *Visual Reception*, *Fine Motor*, *Expressive Language* and *Receptive Language* domains. In the current study, the *Gross Motor* domain was not administered.

Childhood Autism Rating Scale (CARS). The CARS (Schopler, Reichler, DeVellis & Daly, 1980) is a 15-item observation-based rating scale designed to accurately differentiate children with autism from those with developmental delays without features of autism. A total

score is determined by summing the ratings on all 15 items, with total CARS scores ranging from 15 to 60. Higher scores indicate greater severity. Children can be classified as being non-autistic, having mild autism or having severe autism based on established cutoff scores (Schopler, Reichler & Renner, 1988). To better reflect our more current understanding of autism as a spectrum, Chlebowski and colleagues (2010) recommend a cutoff of 25.5 be used to distinguish an ASD from a non-ASD for two year olds and four year olds. To better understand domains within the CARS total score, Magyar and Pandolfi (2007) conducted a factor structure evaluation of the CARS in a sample of four year olds using Principal Axis Factor Analysis (PAF) and found four factors, which accounted for 41.67% of the variance (*Social Communication, Social Interaction, Stereotypies and Sensory Abnormalities* and *Emotional Regulation*).

Results

For the following analyses, if Levene's Test indicated a violation of the assumption of homogeneity of variances, the Games-Howell post-hoc test was used to determine the significance of findings. When the assumption of homogeneity of variances was not violated (non-significant Levene's test), post-hoc comparisons were performed using Tukey's HSD.

Group Comparisons: Age Four Autism Spectrum Disorder Symptomatology

Childhood Autism Rating Scale Profile Analysis. Repeated measures ANOVA (Profile Analysis) was conducted with the between-subjects factor of group (OP, HFA, TD) and within-subjects factors of Magyar and Pandolfi (2007) CARS domain (*Social Communication, Social Interaction, Stereotypies and Sensory Abnormalities, Emotional Regulation*). Results indicated that the group by domain interaction effect was significant ($F(6,153) = 2.28, p = .039$, partial $\eta^2 = .082$), indicating that there are unique profiles of symptom severity among the three groups.

Additional pairwise profile comparisons indicated that the HFA and OP groups displayed similar profiles, with both groups displaying significantly different profiles than the TD group.

In addition to displaying significantly different patterns of scores, there was a significant main effect of group (OP, HFA, TD) ($F(2,51) = 63.25, p < .001, \text{partial } \eta^2 = .713$), indicating group differences in the overall level of CARS symptom severity (collapsed across domains). Games-Howell post-hoc analyses indicated that the HFA group displayed the most severe CARS scores, followed by the OP group, who subsequently showed more severe scores than the TD group. See Table 4 and Figure 1 for additional information about the CARS Factor Severity Score Profile Analysis.

CARS Domain Severity Score Comparisons. Given our finding that overall CARS symptom severity varied significantly across groups, one-way ANOVAs (OP, HFA, TD) were conducted for each CARS domains (*Social Communication, Social Interaction, Stereotypies and Sensory Abnormalities, Emotional Regulation*) to determine the source of these differences. Two patterns of findings emerged. For the *Social Communication* and *Stereotypies and Sensory Abnormalities* domains, all groups significantly differed from each other (HFA > OP > TD). For the *Social Interaction* and *Emotional Regulation* domains, the HFA group displayed more severe scores than the OP and TD groups, who did not differ (see Table 4 and Figure 1).

To further explore significant differences between the OP and TD groups in the *Social Communication* and *Stereotypies and Sensory Abnormalities* domains, supplementary and exploratory item-level analyses were conducted for the items included in these domains (see Table S1). Within the *Social Communication* domain, the OP and TD groups did not differ on five out of six items, with a strong trend ($p = .064$) toward more severe scores for the OP group on the item assessing *Verbal Communication* (#11). Within the *Stereotypies and Sensory*

Abnormalities domain, the OP group displayed more severe scores than the TD group on two out of three items (*Body Use* [#4], *Listening Response* [#8]), with a trend toward more severe scores on the third item (*Taste, Smell and Touch Response* [#9]; $p = .091$).

Group Comparisons: Age Four Cognitive and Language Abilities

Mullen Scales of Early Learning Profile Analysis. The following comparisons include 17 TD children, 18 OP children and 18 HFA children. One child in the TD group was outside the age range of the Mullen (age > 60 months), and therefore, was administered the Differential Ability Scales. Repeated measures ANOVA (Profile Analysis) was conducted with the between-subjects factor of group (OP, HFA, TD) and within-subjects factors of Mullen domains (*Fine Motor, Visual Reception, Expressive Language, Receptive Language*). Following a significant Mauchly's Test of Sphericity ($\chi^2(5) = 22.24, p < .001, \epsilon = 0.764$), a Greenhouse-Geisser correction was used (Greenhouse & Geisser, 1959). The group by domain interaction effect was not significant ($F(4.58, 114.59) = 1.584, p = .176, \text{partial } \eta^2 = .060$), indicating that there were no unique profiles of cognitive abilities among the three groups. Across groups, the pattern displayed appears to follow a second degree polynomial (quadratic, $p = .047$), rather than linear, pattern (see Figure 2), with stronger scores in the *Visual Reception* domain. Results indicated a significant main effect of group (OP, HFA, TD) ($F(2,51) = 63.25, p < .001, \text{partial } \eta^2 = .713$), with groups differing in overall level of cognitive and language ability on the Mullen. Tukey's HSD post-hoc analyses indicated that the HFA group displayed weaker overall cognitive and language abilities than the TD group; the HFA and OP groups did not differ, nor did the OP and TD groups. See Table 5 and Figure 2 for additional information about the Mullen Profile Analysis.

Mullen Domain Comparisons. Given our finding that overall cognitive and language abilities varied significantly across groups, one-way ANOVAs were conducted for each Mullen domain (*Fine Motor*, *Visual Reception*, *Expressive Language*, *Receptive Language*) to determine the source of these differences. For the *Visual Reception*, *Expressive Language* and *Receptive Language* domains, no significant group differences were identified. In the *Fine Motor* domain, significant group differences were found ($F(2, 50) = 3.90, p = .027, \eta^2 = .135$) such that the HFA group displayed weaker fine motor abilities than the TD group. The HFA and OP groups did not differ, nor did the OP and TD groups (see Table 5).

To further explore significant differences on the *Fine Motor* domain, supplementary and exploratory item-level analyses were conducted for the most discriminating items in this domain (highest six items; see Table S2). The three groups did not significantly differ on five of the six items. On an item that requires children to touch each of their fingers to their thumb in response to an examiner's modeling, the HFA group performed significantly weaker than TD and OP peers, who did not differ.

Given the author's hypotheses that subtle weaknesses may emerge for the OP group in the *Expressive Language* domain, supplementary and exploratory item-level analyses were also conducted for the most discriminating items on this domain (highest six items; see Table S3). The three groups did not significantly differ on five of the six items. On an item that requires children to answer simple practical reasoning questions (e.g., "What should you do if your hands are dirty?"), there was a trend such that the HFA group performed less well than TD peers ($p = .094$), with no other significant group differences.

Group Comparisons: Age Four Adaptive Skills

Vineland Adaptive Behavior Scales(-II) Profile Analysis. Repeated measures ANOVA (Profile Analysis) was conducted with the between-subjects factor of group (OP, HFA, TD) and within-subjects factors of VABS (-II) domains (*Motor, Daily Living, Socialization, Communication*). Following a significant Mauchly's Test of Sphericity ($\chi^2(5) = 22.24, p = .005, \epsilon = 0.825$), a Greenhouse-Geisser correction was used (Greenhouse & Geisser, 1959). A significant group by domain interaction effect was found ($F(4.95, 126.30) = 2.54, p = .032, \text{partial } \eta^2 = .090$), indicating that there were different profiles of adaptive abilities among the three groups. Additional pairwise profile comparisons indicated that the HFA and OP groups displayed similar profiles, with both groups displaying significantly different profiles than the TD group. The pattern displayed by the HFA and OP groups appeared to follow a second degree polynomial (quadratic, $p = .036$), rather than linear, pattern (see Figure 3). In addition to displaying significantly different patterns of scores, results indicated a significant main effect of group (OP, HFA, TD) ($F(2,51) = 26.66, p < .001, \text{partial } \eta^2 = .511$). Tukey's HSD post-hoc analyses indicated that the HFA group displayed weaker overall adaptive skills than the OP group and the TD group, who did not differ from each other. See Table 6 and Figure 2 for additional information about the VABS(-II) Profile Analysis.

