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Predicting Children Missed by an Early Autism Screener

Cara Cordeaux
cara.cordeaux@uconn.edu

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Cara Cordeaux

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Presented by Cara Cordeaux, B.S.

Major Advisor_____
Marianne Barton

Associate Advisor_____
Jeffrey Burke

Associate Advisor_____
Letitia Nagles

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Abstract

Recent clinical best-practice guidelines from the American Academy of Pediatrics recommend that all children be screened for ASD at 18 and 24 months of age (Johnson & Myers, 2007), and those have contributed to an emphasis on early screening and diagnosis. However, no screening instrument can identify all cases at 18-24 months. This study examined profiles of 135 children who participated in validation studies of the Modified Checklist for Autism in Toddlers (MCHAT, MCHAT-R/F), an ASD specific screening instrument. Participants were screened at 18-24 months (Time 1) and again at 36-48 months (Time 2). Children who screened negative at 18-24 months old but later screened positive at 30-48 months old (Missed group, N=25) provide important information about the natural course of ASD and potentially about the limitations of early screening efforts. Analyses indicate that child-level variables (adaptive skills, language development milestones) as well as family level variables (maternal education) predicted whether children were missed or detected by an early autism screener. In a combined model, the age at which first words emerged best predicted whether the screener missed a child at 18-24 months. Clinical implications are important to consider in the context of AAP recommendations and a recent focus in the field on universal screening.

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Introduction

Autism spectrum disorder (ASD) is a developmental disorder characterized by social communication impairments and the presence of restricted interests and repetitive behaviors (American Psychiatric Association, 2013). ASD affects approximately 1 in 68 children in the United States (Centers for Disease Control and Prevention, 2014). ASD is a behaviorally defined and diagnosed disorder, with deficits evident before the age of three in communication, play, attention, cognition, and sensory abilities (American Psychiatric Association, 2013).

The stability of autism spectrum disorder (ASD) diagnoses made before age three is well documented in the literature (Chawarska et al. 2009; Guthrie et al., 2012; Landa, 2008). Children may now receive diagnoses of ASD after screening indicates risk at approximately two years old (Eaves & Ho, 2004; Guthrie et al., 2012) or younger (Kleinman et al., 2008a), well below the national average age of first diagnosis (CDC, 2014). This trend reflects increasing efforts to identify children earlier in development, in part because evidence suggests that interventions delivered during early childhood have an especially powerful impact on later development. Multiple studies demonstrate that early engagement with services in the first 24 months of life may shift the developmental trajectory for children with ASD as they demonstrate improvements in social communication, play, and cognitive abilities (Dawson, 2008; Landa, 2008; MacDonald, Parry-Cruwys, Dupere, & Ahearn, 2014; Rogers, et al., 2012).

The potential impact of early intervention hinges on identifying children at risk for ASD as early as possible; in many states, an ASD diagnosis is required for eligibility to receive some services or levels of service intensity. Early diagnosis can also provide targeted recommendations important prognostic information, and shape treatment planning (Huerta & Lord, 2012). The development of ASD-specific screening measures to aid identification in

children younger than 36 months facilitates the process of early detection, as does the current recommendation of the American Academy of Pediatrics for universal screening for ASDs at 18 and 24 months. Universal screening refers to the standardized practice of implementing ASD-specific screening measures for all children during well-child pediatrician visits at ages 18 and 24 months (Zwaigenbaum, et al. 2015). A recent review indicates ample evidence in the literature that screening at ages 18-24 months assists in early detection (Zwaigenbaum, et al. 2015). Yet, some children are missed by early screening measures at or before two years of age. It is important understand what variables contribute to successful early detection and how these variables may function in the context of universal screening, as they may affect downstream access to and use of intervention services.

In addition, characterizing the profiles of children missed by early screening relative to early-detected peers contributes to our understanding of different developmental trajectories within the autism spectrum. There is some evidence in the literature that suggests multiple trajectories and timelines of the development of ASD symptoms, which may influence the function of screening instruments. A close examination of a pre-school sample of children with ASD will expand our understanding of very early trajectories of ASD development and the ways in which different trajectories interact with commonly used universal screening instruments.

Detection of ASD at an Early Age. The Modified Checklist for Autism in Toddlers (M-CHAT) and the Modified Checklist for Autism in Toddlers, Revised with Follow-Up (MCHAT-R/F) are valid screening tools for ASD at 18-30 months (Robins et al., 2001, Robins et al., 2014). However, no screening instrument can identify all potential ASD cases: initial data on these instruments suggest that they have good specificity but relatively lower sensitivity in the general