VABS(-II) Domain Comparisons. Given our finding that overall adaptive abilities varied significantly across groups, one-way ANOVAs were conducted for each VABS(-II) domain (*Motor Skills, Daily Living Skills, Socialization, Communication*) to determine the source of these differences. Two patterns of findings emerged. For the *Socialization, Communication* and *Motor Skills* domains, the HFA groups displayed weaker abilities than the OP and TD groups, who did not significantly differ from each other. In the *Daily Living Skills* domain, the

HFA group displayed weaker abilities than the OP group, who subsequently displayed weaker abilities than the TD group. See Table 6 for additional information.

To further explore significant differences on the *Daily Living Skills* domain, supplementary and exploratory item-level analyses were conducted for the three subdomains that comprise the *Daily Living Skills* domain on the VABS(-II). These include *Community* skills, *Domestic* skills, and *Personal* skills (see Table S4). Given differences in the scores provided for subdomains on the VABS and VABS-II, ratio IQ scores were calculated (age equivalent / chronological age x 100). On the *Community* and *Personal* subdomains, the HFA group displayed significantly weaker abilities than the TD and OP groups, who did not differ. On the *Domestic* domain, the HFA and OP groups performed equivalently, with weaker skills than the TD group.

Within-Group Cognitive and Adaptive Profile Descriptions

Repeated measures ANOVAs were conducted to examine possible within-group differences in Mullen and VABS(-II) domain scores. Bonferroni corrections for multiple comparisons were employed for all pairwise domain comparisons. See Table 5 and Figure 2 for Mullen domain scores by group; see Table 6 and Figure 3 for VABS(-II) domain scores by group. Mullen T scores have a mean of 50 and a standard deviation of 10; scores of 40 to 60 are considered to be within the average range. VABS(-II) Standard Scores have a mean of 100 and a standard deviation of 15; scores of 85 to 115 are considered to be within the average range.

Typically Developing Group.

Mullen Scales of Early Learning. Mean Mullen T scores for the TD group were all within the average range, ranging from 50.65 (*Expressive Language*) to 55.06 (*Visual Reception*). Following a significant Mauchly's Test of Sphericity ($\chi^2(5) = 18.611, p = .002, \epsilon =$

0.621), a Greenhouse-Geisser correction was used (Greenhouse & Geisser, 1959). Results were non-significant ($F(1.86, 29.82) = 1.03, p = .367, \text{partial } \eta^2 = .060$), supportive of a flat profile of cognitive abilities, with no significant differences between domains.

Vineland Adaptive Behavior Scales (-II). Mean VABS(-II) Standard Scores for the TD group were all within the average range, ranging from 95.28 (*Socialization*) to 101.44 (*Communication*). Results were non-significant ($F(3, 51) = 1.31, p = .281, \text{partial } \eta^2 = .072$), supportive of a flat profile of adaptive skills, with no significant differences between domains.

High Functioning Autism Group.

Mullen Scales of Early Learning. Mean Mullen T scores for the HFA group were all broadly within the average range, ranging from 40.94 (*Expressive Language*) to 54.28 (*Visual Reception*). Results indicated significant within-group differences in Mullen domain scores ($F(3, 51) = 6.62, p = .001, \text{partial } \eta^2 = .280$), supportive of an uneven profile of cognitive abilities. Pairwise comparisons indicated that the HFA group's *Visual Reception* abilities were significantly stronger than their *Expressive Language* ($p = .010$) and *Fine Motor abilities* ($p = .013$).

Vineland Adaptive Behavior Scales (-II). Mean VABS(-II) Standard Scores for the HFA group fell within the moderately low range, except for *Communication*, which was within the average range. Scores ranged from 71.67 (*Daily Living Skills*) to 89.67 (*Communication*). Following a significant Mauchly's Test of Sphericity ($\chi^2(5) = 12.41, p = .030, \epsilon = 0.640$), a Greenhouse-Geisser correction was used (Greenhouse & Geisser, 1959). Results indicated significant within-group differences in VABS(-II) domain scores ($F(1.92, 32.64) = 10.70, p < .001, \text{partial } \eta^2 = .386$), supportive of an uneven profile of adaptive skills. Pairwise comparisons

indicated that the HFA group's *Communication* skills were significantly stronger than their *Daily Living Skills* ($p < .001$) and their *Socialization* skills ($p < .001$).

Optimal Progress Group.

Mullen Scales of Early Learning. Mean Mullen T scores for the OP group were all within the average range, ranging from 46.11 (*Expressive Language*) to 56.28 (*Visual Reception*). Following a significant Mauchly's Test of Sphericity ($\chi^2(5) = 14.32, p = .014, \epsilon = 0.665$), a Greenhouse-Geisser correction was used (Greenhouse & Geisser, 1959). Results indicated significant within-group differences in Mullen domain scores ($F(2.00, 33.91) = 4.96, p = .013, \text{partial } \eta^2 = .226$), supportive of an uneven, rather than flat, profile of cognitive abilities. Pairwise comparisons indicated that the OP group's *Visual Reception* abilities were significantly stronger than their *Expressive Language* ($p = .008$) and *Fine Motor* abilities ($p = .022$).

Vineland Adaptive Behavior Scales (-II). Mean VABS(-II) Standard Scores for the OP group all fell within the average range, except for *Daily Living Skills*, which was within the moderately low range. Scores ranged from 83.50 (*Daily Living Skills*) to 101.94 (*Communication*). Results indicated significant within-group differences in VABS(-II) domain scores ($F(3, 51) = 12.20, p < .001, \text{partial } \eta^2 = .418$), supportive of an uneven profile of adaptive skills. Pairwise comparisons indicated that the OP group's *Communication* skills were significantly stronger than their *Daily Living Skills* ($p = .001$) and their *Socialization* skills ($p = .003$). OP children's *Daily Living Skills* were also significantly weaker than their *Motor* skills ($p = .035$).

Discussion

Summary of Previous Findings

Between three and 25% of children diagnosed with an ASD appear to no longer meet criteria for the diagnosis sometime in development, and to demonstrate functioning in the average range cognitively, adaptively and socially (Helt et al., 2008). For children diagnosed with an ASD around age two years, approximately nine percent of children demonstrate this type of outcome by age four (Moulton et al., 2016) or by age 19 (Anderson et al., 2014). Predictors of this outcome include earlier and more intensive intervention, an initial diagnosis of PDD-NOS (vs. Autistic Disorder), stronger early adaptive skills, particularly in the motor domain, and lesser early symptom severity, particularly in the domain of RRBI (Anderson et al., 2014; Orinstein et al., 2014; Moulton et al., 2016; Suter et al., 2007).

Previous work has thoroughly described the current functioning of adolescents with Optimal Outcomes (or “very positive outcomes”) from an early ASD diagnosis by comparing their functioning to peers with HFA and peers with a history of typical development. Across studies, OO children appear to be functioning very similarly to TD peers in the domains of cognitive and language abilities, adaptive skills, and ASD symptomatology (Anderson et al., 2014; Canfield et al., 2016; Fein et al., 2013; Kelley et al., 2010; Naigles et al., 2013; Orinstein et al., 2014; Orinstein, Suh et al. 2015; Orinstein, Tyson et al. 2015; Troyb et al., 2014; Tyson et al., 2014).

Differences between OO and TD children have only been found in fine-grained analyses of higher-level social abilities (e.g., the ability to describe typical social relationships [Orinstein, Suh, et al., 2015]), and higher-level language abilities (e.g., categorical induction abilities [Naigles et al., 2013]; narrative quality [Suh et al., 2014; Canfield et al., 2016]). Psychiatrically,

evidence indicates that OO children show greater rates of attention regulation difficulties and specific phobias than TD children, but have no other significant psychiatric concerns in the late childhood to adolescent years (Orinstein, Tyson, et al., 2015).

Current Study Findings

Given the state of the literature, the current study sought to extend existing work with adolescents with optimal outcomes by conducting similar analyses with preschool-aged children who have demonstrated Optimal Progress from an age two ASD diagnosis. Specifically, we sought to thoroughly describe the age four functioning of children with OP through comparisons to HFA and TD peers in three critical domains (cognitive, adaptive, ASD symptomatology).

Age Four Autism Spectrum Disorder Symptomatology. At age four years, on the clinician-rated Childhood Autism Rating Scale (CARS), children in the Optimal Progress group displayed lesser ASD symptom severity than peers with HFA, but greater symptom severity than peers with TD. While this is consistent with our hypothesis, based on study inclusion criteria, that children in the OP group would display lesser symptomatology than peers with HFA, this finding is counter to our hypothesis that children in the OP group would be broadly indistinguishable from TD peers on this measure. The OP group had a mean CARS *Total Score* of 18.64, which is well within the typical range (15 to 25.5, Chlebowski et al., 2010); however, this overall score indicates that clinicians are rating mild atypicalities in OP children that differentiate them from TD peers in some areas (TD CARS *Total Score M* = 16.53).

Additional findings of the CARS Profile Analysis indicate that the OP and HFA groups maintained a similar pattern of scores, which differed from the TD group. This suggests that while the OP group no longer displays symptom severity similar to peers with HFA, as would be expected based on OP inclusion criteria, they continue to maintain a varied, non-typical profile

(see Figure 1). In sum, these findings indicate that by age four, OP children have significantly diverged from HFA peers in the severity of their ASD symptoms; however, at this developmental time point, they have not yet lost all evidence of their prior diagnosis.

The domain-level findings help us to understand the specific areas in which OP children continue to differ from TD peers. At age four, clinician's rate OP children comparably to their TD peers in their overall *Social Interaction* abilities and *Emotion Regulation* skills; however significant differences remain present in the *Stereotypies and Sensory Abnormalities* and *Social Communication* domains. Our finding of equivalent clinician ratings in the *Emotion Regulation* domain is counter to our initial hypothesis. We hypothesized that children in the OP group may display mild challenges in this area, based on evidence of difficulties with attention regulation and some aspects of self-control in adolescents with OO (e.g., laughing inappropriately, giggling too much, acting too young for their age; Orinstein, Suh, et al., 2015). It is possible that the CARS *Emotion Regulation* domain items are too broad to adequately assess these more specific areas of self-regulation, or that at age four, these differences are not yet apparent.

Further exploratory analyses indicated that within the *Stereotypies and Sensory Abnormalities* domain, the OP group displayed more severe scores than the TD group on two out of three items (*Body Use* [#4] and *Listening Response* [#8]). The *Body Use* item addresses both a child's physical coordination, and the presence of repetitive or unusual movements. Given an absence of statistical differences between the two groups on the Mullen *Fine Motor* domain, or the VABS(-II) *Motor* domain (discussed further below), this finding is likely not reflective of overt, functional differences in motor coordination between the OP and TD groups. It is more likely that this finding reflects the presence of some repetitive or unusual motor movements, particularly given that children in the OP group also displayed higher ADOS RRB CSS scores

than TD peers (see Table 3). Abnormal motor movements are common across individuals with neurodevelopmental disorders, and range from very mild to very severe (Johnson, Gliga, Jones & Charman, 2015). When observing children in the OP group, clinicians may be picking up on mild abnormalities or atypicalities in motor movements or behaviors that would not be detected on standardized testing (e.g., the Mullen, VABS(-II)).

The presence of persistent, albeit mild differences in motor behaviors (e.g., repetitive behaviors, unusual motor movements) may be explained in a number of ways. Abnormal motor development and activity is common in ASD (Downey & Rapport, 2012), and can be one of the earliest emerging markers of the disorder (Bhat, Galloway, & Landa, 2012). Motor system impairment has been described as a “defining biological feature of the disorder” (Mostofsky, Burgess, & Gidley Larson, 2007, p.2121), with downstream effects on social and language development. It is possible that for the OP group, motor activity abnormalities have persisted more so than social or language difficulties because aberrant neurological functioning of the motor system (e.g., increased white matter volume in the precentral cortex, see Mostofsky et al., 2007) is more neurologically fundamental and less amenable to change. It is also possible that mild restricted, repetitive behaviors have persisted because of the ongoing function that they serve. While the function of repetitive behaviors in ASD is not known, it has been hypothesized that repetitive behaviors may serve as a self-regulation strategy to manage anxiety or heightened arousal (Joosten, Bundy & Einfield, 2009). While children in the OP group appear to have lost any significant repetitive behaviors that they may have displayed previously, perhaps they have retained mild repetitive behaviors or motor mannerisms as a coping mechanism, or regulatory strategy.

Within the CARS *Stereotypies and Sensory Abnormalities* domain, as noted above, the OP group also demonstrated significantly higher scores than TD peers on the *Listening Response* item. This item addresses a child's broad listening behavior (e.g., use of listening with other senses, degree and timing of response to sound). Given previous findings that adolescents with Optimal Outcome have greater attention regulation weaknesses than their TD peers (Orinstein, Suh, et al., 2015; Orinstein, Tyson, et al., 2015), it is possible that OP children's mild elevations on the *Listening Response* item are reflective of the presence of general attention regulation difficulties. Attention regulation difficulties are commonly seen in individuals with ASD (Salazar et al., 2015), possibly as a result of a shared multifactorial genetic etiology (Rommelse, Franke, Geurta, Hartman & Buitelaar, 2010) and/or shared developmental pathways and risk factors between ASD and ADHD (Johnson et al., 2015). The presence of attention regulation challenges in children who demonstrate Optimal Progress or Optimal Outcome indicates that these difficulties may be harder to remediate than other aspects of the disorder (Orinstein, Suh et al., 2015). Attention regulation difficulties often become more pronounced over the course of childhood as attentional demands increase, and therefore, any challenges in this area should be monitored.

Within the *Social Communication* domain, the OP group displayed more severe scores than the TD group only one out of six items (*Verbal Communication* [#9]), which addresses the presence of age and situation-appropriate speech, including whether children employ any echolalia, or any peculiar words or jargon. This finding is consistent with the presence of higher clinician-rated mean DSM-IV-TR *Communication* symptom totals for the OP group (OP $M = 0.63$, TD $M = 0.06$; see Table 3). Given that the CARS *Verbal Communication* item and the DSM-IV-TR *Communication* domain both assess a wide range of communication skills and

symptoms, it is not immediately clear what is driving this finding; however, both findings may have been driven by the fact that four children in the OP group displayed some clinician-reported stereotyped/repetitive or idiosyncratic language at age four. This is consistent with the finding that adolescents with Optimal Outcomes were nine times more likely to use idiosyncratic language when telling a story than their TD peers (Suh et al., 2014). Suh et al. (2014) hypothesize that residual idiosyncratic language may reflect reduced familiarity with conventional ways of communicating. Given that children with ASD often have reduced interactions with typically developing peers, it is likely that children in the Optimal Progress group would have less familiarity and practice with conventional communication, possibly driving their continued use of idiosyncratic or repetitive language at age four.

Age Four Cognitive and Language Abilities. At age four years, on the Mullen Scales of Early Learning, the OP, HFA and TD groups all demonstrated similar profiles, with all groups displaying the strongest scores in the *Visual Reception* domain. This may be reflective of our study inclusion criteria, which required children in all three groups to demonstrate *Visual Reception* T scores ≥ 35 (see Table 1). Collapsing across domains on the Mullen, the OP and TD groups did not differ in their overall level of functioning, while as we hypothesized, the HFA group displayed weaker abilities than the TD group. Follow-up domain analyses indicated that the OP and TD groups did not differ on any individual domain, including *Fine Motor* (OP $M = 49.89$, TD $M = 53.00$), for which there were no OP group inclusion requirements. For the *Visual Reception*, *Expressive Language* and *Receptive Language* domains, children in the OP group were required to have T scores ≥ 35 . Our findings indicate that the OP group is functioning well above this threshold across all domains, with average T scores ranging from 46.11 (*Expressive Language*) to 56.28 (*Visual Reception*).

Additional follow-up domain analyses indicated that the HFA group displayed equivalent abilities to the OP and TD groups in the *Visual Reception*, *Expressive Language* and *Receptive Language* domains, with weaker abilities than the TD group only in the *Fine Motor* domain (HFA $M = 40.94$). It is notable that the HFA group displayed similar expressive and receptive language abilities to TD peers, given that there were no HFA group inclusion requirements for language functioning.

Pairwise within-group domain comparisons indicated a more uneven Mullen profile for children in the HFA and OP groups than those in the TD group, who displayed a flat profile of abilities. Specifically, both the HFA and OP groups displayed significantly stronger *Visual Reception* scores than *Expressive Language* and *Fine Motor* scores. This profile is consistent with previous investigations of children with HFA, which indicate strengths in nonverbal problem-solving and weaknesses in language and motor functioning (Fein et al., 2013; Planche & Lemonnier, 2012).