population (Kleinman et al., 2008; Robins et al., 2014). That is, the screeners are better able to identify true negatives (children without ASD) than true positives (children with ASD). Therefore, some number of children with ASD in the general population will go undetected by these screeners. Further issues that arise with ASD screening are false-positives (children who fail a screener but do not have ASD) and false-negatives (children with ASD who pass a screener). Strategies aimed at decreasing false-positives, such as conducting a brief interview with parents if their child's score on an ASD-specific screening tool raises suspicions about an ASD, considerably improve the positive predictive value of the MCHAT(-R/F) (Kleinman et al., 2008b; Robins et al., 2014). False-negatives are more problematic, and may occur for a variety of reasons. For example, parents may overestimate a child's frequency of behavior, or skew responses more positively based on limited knowledge of typical development (i.e., misinterpret atypical behavior as typical). Parents may also misread or misinterpret items and rate behaviors other than those targeted by the screener. False-negatives occur at the inverse rate of true positives; that is, if a screener has lower sensitivity, we expect more false-negatives. In the above studies, the number of false-negative children missed by these screeners is unknown as it was not possible to evaluate all children who passed the screener to confirm diagnostic status (Kleinman et al., 2008).

Parent report and early detection. The reliance of many screening tools for ASDs on parent report may be a primary reason for false negatives. Parent inaccuracy in reporting early signs of ASD may occur due to a failure to fully understand the question asked, a lack of knowledge about developmental expectations, or misinterpretation of the child's behavior (Cox et al., 1999). Even when parents are acquainted with the symptoms of autism, they may struggle

to detect early symptoms. One study found that for children with older siblings on the spectrum, parent concern had better specificity than sensitivity and was better for communication than social ability; in other words, parents were better at deeming their child "typical" than "atypical," and better at recognizing typical communication development than typical social development (Hess & Landa, 2012).

Different ASD trajectories. Additionally, there is a certain amount of fluidity inherent in development that may make ASDs more difficult to detect. One study found that between 13 and 30 months, a sample of toddlers with ASDs and other developmental delays showed increases, decreases, and both increases and decreases in different ability areas (i.e., a decrease in expressive language ability and fine motor skills but an increase in receptive language ability) with no pattern characteristic of diagnosis at 30 months (Ben-Sasson & Gill, 2014). Another source of false-negatives may be the sometimes gradual, progressive nature of ASDs, which underlines the need for repeated screening (Landa, Holman, & Garrett-Mayer, 2007). Landa and colleagues (2007) suggest that toddlers diagnosed with ASD later relative to peers may fail to show early symptoms involving impaired social or communication abilities before 24 months, and only begin to show signs detectable by a non-expert observer after their second birthday. A subsequent review suggests that late symptom detection between ages two and three is borne out by other studies (Landa, 2008). Therefore, inaccurate parental report may not be the sole source of later detection of diagnostic risk for these children; rather, children may not yet be manifesting symptoms of concern at the time of initial screening, or they may demonstrate milder symptoms.

Further complicating the reliance on parent report is a more recent analysis of early trajectories to an ASD diagnosis, which suggests that an older two-pattern model (early onset and regression) does not adequately capture the emergence of ASD symptoms, especially within the second year of life. Ozonoff and colleagues (2011) found three trajectories in the first two years of development: early onset, with low social-communication behavior from 6 months onward; regression, with high social-communication behavior at 6 months that declines over time; and plateau, with typical social-communication behavior at 6 months that fails to progress typically over the second year of life. Another prospective longitudinal study found two trajectories: early (onset of symptoms and developmental disruption between six and 14 months) and late (more gradual developmental deceleration after approximately 14 months) (Landa Gross, Stuart, & Faherty, 2012). The authors further note that children in each group displayed some degree of plateau or reduction in communication or social engagement (Landa Gross, Stuart, & Faherty, 2012). In concert with results showing poor concordance between parent report and home video data, these data suggest that parents have difficulty assessing developmental progress over many months, especially when the reference period of typical behavior is brief (as in regression) or when a longer period of typical development slows over time (as in plateau).

***Child Characteristics contributing to a later age of diagnosis*.** In addition to potential complications due to reliance on parent report and variable trajectories of development, other evidence suggests that children who receive an ASD diagnosis later or whose parents express concern at a later age do in fact differ from earlier detected or diagnosed peers in a number of areas, including language, symptom severity, adaptive skills, cognition, and regression.

Considered together, these data suggest that child-level variation in skills across domains may influence the way parent report interacts with the early detection screening measures. The following sections summarize key areas in which variation in skills may influence the early detection process.

Language Development. Often, parent concerns are language-based (Chawarska et al., 2007; Chawarska et al., 2009; Herlihy, Knoch, Vibart, & Fein, 2013), with some evidence to suggest communication concerns (but not social concerns) at age 24 months predict ASD diagnostic outcome at 36 months with good specificity (Hess & Landa, 2012). Additionally, greater speech deficits are associated with an earlier age of parent concern (Baghdadli et al, 2003). A cohort study from the California Department of Developmental Services (DDS) from 1992-2001 found that children with higher communication ability were more likely to have a later age of diagnosis, though the disparity fell to a two-month difference by the 2001 cohort (Fountain, King, & Bearman, 2011).