All children in the OP group have demonstrated significant improvements across all domains since their initial ASD diagnosis at age two such that all age four Mullen scores are solidly within the average range (see Moulton et al., 2016 for age two scores); however, our findings indicate that children who demonstrate OP continue to display an uneven cognitive profile that is consistent with that seen in children with HFA. The gap between *Visual Reception* abilities and *Fine Motor* abilities is less pronounced for the OP group than for the HFA group (OP = -0.64 Standard Deviation [SD], HFA = -1.33 SD); however, the gap between *Visual Reception* and *Expressive Language* skills is equivalent for the two groups (OP = -1.0 SD, HFA = -0.89 SD). Despite this, since age two, the gap between the OP group's *Visual Reception* abilities and their language abilities has substantially narrowed, possibly indicating a normalizing

of their profile over time (see Moulton et al., 2016). We hypothesize that children in the OP group will continue to show age-appropriate development in their language abilities, such that they will continue to function broadly equivalently to TD peers (Fein et al., 2013; Kelley et al., 2010; Kelley et al., 2006; Tyson et al., 2014), and may demonstrate a closing of the small remaining gap between their non-verbal and verbal abilities over time. Based on previous findings, we hypothesize that subtle weaknesses may emerge in certain specific, higher-level areas (e.g., categorical induction abilities [Naigles et al., 2013]; and narrative quality [Suh et al., 2014; Canfield et al., 2016]); however, we believe that any subtle weaknesses in these areas are unlikely to be significantly impairing.

Age Four Adaptive Skills. On the Vineland Adaptive Behavior Scales (VABS[-II]) parent interview, collapsing across domains, the OP and TD groups displayed similar scores, with the HFA group demonstrating significantly weaker overall adaptive abilities. Consistent with our hypotheses, follow-up domain analyses indicated the OP and TD groups did not differ in *Socialization* or *Communication* scores, nor did they differ in *Motor* scores, for which there were no OP group inclusion requirements. In all three of these domains, the OP and TD groups performed solidly within the average range. In the *Daily Living Skills* domain, however, counter to our hypothesis, the OP group performed in the moderately low range, and as a result, differed significantly from TD peers.

Additional exploratory analyses indicated that within the *Daily Living Skills* domain, the OP group displayed similar scores to the TD group on the *Community* and *Personal* subdomains, but weaker scores on the *Domestic* subdomain. This subdomain assesses a child's participation in household chores, including cleaning up their own play space and putting away personal possessions. While many child characteristics influence the performance of these skills (e.g., fine

and gross motor skills, cognitive abilities, behavioral regulation), these skills are likely highly influenced by parent characteristics, including what demands or requests parents place upon on their children for participation in household chores. Given the significant intervention needs of children with ASD, it is likely that parents of toddlers with ASD have needed to prioritize other skills (e.g., language, social interaction) over daily living skills.

The results of the VABS(-II) Profile Analysis indicated that the OP and HFA groups demonstrated similar profiles of scores, which differed from the TD group. Both the HFA and OP groups displayed stronger *Communication* abilities than *Socialization* and *Daily Living Skills*, whereas the TD group displayed a statistically flat profile. The OP group's domain scores were all well within the average range (except *Daily Living Skills*, moderately low), and represent significant improvements from age two adaptive functioning (see Moulton et al., 2016).

However, as noted on the Mullen, it appears that children in the OP group continue to show a pattern of abilities similar to HFA peers, who have been found across studies to display relatively weaker VABS *Socialization* scores (Fein et al., 2013; Kjellmer et al., 2012). Given findings of strong social skills in adolescents with Optimal Outcome (Fein et al., 2013), we hypothesize that the OP group will continue to display age-appropriate, average-range social abilities.

Additionally, over time, it is possible that the OP group's profile of abilities will become more uniform like those of their TD peers, as improvements in social and daily living skills continue.

Clinical Implications for Children who Demonstrate Optimal Progress

ASD Symptomatology and Psychiatric Functioning. As required by group inclusion criteria, by age four years, children in the OP group do not display any significant ASD symptomatology. While current ASD symptomatology is not clinically significant, statistical differences from TD peers remain in the domains of *Stereotypies and Sensory Abnormalities* and

Social Communication. These findings appear to be driven by mild, residual motor and language stereotypies/idiosyncrasies, and by mild atypicalities in listening behaviors. Given the near absence of symptoms, and their mild nature, children who demonstrate OP likely will not qualify for continued formal services; however, we encourage parents and caregivers to continue to monitor any residual symptoms or atypicalities closely. We recommend that parents regularly assess whether any remaining repetitive or unusual motor behaviors are interfering with social relationships, or with the use of more adaptive self-regulation or coping strategies. Similarly, while the use of idiosyncratic language may largely be viewed as quirky or endearing, parents should monitor whether its use is interfering socially with peers. Additionally, given findings of increased rates of ADHD in adolescents with Optimal Outcomes (Orinstein, Tyson et al., 2015), it will be important for parents of children who demonstrate Optimal Progress to monitor their child's attention regulation abilities over time, to assess whether mild differences in listening behaviors dissipate, remain mild, or become more pronounced. If attention difficulties begin to interfere socially or academically, a comprehensive evaluation for Attention-Deficit/Hyperactivity Disorder should be considered. While the current study was unable to thoroughly assess the presence of anxiety disorders, given findings of increased rates of specific phobias in adolescents with Optimal Outcomes (Orinstein, Tyson et al., 2015), symptoms of anxiety should also be monitored in children who demonstrate Optimal Progress.

Cognitive and Adaptive Abilities. Children who demonstrate Optimal Progress are functioning well within the average range, and equivalently to TD peers, in their early nonverbal problem-solving abilities (Mullen *Visual Reception*), language abilities (Mullen *Expressive Language*, Mullen *Receptive Language*, VABS(-II) *Communication*), and motor skills (Mullen *Fine Motor*, VABS(-II) *Motor*). As above, parents and caregivers should monitor their child's

progress, to ensure that children continue to keep up with TD peers. OP children's daily living skills (VABS(-II) *Daily Living Skills*) were found to be in the moderately low range, and weaker than TD peers, reflecting the only domain of below average range functioning. As noted above, this may be due in part to differences in the priorities of parents of children with ASD; it is likely that parents of toddlers with ASD need to prioritize other skills (e.g., cognitive, language, social interaction) over daily living skills. We hypothesize that as language, social and behavioral intervention needs decrease for the OP group, daily living skills may naturally become more of a focus. If seen as a priority for families, children in the OP group, given their cognitive strengths, should have no difficulties in learning age-appropriate daily living skills.

Limitations and Future Directions

There are several limitations to the current study. First, while a sample size of 18 is reasonable given the rate of OP in toddlers with an early ASD diagnosis, it remains a small sample with limited power. Our sample size may have limited our ability to detect differences between children in the OP and TD groups; however, we believe that by describing group profiles and discussing clinical significance, this limitation is minimized. Future studies should seek to study a larger group of children who demonstrate this type of outcome in order to increase the power of analyses, possibly through collaboration across multiple clinics or universities. Second, our sample is likely not representative of the broader population of children diagnosed with an ASD, given that our sample was predominantly white, and had, on average, a median income \$18,425 higher than the median for the state of Connecticut (from which the sample was drawn). It will be important to extend this research to include a more diverse, representative sample, particularly given evidence of health disparities for minority children and

children of families with lower socioeconomic status (Fombonne, 2003; Herlihy et al., 2014; Mandell et al., 2001) that may influence the occurrence of highly positive outcomes.

Third, we have little information about the interventions received by the OP group between their age two ASD diagnosis and age four evaluation, and therefore, cannot speak to the role of intervention in producing these children's positive outcomes. The large majority of children in our sample received early intervention (e.g., speech therapy, occupational therapy, ABA), and based on previous research (Orinstein et al. 2014; Anderson et al. 2014) it is likely that early intervention plays a large role in producing highly positive outcomes. High-quality early intervention for ASD often focuses on enhancing social attention and social engagement, and in turn, works to additionally enhance language and cognitive development, which largely occurs through social mechanisms. By enhancing early social engagement, it is hypothesized that children are set on an altered developmental trajectory that is more similar to typically developing peers (Dawson et al., 2008). On a neural level, both normalization of brain circuits and use of compensatory circuits have been hypothesized as the mechanism of behavioral change following intensive early intervention. Few studies have investigated this empirically; however, one study of 18 to 30-month-old children with ASD who received a developmental behavioral intervention (Early Start Denver Model) for two years found a normalization of brain activity related to social attention and engagement, which was correlated with significant behavioral improvement (Dawson et al., 2012). Only one study has addressed this question with a sample of individuals with Optimal Outcomes (Eigsti et al., 2016), and found that in the domain of language, behavioral normalization of language abilities was associated with atypical brain networks, providing support for the use of compensatory, rather than normalized neural

mechanisms. Additional research will be needed, both with children with stable ASD and those with Optimal Outcomes, to further address this important question.