A perceived contrast between cognitive or adaptive skill and language ability may act as a cue to parents. One study found that children under 36 months of age with stronger cognitive and adaptive skills but weaker expressive and receptive language skills had an earlier age of diagnosis (Bickel, Bridgemohan, Sideridis, & Huntingdon, 2015). For some children, ASD-related language impairments may only manifest at later ages; one study found that a later age of diagnosis was associated with impaired peer relationships and poor conversation skills as well as increased restricted interests (Maenner et al., 2013). This suggests that more complex social

communication deficits become clearer as children age and social communication demands exceed skill capacity.

Symptom Severity. In general, children with less severe symptoms are identified later (Mandell, Novak, & Zubritsky, 2005; Mazurek et al., 2014). Several studies suggest that a strong presence of symptoms associated with ASD is associated with an earlier age of diagnosis (Maenner et al., 2013; Mandell, Novak, & Zubritsky, 2005). However, it may be that the nature of symptoms differentially cues ASD-specific concern; for example, more impaired social ability, but not severe restricted/repetitive behaviors, was associated with earlier diagnosis (Mishaal, Ben-Itzchak, & Zachor, 2014) and parents of children diagnosed earlier than peers had social development concerns earlier (Twyman, Maxim, Leet, & Ultmann, 2009). In one study, children with language delays and ASD were diagnosed 1.2 years earlier relative to other children, while behavioral symptoms such as odd play or hand flapping reduced age of diagnosis by four or three months, respectively (Mandell, Novak, & Zubritsky, 2005). This suggests that for children with largely intact language skills, the presence of other symptomatic behaviors may not trigger parent concern at the same level.

Adaptive Skills. Some evidence suggests adaptive skill level may contribute to the age of diagnosis. Extensive impairment in adaptive skills has predicted an early age of parental concern, which is associated with an earlier age of diagnosis (Baghdadli et al, 2003). However, another study found no relationship between adaptive skills and parental age of concern about ASD symptoms (Chawarksa et al., 2007). This may be due to a non-linear pattern of adaptive skill association with ASD: a large Israeli study found that children with adaptive skills two standard

deviations or more above the group mean (above a standard score of 70) and children with adaptive skills two standard deviations or more below the group mean were diagnosed later. The authors posit that the lower functioning children were missed due to a confound with global developmental delay such that ASD symptoms were not recognized until later (Mishaal, Ben-Itzchak, & Zachor, 2014). On the opposite end, similarly to language skills, intact adaptive skills may have masked the presence of ASD symptoms and delayed the age of detection for higher functioning children.

Regression. There is some evidence to suggest that regression is associated with diagnosis such that children with a history of developmental regression are diagnosed earlier than peers with no regression concerns (Jonsdottir et al., 2010; Mishaal, Ben-Itzchak, & Zachor, 2014; Shattuck et al., 2009). However, the presence of regression concerns may function differently in a universal screening model, where all children are screened at the same time point, versus in a population-based surveillance study where screening and diagnosis occur at different times. Of note, the average age of parent-reported regression overlaps with ages targeted for initial autism screening: a recent meta-analysis of parent-reported regression found that the average age of language regression was 21.8 months, and the average age of mixed skill regression occurred at 21.1 months (Barger, Campbell, & McDonough, 2013). Parents are poor reporters of regression, and retrospective report is particularly poor at capturing decline in social communication skills (Ozonoff et al., 2010). It is possible that parents are not fully attuned to signs of skill loss or plateau at the time when screeners are completed. Thus, they may not report skills as lost or failing to develop on early screeners. Conversely, regression may occur at or after

an 18-24 month screening time point, therefore accounting for children who are detected at later ages.

Cognitive Functioning. Evidence linking cognitive functioning to age of diagnosis is mixed. A recent review notes that two studies show children with lower IQ or intellectual disability have an earlier age of diagnosis, while four studies find no association between low IQ and age of diagnosis (Daniels & Mandell, 2014). A study of four Icelandic birth cohorts found that children with lower IQ and verbal abilities were more likely to have an earlier age of diagnosis; the authors speculate that relatively intact cognitive and verbal ability of children diagnosed after age six may have delayed diagnosis (Jonsdottir et al., 2010). A large US study also found that higher IQ was associated with later age of diagnosis, though the age of diagnosis is decreasing such that higher functioning children are being diagnosed earlier than in years past (Mazurek et al., 2014). It is possible that other features, such as language development or the presence of social impairment, more strongly affect the age at which ASD symptoms are first detected relative to cognitive function.

Demographic variables. The role of demographic variables on disparities in ASD diagnosis and service use is well-represented in the literature, with some evidence suggesting that factors such as race/ethnicity or income disproportionately impact access to care (Irvin et al., 2012; Mehta, Lee, & Ylitalo, 2013; Travers, Tincani, Krezmien, 2011). These demographic variables potentially contribute to differences in the early detection process.

Race and Ethnicity. The association between age of diagnosis and race or ethnicity has mixed support in the literature. In a review, Daniels and Mandell (2014) note that five studies reported minority children in their samples were diagnosed later relative to White children, yet six others found no association between race/ethnicity and age at diagnosis. They also report at least three studies where Non-White children were diagnosed earlier than White peers. National survey-based studies indicate that across the country, age of first diagnosis varies considerably by location. In one study, race/ethnic differences disappeared when location was included in the model (Shattuck et al., 2009), and in another, geographic factors contributed to age of diagnosis significantly more than individual or family-level characteristics, with location in the Northeast USA resulting in earlier diagnosis (Rosenberg et al., 2011). This suggests that disparities in timeliness of detection or diagnoses received prior to ASD diagnosis may have more to do with access to well-timed screening and adequate diagnostic resources than minority status alone. A recent study using a sample from the M-CHAT(-R/F) validation study found a significant effect for minority status on age of diagnosis, yet the magnitude of the effect was small and translated into a one-month difference in age at diagnosis, which is unlikely to have clinical significance (Herlihy et al., 2014).

Socioeconomic status (SES). It is difficult to disentangle socioeconomic status from other variables such as geographic location, education, and access to care/services. A recent review notes three American and three international studies published between 2009 and 2012 that indicated no link between SES and age at diagnosis (Daniels & Mandell, 2014). An additional study in a Czech cohort found that family SES and number of available ASD education sources for parents were not associated with an earlier age of diagnosis (Hrdlicka et al., 2016). In

contrast, Fountain, King, and Bearman (2011) found a 16-month socio-economic "advantage gap" initially present in a long-term Californian cohort study such that higher SES children were diagnosed earlier, but the gap reduced to six months over a decade (1992-2001). Another study of over 1,700 children with ASD between 2008 and 2011 across several states revealed that lower SES was associated with a later age of diagnosis (Mazurek et al., 2014). It may be that SES interacts with other, national-level variables such as insurance and geographic differences in access to appropriate care and services. For instance, it is notable that within one state, the SES gap closed substantially over a decade, but when various states were examined together, SES disparities remained. This suggests other, structural-level variables are at play, such as insurance and access infrastructure. In addition, the impact of SES may also have lessened over time as ASD awareness and screening efforts have increased nationally.

Family level variables. The literature indicates that for children under age three, factors that drive timely detection and diagnosis differ from those that predict diagnosis in older children. One study of children aged five months to 13 years found that family characteristics (insurance, maternal age and education, ASD present in siblings or extended family, and number of siblings) accounted for 12% of the variance associated with age at diagnosis versus child characteristics, which accounted for 1% of variance. However, for children under 36 months, family variables such as maternal age accounted for less variance, with sibling risk status, cognitive ability, and receptive language best predicting age of diagnosis (Bickel et al., 2015). Further evidence for the impact of family-level variables such as birth order and maternal age suggests these factors may impact age of ASD detection.

Birth order. Comparison to older siblings may sensitize parental attention to atypical development. Cohort studies suggest that first-born children were more likely to be diagnosed later (Fountain, King, & Bearman, 2011; Frenette, 2010). In more recent studies, children with older siblings were more likely to be diagnosed earlier (Bickel et al., 2015; Mishaal, Ben-Itzchak, & Zachor, 2014) and trigger parental concerns earlier (Rosenberg et al., 2011). Additionally, children with a sibling on the spectrum were shown to have an earlier age of diagnosis relative to children with typically developing older siblings or only children (Herlihy, Knoch, Vibert, & Fein, 2013). It may be that comparison to younger sibling or peer development becomes more salient as the child approaches preschool age, so that concern about developmental milestones is not captured at the time early screeners are administered to first-born children.

Maternal age. The role of maternal age in early detection and diagnosis of ASDs is unclear. One study found that maternal age was related to the language development of the child when initial concerns began, such that mothers who first recognized concerns in the verbal stage (>18 months) were older than mothers who had concerns earlier in development (Chawarska et al., 2007). A large national study reported the opposite finding that younger maternal age was associated with later age of diagnosis (Shattuck et al., 2009). Similarly, a Canadian study found that increases in maternal age were associated with decreases in age at diagnosis for cohorts from 1992-2000 (Frenette et al., 2011). However, recent studies did not find that maternal age predicted age of diagnosis (Bickel et al., 2015; Daniels & Mandell, 2014; Mishaal, Ben-Itzchak, & Zachor, 2014). Within the universal screening model, few studies have examined the

relationship between maternal age and age of first parental concern; available data suggests that maternal age does not predict age of concern (Herlihy, Knoch, Vibert, & Fein, 2015).

Maternal education. Some evidence suggests that children with more educated parents are diagnosed earlier. Recent studies found that greater maternal or parental education predicted earlier diagnosis (Bickel et al., 2015; Mazurek et al., 2014). A review of state records for ten Californian birth cohorts reported contradictory findings that families living in census tract areas with more education had later ages of diagnosis, though this was marginally significant in 1992 and the effect diminished over time. This latter finding was consistent with the effect of other community level variables (access to psychiatric professionals, community wealth) fading over time (Fountain, King, & Bearman, 2011). However, these data may reflect a broader effect related to state- or nation-level factors such as access to care or services; Studies in Icelandic and Israeli cohorts find no association between parental education and age of diagnosis (Jonsdottir et al., 2010; Mishaal, Ben-Itzchak, & Zachor, 2014). In a similar fashion to the role of SES in early detection, taken together these data suggest that individual level resources may matter less for timely detection than resource access and availability.