Finally, while the current study has substantial evaluation data from ages two and four years, and carefully details the current, age-four functioning of children with OP, it cannot determine how the OP group will look later in development. We hypothesize that this group is on a trajectory that will lead to outcomes like those of adolescents with Optimal Outcomes (Fein et al., 2013); however, we cannot address this with our current data. We believe that children in the OP group will continue to display improvements in their verbal communication skills, and in any residual stereotypies or motor abnormalities, such that it will be exceedingly difficult to differentiate them from TD peers in the domains of cognitive, adaptive, social and language abilities using standardized assessment measures. In contrast, evidence from work with children with OO indicates that attention regulation difficulties may become more pronounced in the adolescent years (Orinstein, Suh, et al., 2015; Orinstein, Tyson, et al., 2015). While it is challenging given the expected rates of Optimal Outcome, future work should seek to follow children from the time of first ASD diagnosis, around age two years, through early childhood and adolescence, in order to better understand the longer-term cognitive, adaptive, and symptomological trajectories of children with optimal outcomes.

Broader Implications for ASD

This work supports previous work that indicates that children with a clear, documented ASD diagnosis can attain a highly positive outcome in which they no longer meet diagnostic criteria and are functioning within the average range across critical domains of development (Anderson et al., 2014; Fein et al., 2013). While ASDs are still broadly viewed to be life-long disorders, this emerging work provides evidence that, for some children, all ASD symptom

domains (Social Communication, RRBI) are amenable to significant improvement and change. Collectively, work investigating highly positive outcomes contributes to our growing understanding of the significant heterogeneity of diagnostic presentation and developmental trajectories in ASD.

As distinct groups in the field begin to investigate this type of outcome using similar criteria, we are beginning to discern the percentage of children for whom this type of outcome occurs (9% in Anderson et al., 2014 and Moulton et al., 2016). While general information about diagnostic stability and the rates of different types of outcomes is critical to clinicians and parents, we still have a great deal to learn about when, how, and under what circumstances highly positive outcomes occur. An important next step should include further elucidation of the developmental time frame of highly positive outcomes. Elucidating the most likely timing of this outcome may provide the first steps toward understanding the neurodevelopmental window for achieving Optimal Progress or Optimal Outcome, which in turn, may provide insights into the types of neurological changes that are required.

Due to the confines of our broader longitudinal project (University of Connecticut Early Detection Study), children identified as meeting criteria for Optimal Progress in the current study all were required to do so by age four. As we did not follow children past age four, we cannot determine whether, or how many, additional children would have met criteria for Optimal Progress or Optimal Outcome later in development. Anderson and colleagues (2014) followed children from age two to age 19, thereby allowing for greater variability in the timing of the loss of an ASD diagnosis. Two of the eight children who demonstrated a “Very Positive Outcome” appeared to achieve this outcome around age nine, while the remaining six did not achieve this outcome until adolescence (Anderson et al., 2014). What differentiates children who may show

this outcome earlier versus later? Do all children who display this type of outcome demonstrate similar neurological changes, or are there distinct neurological changes that accompany this type of outcome at different time periods in development?

Long-term goals of the field should include discerning the mechanisms by which highly positive outcomes occur, with the goal of eventually utilizing this knowledge to help to increase the rate of highly positive outcomes in the broader population of individuals with ASD. We hypothesize that there are numerous contributing factors including child characteristics (e.g., early cognitive abilities, adaptive skills, ASD symptom severity), intervention timing, type, intensity and duration, and family and environmental characteristics (e.g., access to intervention resources, socioeconomic status, caregiver mental health). Significant future work will be needed to continue to illuminate the various pieces of this complex puzzle.

Summary and Conclusions

The current study extends the existing literature investigating optimal outcomes following an early ASD diagnosis, and thoroughly describes the functioning of children who lose their diagnosis by an early developmental time point. This study provides additional support and evidence for the possibility that children with a clearly documented ASD diagnosis may demonstrate a significant amelioration of symptoms, such that they no longer meet criteria for the disorder. Additionally, this study indicates that, for some children who are diagnosed by age two years, this type of outcome may occur by age four.

In the current study, children in the OP group were indistinguishable from TD peers in the domains of cognitive abilities, language skills, and adaptive abilities, with the exception of daily living skills which were in the moderately low range. This may be due in part to differences in the priorities of parents of children with ASD; it is likely that parents of toddlers with ASD

need to prioritize other skills (e.g., language, social interaction) over daily living skills. In regards to ASD symptomatology, clinician's rated children in the OP group as having very mild elevations relative to TD children, particularly in the domains of stereotypies and sensory abnormalities and social communication. In all instances, children in the OP group displayed only mild elevations, which did not reach clinical significance; however, our findings indicate that at this stage of development, sufficient differences remain to differentiate these children statistically from the TD group. These differences appear to be driven by the presence of mild, residual motor and language stereotypies/idiosyncrasies, and by mild atypicalities in listening behaviors. Based on previous research, we hypothesize that these mild differences may dissipate over time, with the exception of attention regulation challenges, which may become more pronounced.

In conclusion, children in the OP group appear to be performing well across domains, and are only distinguishable from TD peers in a few select domains using fine-grained measures. It is encouraging to see this type of outcome so early in development, only two years after an ASD diagnosis was provided. Based on previous research, we hypothesize that these children will continue to display strong skills and abilities, and become increasingly difficult to differentiate from TD peers. As children continue to develop, and to reach important milestones, such as beginning formal schooling, caregivers and clinicians are encouraged to continue to closely monitor any mild residual ASD symptoms. Future work should seek to follow these children over the course of development, to assess long-term outcomes, and to continue to develop our understanding of this promising developmental trajectory.

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Appendix A

Table 1

Group Inclusion Criteria

Group	Diagnostic	Cognitive	Adaptive
Optimal Progress	Age 2: Diagnosed with DSM-IV-TR AD or PDD-NOS. Age 4: No longer met criteria for DSM-IV-TR AD or PDD-NOS.	No requirements Age 4 MSEL: VR, EL, RL all ≥ 35	No requirements Age 4 VABS: Communication, Socialization > 77
High Functioning Autism	Age 2: Met DSM-IV-TR criteria for AD, PDD-NOS or Asperger's. Age 4: Continued to meet criteria for DSM-IV-TR AD, PDD-NOS or Asperger's.	No requirements Age 4 MSEL: VR ≥ 35	No requirements
Typical Development	Age 2/Age 4: Never met criteria for any clinical diagnosis. No clinical concerns. No known siblings with ASD.	Age 4 MSEL: VR, EL, RL, FM all ≥ 35	Age 4 VABS: Communication, Socialization, Motor > 77

AD, Autistic Disorder; DSM-IV-TR, Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision; MSEL, Mullen Scales of Early Learning; PDD-NOS, Pervasive Developmental Disorder - Not Otherwise Specified; VABS, Vineland Adaptive Behavior Scales.

Table 2

Sample Demographics

	Optimal Progress n = 18	High Functioning Autism n = 18	Typical Development n = 18	<i>Statistics</i>
Age in Months:				<i>F</i> (2,51) = .015 <i>p</i> = .985
Mean (SD)	50.72 (5.82)	50.44 (4.40)	50.50 (5.07)	
Range	38 to 63	44 to 62	44 to 64	
Gender: N (%)				Exact Match
Male	12 (66.7)	12 (66.7)	12 (66.7)	
Female	6 (33.3)	6 (33.3)	6 (33.3)	
Race/Ethnicity: N (%)				Fisher's Exact = 6.88 <i>p</i> = .565
White	15 (83.3)	16 (88.9)	12 (66.7)	
Hispanic/Latino	1 (5.6)	1 (5.6)	3 (16.7)	
Black or African American	0 (0)	1 (5.6)	2 (11.1)	
Asian or Pacific Islander	1 (5.6)	0 (0)	1 (5.6)	
Biracial	1 (5.6)	0 (0)	0 (0)	
Median Household Income:				<i>F</i> (2,51) = .211 <i>p</i> = .811
Census Tract Estimates				
Adjusted to 2014 USD				
Mean	\$85,855.25	\$92,300.85	\$86,814.97	
(SD)	(\$31,909.05)	(\$28,144.35)	(\$35,929.29)	
Range	\$22,100.00 to \$129,501.21	\$39,582.45 to \$142,431.21	\$36,138.61 to \$164,314.18	

SD, Standard Deviation. USD, United States Dollars.