The role of Universal Screening. Routine ASD screening at 18 and 24 months is not consistently practiced, though AAP guidelines are clear and research suggests compliance with the guidelines reduces the age of first diagnosis (Daniels & Mandell, 2014). A recent study suggests that universal, population-based screening reduces disparities in age of first diagnosis for lower SES and minority toddlers. Herlihy and colleagues (2015) found that while lower SES predicted a later age at evaluation, the effect was small and not likely to be clinically significant

within the universal screening model. They also found that minority status did not predict the likelihood of receiving an ASD diagnosis, in contrast to prior evidence suggesting minority status acts as a barrier to timely diagnosis. This study appears to demonstrate the equalizing potential of universal screening; that is, when routine, standardized measures and timely evaluations are available, racial/ethnic and SES disparities in detection and diagnosis may appreciably diminish. In addition, children detected by population-based screening are often younger than children detected through other strategies, and therefore may be detected before parent or health professionals register concerns (Pierce, Courchesne, & Bacon, 2016; Robins et al., 2016). This suggests that universal screening has good potential to materially increase efficiency in early ASD-risk identification.

Current Study Aims. Taken together, this review of the existing literature suggests that multiple factors contribute to the later identification of children with ASD. Child-level variables such as language delay, the presence of ASD symptoms or regression, and low cognitive or adaptive skill levels may cue parental concern and lead to early detection with an ASD screener. Additionally, certain family-level variables (e.g., birth order, maternal education) may increase the likelihood that parent-report screeners identify at-risk children at an early age. However, differential trajectories of ASD symptom development, in conjunction with child, family, or demographic factors, have the potential to complicate the function of a parent-report screener. Some children may not exhibit a level of delay or impairment at the time when early screeners are administered. Others may show a higher level of delay or impairment, but family or demographic factors may interfere such that the early screeners do not function as intended. The current study seeks to better understand the profile of low-risk children who are detected and

diagnosed between the ages of three and four ("Missed") relative to peers with ASD who are detected and diagnosed between ages one and two ("ASD") within a universal screening model. Considering the profiles of these Missed children in comparison to their early-detected ASD peers can provide insight into the natural course of ASD development, and additionally provide information about the limitations of the universal screening model.

Aim One: Child Variables. First, the current study seeks to explore whether cognitive, adaptive, symptom, or developmental differences distinguish Missed from ASD peers. We hypothesize that Missed children will have a) higher language functioning, b) show fewer adaptive skill deficits than early-detected peers, c) have fewer symptoms of ASD, and d) fewer milestone delays relative to ASD peers.

Aim Two: Demographic and Family Variables. Second, we aim to assess demographic variables and family-level variables such as race/ethnicity, birth order, maternal age, maternal education, and income level to determine whether any of these factors may distinguish Missed from ASD children. We expect the universal screening model to minimize disparities related to demographic variables (Herlihy et al., 2014). However, previous research suggests family-level factors such as birth order may affect age of detection and diagnosis (Bickel, et al., 2015). Therefore, we hypothesize that birth order will predict group membership.

Aim Three: Combined Model. Third, we seek to assess what variables best distinguish Missed from ASD children when child, demographic, and family variables are considered together. We hypothesize that child variables and birth order will best predict group membership.

Methods

Participants. Participants were drawn from a sample of children participating in the Early Detection study, an ongoing population-based study to evaluate the psychometric properties of an autism-specific screening questionnaire, the Modified Checklist for Autism in Toddlers (M-CHAT, Robins, Fein, Barton, & Green, 2001) and its revision, the M-CHAT-Revised/Follow-up (M-CHAT-R/F; Robins et al., 2014). Children enrolled in the present study via three primary sources: pediatrician well-child visit ASD screening, an Early Intervention service provider ASD screening, or referral from a psychologist at age 18-24 months. At the pediatrician well-child visit, the pediatrician could indicate ASD-specific concerns, which resulted in an evaluation offered to the child regardless of performance on a screener.

Caregivers were given the M-CHAT (n=22,462) or the M-CHAT-R/F (n=11,195) to complete at their child's 18-24 month (Time 1) well-child pediatric visit, at an early intervention site, or by a psychologist; completed screeners were scored at the University of Connecticut Early Detection Laboratory. If a child screened positive at Time 1 (i.e., failed the screener), a graduate student contacted the caregiver via telephone to confirm failed items. If a child was confirmed to screen positive during the follow-up phone interview, he or she was invited to attend a free developmental and diagnostic evaluation at the University of Connecticut.

Missed Group. Children who screened negative at Time 1 (n=21,146) were mailed a rescreening packet with a stamped return envelope including the M-CHAT or M-CHAT-R/F, and the Social Communication Questionnaire (SCQ, Rutter, Bailey, & Lord, 2003) at 36-48 months (Time 2). Screeners were then returned (n=5,595) to the Early Detection Laboratory for

scoring, and the procedure described above was followed if the child screened positive on either measure. Families unable to attend evaluations due to transportation or distance issues were offered study-provided transportation or an evaluation located at the family's pediatric site.

Children who screened positive on an ASD screening measure at age 36-48 months for the first time (n=119) were invited to receive an evaluation. Some children received non-ASD diagnoses or no diagnosis (n=52). Additionally, a subset of the group who screened positive on an ASD screening measure at age 36-48 months was lost to attrition (n=25) before evaluation; thus, their diagnostic status is unknown. Fifteen children were evaluated in a different state or at a collaborating site and were excluded from the current study due to missing data. Children who received an ASD diagnosis constitute the group "missed" by early screening and are the subjects of the current study (Missed, n=25). One child was excluded from final analyses in the Missed group due to extenuating circumstances that delayed a timely evaluation, resulting in deviation from study protocol. Another child was excluded because he was adopted. Within the Missed group, 18 children failed the M-CHAT(R/F) screeners and five failed the SCQ. Three children were evaluated because a parent reported autism concerns on a checklist at rescreening. No child in the Missed group was a younger sibling of a child with ASD; therefore, the final group represents a low-risk, population based sample.

ASD Group. A portion of children who screened positive at Time 1 were evaluated and received an ASD diagnosis; they were then invited to return for an evaluation at 36-48 months (Time 2) and some again received an ASD diagnosis (n=165). Nineteen children were evaluated in a different state or at a collaborating site and were excluded from the current study due to missing data. An additional 14 children evaluated at the University of Connecticut were excluded

due to incomplete data. 11.5% of the sample were younger siblings of children with confirmed ASD diagnoses (n=19). Because this study focused on factors that might delay detection in a low-risk sample, children with an older sibling on the autism spectrum were excluded. The low-risk children who received an ASD diagnosis at Time 1 and Time 2 (ASD; n=110) constitute the comparison group for the Missed children. Three children were excluded from final analyses in the ASD group due to extenuating circumstances that delayed a timely evaluation, resulting in deviation from study protocol. The majority of the ASD group (97.5%) enrolled in the current study after screening positive on the M-CHAT-R/F or M-CHAT. Four children in the ASD group enrolled in the study following pediatrician referral.

A total of 135 children, including 25 children who were missed by an early screening measure at Time 1 and 110 children demonstrating diagnostic stability from Time 1 to Time 2, are the focus of the current analyses. Children who were non-fluent English speakers were also excluded from this study because the screening measures were normed on an English-speaking sample. The overall sample is 85.9% male (n = 116), which approximates the current estimated gender ratio in the wider population of children with ASD of 4.6:1 (CDC, 2012). The majority of children in the sample are White (n = 113, 83.7%), as indicated by their caregivers. For the purposes of this study, all minority races/ethnicities were collapsed into one category (non-White) due to small cell numbers.

At the Time 1 screening, the Missed group was on average 21.4 months old (SD =4.9) and the ASD group was 23.1 months old (SD = 3.9). At the Time 2 evaluation, the Missed group

was on average 50.7 months old (SD =5.6) and the ASD group was 51.0 months old (SD =6.3). See Table 1 for a summary of participant characteristics.

Procedures. A licensed clinical psychologist or developmental pediatrician and a graduate student in the clinical psychology program at the University of Connecticut conducted the evaluations; each evaluation consisted of parent interviews and child testing to assess the child's cognitive, adaptive, and language skills as well as ASD-specific measures. Caregivers received diagnostic feedback and recommendations for treatment at the conclusion of the evaluation and received a written report approximately six weeks later.

ASD was diagnosed based on the clinical judgment of experienced clinicians following DSM-IV-TR criteria (American Psychiatric Association, 2000). At the time of data collection, ASD diagnoses included a diagnosis of Autistic Disorder (AD), pervasive developmental disorder, not otherwise specified (PDD-NOS), or Asperger's Disorder. A research diagnosis, ASD-Low Mental Age, was assigned to children who met DSM-IV criteria for an AD and had scores below the 12-month level on all cognitive domains assessed with the Mullen Scales of Early Learning (MSEL).

For all children, Time 2 evaluations included the Autism Diagnostic Interview, Revised (ADI-R) or an earlier version, the Vineland Adaptive Behavior Scales, the Mullen Scales of Early learning, the Autism Diagnostic Observation Scales, and the Childhood Autism Rating Scale.