Table 3

PDD Diagnostic and Symptom Severity Information

	Optimal Progress	High Functioning Autism	Typical Development	<i>Statistics</i>	<i>Post- Hoc</i>
DSM-IV-TR PDD Symptoms:	n = 16	n = 18	n = 18		
M (SD)					
Total	1.44 (1.09)	4.61 (1.15)	0.11(.33)	<i>F</i> (2,49) =111.84, <i>p</i> <.001, η^2 =.820	G-H: HFA>OP HFA>TD OP>TD
Social Interaction	0.13(.34)	1.67 (.84)	0.06 (.24)	<i>F</i> (2,49) =48.96, <i>p</i> <.001, η^2 =.666	G-H: HFA>OP HFA>TD OP=TD
Communication	0.63 (.62)	1.61 (.61)	0.06 (.24)	<i>F</i> (2,49) =42.039, <i>p</i> <.001, η^2 =.632	G-H: HFA>OP HFA>TD OP>TD
RRBIs	0.69 (1.08)	1.33 (.91)	0 (0) Excluded	<i>t</i> (32)=1.90 <i>p</i> = .067, η^2 =.101	N/A
ADOS CSS:	n = 18	n = 18	n = 18		
M (SD)					
Total	1.56 (.86)	4.94 (1.43)	1.11(.32)	<i>F</i> (2,51) =82.08, <i>p</i> <.001, η^2 =.762	G-H: HFA>OP HFA>TD OP=TD
Social Affect	1.83 (1.04)	5.00 (1.53)	1.39 (.70)	<i>F</i> (2,51) =53.31, <i>p</i> <.001, η^2 =.676	G-H: HFA>OP HFA>TD OP=TD
RRB	3.28 (2.37)	5.00 (1.94)	1.67 (1.53)	<i>F</i> (2,51) =12.78, <i>p</i> <.001, η^2 =.334	G-H: HFA>*OP HFA>*TD OP>*TD
CARS:	n = 18	n = 18	n = 18		
M (SD)					
Total	18.64 (1.92)	25.58 (3.22)	16.53 (1.08)	<i>F</i> (2,51) =79.33, <i>p</i> <.001, η^2 =.757	G-H: HFA>OP HFA>TD OP>TD

>*, Trend Level Finding (.05 ≤ *p* ≤ .10); η^2 , Eta Squared; ADOS CSS, Autism Diagnostic Observation Schedule Calibrated Severity Score; CARS, Childhood Autism Rating Scale; DSM-IV-TR, Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision; G-H, Games-Howell; M, Mean; PDD, Pervasive Developmental Disorder, RRBIs, Restricted, Repetitive Behaviors and Interests; SD, Standard Deviation

Table 4

Age Four ASD Symptom Severity Profile Analysis – Childhood Autism Rating Scale

	OP	HFA	TD	<i>Statistics</i>	<i>Effect Size</i>	<i>Post-Hoc</i>
CARS Severity Score M (SD)	n = 18	n = 18	n = 18	Group: $F(2,51) = 63.25, p < .001$	$p\eta^2 = .713$	G-H: HFA>OP HFA>TD OP>TD
				Domain x Group: $F(6,153) = 2.28, p = .039$	$p\eta^2 = .082$	Pairwise: HFA=OP HFA≠TD OP≠TD
Social Communication	1.16 (.14)	1.69 (.29)	1.05 (.10)	Group: $F(2,51) = 54.42, p < .001$	$\eta^2 = .681$	G-H: HFA>OP HFA>TD OP>TD
Social Interaction	1.14 (.21)	1.74 (.47)	1.14 (.24)	Group: $F(2,51) = 20.83, p < .001$	$\eta^2 = .450$	G-H: HFA>OP HFA>TD OP=TD
Stereotypies and Sensory Abnormalities	1.44 (.34)	1.80 (.42)	1.08 (.14)	Group: $F(2,51) = 21.92, p < .001$	$\eta^2 = .462$	G-H: HFA>OP HFA>TD OP>TD
Emotional Regulation	1.26 (.22)	1.69 (.21)	1.19 (.22)	Group: $F(2,51) = 28.27, p < .001$	$\eta^2 = .526$	Tukey's: HFA>OP HFA>TD OP=TD

η^2 , Eta Squared; $p\eta^2$; Partial Eta Squared; G-H, Games-Howell; HFA, High Functioning Autism; OP, Optimal Progress; Pairwise, Pairwise Interaction Analysis; SD, Standard Deviation; TD, Typical Development; Tukey's, Tukey's HSD; VABS(-II), Vineland Adaptive Behavior Scales, Versions I or II.

Table 5

Age Four Cognitive Profile Analysis

	OP	HFA	TD	Statistics	Effect Size	Post-Hoc
Mullen T-Score Mean (SD)	n = 18	n = 18	n = 17			
				Group: <i>F</i> (2,50) = 4.16, <i>p</i> =.021	<i>p</i> η^2 =.143	Tukey's: HFA=OP HFA<TD OP=TD
				Domain x Group: <i>F</i> (4.58, 114.59) = 1.58, <i>p</i> = .176	<i>p</i> η^2 =.060	N/A
Fine Motor	49.89 (12.64)	40.94 (14.66)	53.00 (12.54)	Group: <i>F</i> (2,50) =3.90, <i>p</i> =.027	η^2 =.135	Tukey's: HFA=OP HFA<TD OP=TD
Visual Reception	56.28 (8.41)	54.28 (9.96)	55.06 (8.34)	Group: <i>F</i> (2,50) =.228, <i>p</i> =.797	η^2 =.009	N/A
Expressive Language	46.11 (5.31)	45.39 (8.22)	50.65 (7.79)	Group: <i>F</i> (2,50) =2.71, <i>p</i> =.076	η^2 =.098	N/A
Receptive Language	52.67 (7.72)	50.17 (9.24)	55.00 (6.35)	Group: <i>F</i> (2,50) =1.64, <i>p</i> =.204	η^2 =.062	N/A

η^2 , Eta Squared; $p\eta^2$: Partial Eta Squared; HFA, High Functioning Autism; Mullen, Mullen Scales of Early Learning; OP, Optimal Progress; SD, Standard Deviation; TD, Typical Development; Tukey's, Tukey's HSD

Table 6

Age Four Adaptive Profile Analysis

	OP	HFA	TD	Statistics	Effect Size	Post-Hoc
VABS(-II) Standard Score M (SD)	n = 18	n = 18	n = 18			
				Group: $F(2,51) = 26.66, p < .001$	$p\eta^2 = .511$	Tukey's: HFA<OP HFA<TD OP=TD
				Domain x Group: $F(4.95, 126.30) = 2.54, p = .032$	$p\eta^2 = .090$	Pairwise: HFA=OP HFA≠TD OP≠TD
Motor	93.89 (12.12)	78.28 (15.61)	98.78 (11.80)	Group: $F(2,51) = 11.89, p < .001$	$\eta^2 = .314$	Tukey's: HFA<OP HFA<TD OP=TD
Daily Living	83.50 (14.45)	71.67 (9.11)	97.78 (9.69)	Group: $F(2,51) = 23.93, p < .001$	$\eta^2 = .484$	Tukey's: HFA<OP HFA<TD OP<TD
Socialization	91.28 (9.01)	76.06 (10.16)	95.28 (11.37)	Group: $F(2,51) = 17.72, p < .001$	$\eta^2 = .410$	Tukey's: HFA<OP HFA<TD OP=TD
Communication	101.94 (12.77)	89.67 (11.82)	101.44 (9.80)	Group: $F(2,51) = 6.54, p = .003$	$\eta^2 = .204$	Tukey's: HFA<OP HFA<TD OP=TD

≠, Significant Pairwise Interaction Effect; η^2 , *Eta Squared*; $p\eta^2$, Partial Eta Squared; G-H, Games-Howell; HFA, High Functioning Autism; OP, Optimal Progress; Pairwise, Pairwise Interaction Analysis; TD, Typical Development; Tukey's, Tukey's HSD; VABS(-II), Vineland Adaptive Behavior Scales, Version I or II