Measures

Autism Diagnostic Interview. The ADI is a semi-structured interview for parents that gathers past and current developmental information that a clinician uses to assess autism symptomatology based on ICD-10 and DSM-IV criteria (Lord et al., 1994). Over the course of this study several versions of the ADI were used (ADI-R, ADI(R), ADI-Toddler, ADI-Short) All versions cover three domains of impairment associated with ASD (i.e., language and communication, reciprocal social interaction, and RRBs). The ADI is meant for use with children who have a mental age over 24. Each version of the ADI has a scoring algorithm, which consists of specific items related to core symptoms and allows the clinician to determine if the ASD criteria are met. Higher scores indicate more ASD symptoms. Items of interest for the current study common to all versions are age at developmental milestones such as first word, age of phrase speech, etc. A version of the ADI was administered to caregivers of children in the ASD group and the Missed group at Time 2.

History Form. A detailed history form was developed in three versions (Time 1, Time 2, and Missed) to gather information about children and families at each time point. The Missed version included portions of the Time 1 form as well as all the information on the Time 2 form and was administered to children who were detected at the Time 2 re-screening. On each form, caregivers indicated data such as age of first concern, age of developmental milestones (age of first words, phrase speech), concerns about regression, and provided demographic information (race/ethnicity, birth order, years of maternal education, yearly income). The average age of first word emergence in the Missed group was 13.8 months (SD=4.96), and the average age of first words in the ASD group was 24.04 months (SD=10.95). The average age of first phrase use in

the Missed group was 25.96 months (SD=8.34), and the average age of first phrases in the ASD group was 35.55 months (SD=11.60). Age of first words and phrase speech were coded as 0 if on time (words, 8-18 months; phrases 18-24 months) and 1 if delayed (words, >18 months; phrases, >24 months) (Matson, Mahan, Kozlowski, & Shoemaker, 2010). Regression concerns were coded as present (1) or absent (0). Birth order was coded 1 if a child was the first-born, and 0 if a child was a younger sibling. Yearly income was collected by tens of thousands (e.g., 10-20K, 21-30K per year).

The Mullen Scales of Early Learning (MSEL). The Mullen Scales of Early Learning (MSEL; Mullen, 1995) is a standardized test of cognitive ability, intended to evaluate children between birth and 68 months. It has five subtests (Gross Motor, Visual Reception, Fine Motor, Expressive Language, and Receptive Language) that reflect domains of cognitive development. All subsets with the exception of the Gross Motor domain were administered in the current study; this domain is only available for children under 33 months (Mullen, 1995). Each subtest yields T-scores, percentile ranks, and age equivalents, which reflect the child's current level of development in comparison to same-aged peers. The MSEL is a frequently used measure of developmental level and cognitive functioning in both typically developing children and children with developmental delays. Due to a large number of t-scores falling at more than three standard deviations below the mean, age-equivalent scores were transformed into developmental quotient scores to allow use of parametric statistical tests. A developmental quotient score was calculated according to the mental age formula: the age-equivalent divided by the chronological age, multiplied by 100 (Guthrie et al., 2012).

Vineland Adaptive Behavior Scales-Interview Edition, versions I and II (VABS). The Vineland Adaptive Behavior Scales (VABS; Sparrow, Balla, & Cicchetti, 1984) is a semi-structured, standardized parent report interview that assesses adaptive function across domains of Communication, Daily Living, Socialization, and Motor Skills. The measure yields domain scores, standard scores for individual subscales, and an overall Adaptive Behavior Composite (ABC) score, which is used to compare a child's skills to same-aged peers. Domain standard scores range from 20-160, with higher scores indicating higher functioning or skill level. For the current study, caregivers were administered the VABS (Sparrow, Balla, & Cicchetti, 1984) or the VABS-II, a revised version (Sparrow, Cicchetti, & Balla, 2005). The VABS is considered a valid instrument when assessing children with developmental delays and ASD, and has good established reliability and validity (Sparrow, Balla, & Cicchetti, 1984. By convention, the current study analyzed Time 2 VABS and VABS-II scores together.

Autism Diagnostic Observation Schedule - Generic (ADOS). The Autism Diagnostic Observation Schedule (ADOS; Lord et al., 2000) is a semi-structured, standardized, play-based assessment that measures individual performance in four domains: Reciprocal Social Interaction, Communication, Stereotyped Behaviors and Restricted Interests and Play. Children are administered one of four modules based on language level. Each module consists of a series of unstructured and structured situations or activities that provide a hierarchy of presses for the behaviors of interest. Higher scores on the four domains indicate greater autism severity

The ADOS Calibrated Severity Score (CSS) is a measure of autism severity that takes into account a child's age and language abilities while allowing for a measure of symptom severity that is less influenced by age or verbal abilities (Gotham et al., 2009). The CSS is

computed from ADOS "raw total scores," which include children's scores on two domains: Social Affect (includes items from the Reciprocal Social Interaction, and Communication domains) and Restricted, Repetitive Behaviors (includes items from the Stereotyped Behaviors and Restricted Interests domain). Use of the CSS allows autism severity to be compared across modules. ADOS Modules 1 or 2 were administered at Time 2 for both groups.