Appendix B

CARS Profile Analysis

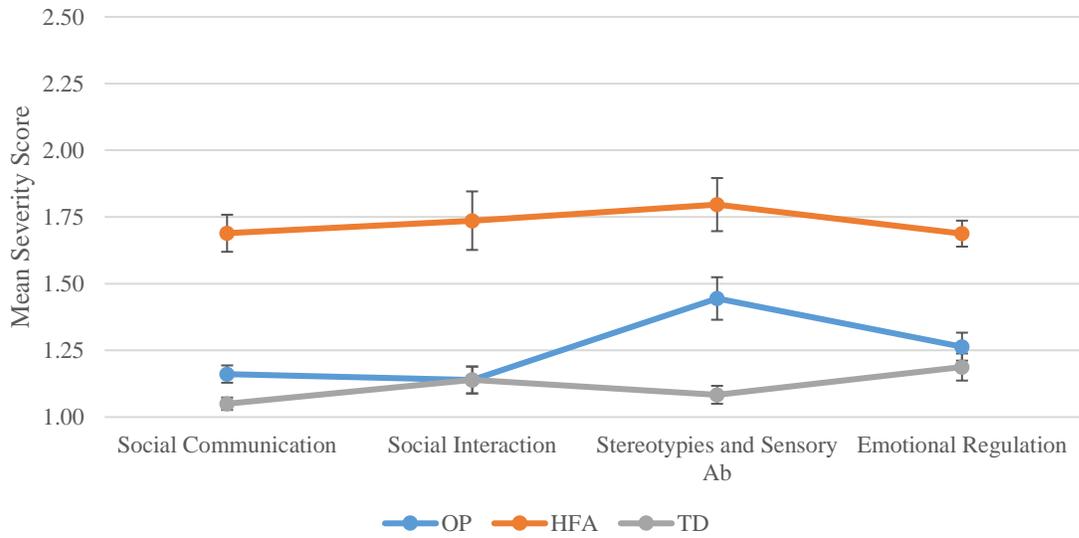


Figure 1. Childhood Autism Rating Scale (CARS) Profile Analysis. Results: Significant group by domain interaction; significant main effect of group.

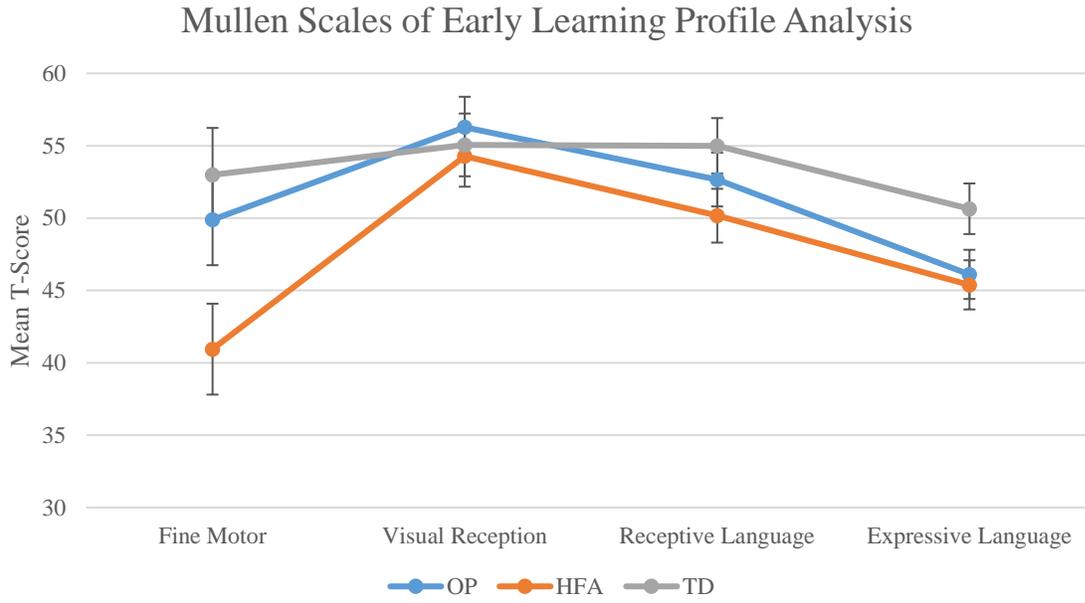


Figure 2. Mullen Scales of Early Learning Profile Analysis. Results: Group by domain interaction effect not significant; significant main effect of group.

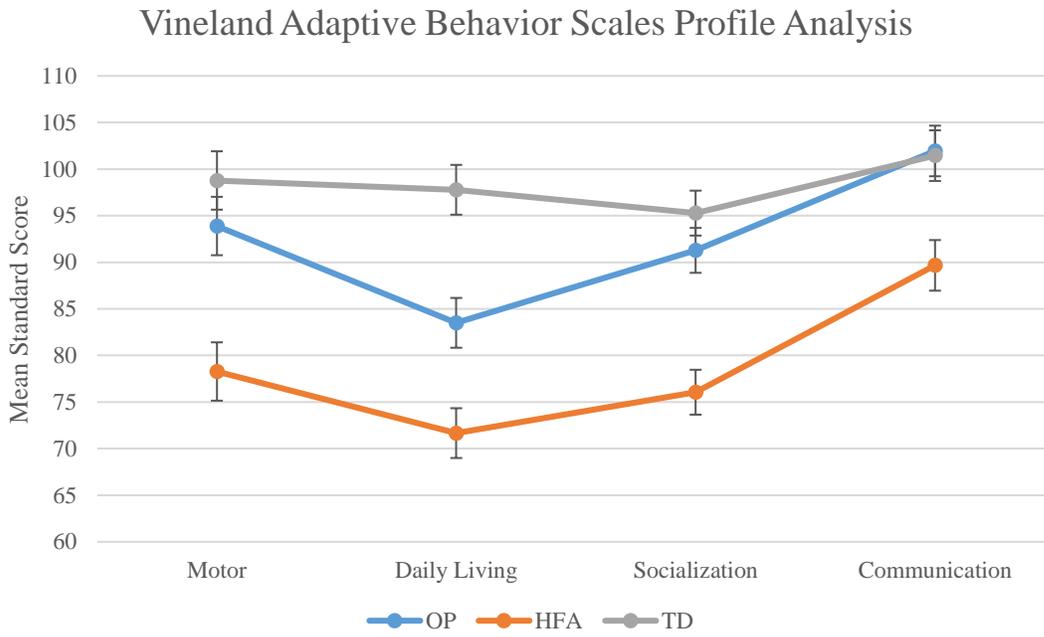


Figure 3. Vineland Adaptive Behavior Scales (-II) Profile Analysis. Results: Significant group by domain interaction; significant main effect of group.

Appendix C

Estimated Median Household Income Methodology

The United States Census Bureau defines a census tract as “a small, relatively permanent statistical subdivision of a county” which is “[d]esigned to be relatively homogeneous...with respect to population characteristics, economic status, and living conditions at the time of establishment” (United States Census Bureau, 2017). The optimum population size of a census tract is 4,000 inhabitants, with a range of 1,200 to 8,000. Census tract boundaries are relatively permanent, allowing for comparisons to be made from census to census. In the absence of participant-reported information about annual household income, census tract-based estimated median household income has been used as a marker of socioeconomic status in a broad range of studies, from studies of preterm birth outcomes (Coley et al., 2015), to studies of healthy food availability (Krukowski, Smith West, Harvey-Berino & Prewitt, 2010), to those of autism prevalence (Pinborough-Zimmerman, Bilder, Satterfield, Hossain & McMahon, 2010).

In the current study, each participant’s family’s census tract was identified using the household address the family provided at the child’s age four evaluation. Census tracts were determined using the United States Census Bureau’s Geocoder (geocoding.geo.census.gov). Participant GEOIDs were subsequently identified by combining an individual’s state code, county code, and census tract number. Following the identification of each participant’s GEOID, one of three United States Census Bureau data files were used to look up estimated median household income. If a child’s age four evaluation was conducted from 1/1/2000 to 12/31/2005, the 2000 Census was used (United States Census Bureau, 2000) (n = 9, 16.67%). For evaluations conducted from 1/1/2006 to 12/31/2010, the 2010 Census was used (United States Census Bureau, 2010) (n = 26, 48.15%). For evaluations conducted from 1/1/2011 to 12/31/2014, the

2010 to 2014 American Community Survey was used (United States Census Bureau, 2014) (n = 19, 35.19%). Using the appropriate data set, each participant's GEOID was used to look up the family's "Median Household Income (Estimate) in Dollars."

Median household income in the 2000 Census is reported in 2000 inflation-adjusted dollars; median household income in the 2010 Census is reported in 2010 inflation-adjusted dollars; median household income in the 2010 to 2014 American Community Survey is reported in 2014 inflation-adjusted dollars. In order to meaningfully combine data from these three time points (2000, 2010, 2014), median household incomes from the 2000 Census and 2010 Census were adjusted to reflect the cumulative rate of inflation from 2000 to 2014, or 2010 to 2014, respectively. The cumulative rate of inflation was determined using the Bureau of Labor Statistics Consumer Price Index Inflation Calculator (https://www.bls.gov/data/inflation_calculator.htm). This tool uses the average Consumer Price Index (CPI) for a given calendar year in the United States, and reflects changes in the prices of all goods and services purchased for consumption by urban households. The cumulative rate of inflation from 2000 to 2014 was 37.48%, and therefore, median household income from the 2000 Census was transformed by multiplying by 1.3748 (e.g., \$10,000 was transformed to \$13,748). The cumulative rate of inflation from 2010 to 2014 was 8.57%, and therefore, median household income from the 2010 Census was transformed by multiplying by 1.0857 (e.g., \$10,000 was transformed to \$10,857). This resulted in all data being in 2014 inflation-adjusted USD. Estimated median household income was then compared across the three groups (OP, HFA, TD) using a one-way ANOVA (see Table 2).

Appendix D

Supplemental Tables

Table S1

Age Four Childhood Autism Rating Scale Item Scores

	OP	HFA	TD	<i>Statistics</i>	<i>Post-Hoc</i>
CARS	n = 18	n = 18	n = 18		
M (SD)					
Social Communication					
<i>#2 - Imitation</i>	1.05 (0.23)	1.36 (0.45)	Excluded	$t(25,76)=2.56,$ $p=.017, \eta^2=.162$	HFA>OP
<i>#11 - Verbal Communication</i>	1.47 (0.50)	1.83 (0.51)	1.14 (0.33)	$F(2,51)=10.41,$ $p<.001, \eta^2=.290$	G-H: HFA>*OP HFA>TD OP>*TD
<i>#12 - Nonverbal Communication</i>	1.14 (0.29)	1.69 (0.42)	1.06 (0.24)	$F(2,51)=20.44,$ $p<.001, \eta^2=.450$	G-H: HFA>OP HFA>TD OP=TD
<i>#14 - Intellectual Response</i>	1.06 (0.16)	1.67 (0.64)	1.03 (0.12)	$F(2,51)=15.59,$ $p<.001, \eta^2=.380$	G-H: HFA>OP HFA>TD OP=TD
<i>#15 - General Impressions</i>	1.08 (0.19)	1.89 (0.19)	1.03 (0.12)	$F(2,51)=99.68,$ $p<.001, \eta^2=.796$	G-H: HFA>OP HFA>TD OP=TD
Stereotypies and Sensory Abnormalities					
<i>#4 - Body Use</i>	1.67 (0.64)	2.11 (0.58)	1.17 (0.34)	$F(2,51)=13.87,$ $p<.001, \eta^2=.352$	Tukey's: HFA>OP HFA>TD OP>TD
<i>#8 - Listening Response</i>	1.34 (0.47)	1.75 (0.43)	1.06 (0.24)	$F(2,51)=14.11,$ $p<.001, \eta^2=.356$	G-H: HFA>*OP HFA>TD OP>TD
<i>#9 - Taste, Smell and Touch Response</i>	1.28 (0.46)	1.53 (0.67)	1.03 (0.12)	$F(2,51)=4.95,$ $p=.011, \eta^2=.163$	G-H: HFA=OP HFA>TD OP>*TD

<*, Trend Level Finding (.05 ≤ p ≤ .10); η^2 , Eta Squared; CARS, Childhood Autism Rating Scale; G-H, Games-Howell; HFA, High Functioning Autism; OP, Optimal Progress; Pairwise, Pairwise Interaction Analysis; SD, Standard Deviation; TD, Typical Development; Tukey's, Tukey's HSD

Table S2

Age Four Mullen Scales of Early Learning Fine Motor Items

	OP	HFA	TD	Statistics	Post-Hoc
Mullen	n = 18	n = 18	n = 17		
Fine Motor: M (SD)					
25. Folds Paper Three Times Possible Score Range: 0 – 1	0.72 (0.46)	0.44 (0.51)	0.65 (0.49)	$F(2,52)=1.55,$ $p=.222, \eta^2=.058$	N/A
26. Imitates Drawings Possible Score Range: 0 – 3	1.83 (1.15)	1.39 (1.24)	2.00 (1.00)	$F(2,52)=1.36,$ $p=.266, \eta^2=.052$	N/A
27. Touches Fingers Possible Score Range: 0 – 1	0.67 (0.49)	0.17 (0.38)	0.69 (0.48)	$F(2,52)=7.55,$ $p=.001, \eta^2=.236$	G-H: HFA<TD HFA<OP OP=TD
28. Touches Fingers (Both Hands) Possible Score Range: 0 – 1	0.39 (0.50)	0.17 (0.38)	0.44 (0.51)	$F(2,52)=1.66,$ $p=.200, \eta^2=.064$	N/A
29. Folds Paper into Square Possible Score Range: 0 – 1	0.17 (0.38)	0.17 (0.38)	0.24 (0.44)	$F(2,52)=0.17,$ $p=.845, \eta^2=.007$	N/A
30. Copies Shapes and Letters Possible Score Range: 0 – 5	1.83 (1.95)	0.83 (1.58)	1.12 (1.41)	$F(2,52)=1.72,$ $p=.190, \eta^2=.064$	N/A

η^2 , Eta Squared; G-H, Games-Howell; HFA, High Functioning Autism; OP, Optimal Progress; Pairwise, Pairwise Interaction Analysis; SD, Standard Deviation; TD, Typical Development

Table S3

Age Four Mullen Scales of Early Learning Expressive Language Items

	OP	HFA	TD	Statistics	Post-Hoc
Mullen	n = 18	n = 18	n = 17		
Expressive Language: M (SD)					
23. Answers Verbal Questions Possible Score Range: 0 – 2	1.78 (0.43)	1.83 (0.51)	1.82 (0.53)	$F(2,50)=0.07,$ $p=.937, \eta^2=.002$	N/A
24. Verbal Analogies Possible Score Range: 0 – 5	2.78 (1.63)	2.72 (1.74)	2.76 (1.60)	$F(2,50)=0.01,$ $p=.995, \eta^2<.001$	N/A
25. Repeats (Short) Sentences Possible Score Range: 0 – 1	0.83 (0.38)	0.83 (0.38)	0.71 (0.47)	$F(2,50)=0.55,$ $p=.581, \eta^2=.022$	N/A
26. Oral Vocabulary Possible Score Range: 0 – 4	0.67 (1.32)	0.50 (1.04)	0.94 (0.90)	$F(2,50)=0.70,$ $p=.500, \eta^2=.027$	N/A
27. Verbal Practical Reasoning Possible Score Range: 0 – 4	0.61 (0.85)	0.28 (0.75)	1.24 (1.64)	$F(2,50)=3.17,$ $p=.051, \eta^2=.112$	G-H: HFA<*TD HFA=OP OP=TD
28. Repeats (Longer) Sentences Possible Score Range: 0 – 2	0.56 (0.78)	0.56 (0.78)	0.53 (0.72)	$F(2,50)=0.01,$ $p=.993, \eta^2<.001$	N/A

<*, Trend Level Finding (.05 ≤ p ≤ .10); η^2 , Eta Squared; G-H, Games-Howell; HFA, High Functioning Autism; OP, Optimal Progress; Pairwise, Pairwise Interaction Analysis; SD, Standard Deviation; TD, Typical Development; Tukey’s, Tukey’s HSD

Table S4

Age Four Vineland Adaptive Behavior Scales Daily Living Skills Subdomain Scores

	OP	HFA	TD	<i>Statistics</i>	<i>Post-Hoc</i>
VABS(-II)	n = 18	n = 18	n = 18		
Ratio IQ: M (SD)					
Daily Living Skills					
<i>Community</i>	83.06 (25.48)	57.95 (18.29)	97.19 (19.45)	$F(2,51)=15.61,$ $p<.001, \eta^2=.380$	Tukey's: HFA<TD HFA<OP OP=TD
<i>Domestic</i>	79.46 (28.71)	60.82 (26.11)	110.09 (34.13)	$F(2,51)=12.16,$ $p<.001, \eta^2=.327$	Tukey's: HFA<TD HFA=OP OP<TD
<i>Personal</i>	74.91 (14.25)	59.72 (14.33)	87.57 (24.81)	$F(2,51)=10.25,$ $p<.001, \eta^2=.287$	Tukey's: HFA<TD HFA<OP OP=TD

η^2 , Eta Squared; G-H, Games-Howell; HFA, High Functioning Autism; OP, Optimal Progress; Pairwise, Pairwise Interaction Analysis; SD, Standard Deviation; TD, Typical Development; Tukey's, Tukey's HSD; VABS(-II), Vineland Adaptive Behavior Scales, Versions I or II