The Childhood Autism Rating Scale (CARS). The CARS (Schopler, 1980) is a 15-item observation-based rating scale designed to differentiate children with autism from those with developmental delays without features of autism. Ratings are assigned based on parent report as well as clinician observation. Each item is a sub-domain (e.g., "verbal communication") that is rated on a seven-point scale ranging from "within normal limits for that age" to "severely abnormal for that age." The total score provides a classification of *non-autistic, mild autism* or *severe autism* based on established cutoff scores. In order to better reflect our more current understanding of autism as a spectrum, Chlebowski et al. (2010) recommend a cutoff of 25.5 be used to distinguish an ASD from a non-ASD for two and four-year-olds.

Results

Data Analytic Plan. Logistic regression analyses were conducted to determine whether child-level variables, demographic variables, or family-level variables distinguish between Missed and ASD groups.

Variable Selection. All data were analyzed to determine whether assumptions of logistic regression were met. All analyses were run using IBM SPSS Statistics for Windows, Version 22.0 (IBM Corporation, 2013).

Initial logistic regressions were conducted for each predictor variable with group membership as the dependent variable. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated to describe how well each level of a variable predicted outcome in comparison with the reference level of the variable (e.g., age of first words, on time vs. delayed).

Due to multiple comparisons, a Bonferroni corrected alpha level of .002 was used to identify variables for retention in final analyses. Exceptions were made to include variables that were theoretically supported in the literature as predictors of early ASD detection despite failure to reach the corrected alpha level (birth order, MSEL expressive language DQ score, CARS total score). Those variables identified within the initial regression models as significant, or as theoretically indicated, were retained and tested together as part of exploratory final model.

Assumptions of collinearity were assessed through the evaluation of variance inflation factor (VIF) and tolerance statistics for each regression with conservative cut-offs of VIF > 4 and tolerance < .20 (Menard, 1995).

Aim One: Child Variables. The potential for child-level variables to distinguish between Missed and ASD groups was examined in a series of bivariate comparison models with ASD as the referent group. Variables included cognitive constructs, adaptive constructs, ASD symptom constructs, and developmental constructs (Table 2). The odds ratio of a child being missed by the MCHAT(-R/F) at 18-24 months was positively related to all VABS-II domain scores. In other words, children with higher adaptive skills scores were more likely to be in the Missed group.

The odds ratio of a child being missed by the MCHAT(-R/F) at 18-24 months was inversely related to age at first word and first phrase. That is, children whose first words and phrases developed on time were more likely to be in the Missed group.

Aim Two: Demographic and Family Variables. Demographic factors and family-level variables (Table 3) were examined for their potential to distinguish between Missed and ASD groups in a series of bivariate comparisons with ASD as the referent group. Of these, the odds ratio of a child being missed by the MCHAT(-R/F) at 18-24 months was positively related to years of maternal education. That is, children whose mothers had more education were more likely to be missed by MCHAT(-R/F).

Aim Three: Combined Model. Child variables that reached significance and those that had theoretical value, birth order, and years of maternal education were held over for further tests across constructs to generate a final model. First, significantly predictive variables were tested within constructs for collinearity. The VABS socialization score displayed evidence of collinearity with the VABS communication score and was initially excluded from the combined model.

All variables that reached significance and those with theoretical value were examined simultaneously in a multivariate logistic regression with ASD as the referent group (Table 4). The combined model was tested for collinearity and the VABS daily living skills and VABS communication scores displayed evidence of collinearity. A number of alternatives were considered; ultimately, the two scores were averaged to create a summary score that was entered into the combined model. A second summary score including the VABS socialization, daily

living skills, and communication scores was also tested in a separate combined model. It has been suggested that the collinearity between early items on the socialization and communication scales is related to a high degree of overlap between item content (Thurm, Lord, Lee, & Newschaffer, 2007). Similarly, the early items in the daily living skills domains are related to both communication and socialization abilities. For example, items such as “lets someone know when he or she has wet or soiled diaper, for instance points, vocalizes, pulls at diaper, etc.” and “talks to familiar person on telephone” are related to communication, and items such as “helps with simple household chores” are related to social ability.

There was no material difference in results of the two combined models when the VABS socialization score was included in the summary score. The final combined model included a VABS summary score consisting of the socialization, daily living, and communication scores (VABS combined).

In the combined model, the age of first words best distinguished children in the Missed group from those in the ASD group. The odds ratio that a child would be missed by the MCHAT(-R/F) at 18-24 months was inversely related to age of first words. In other words, if a child attained first words on time, it was more likely that the screener did not detect the child.

Discussion

In the present study, we explored the potential for child factors, demographic factors, family factors, or a combination of these to distinguish Missed children from early-detected ASD peers at an 18-24 month screening within a universal screening model. Previous research suggests that a number of variables may play a role in the early detection process, and at multiple levels.

Aim One: Child Variables. As hypothesized, we found that at age four, Missed children showed stronger adaptive skills than early-detected peers, and were less likely to have milestone delays in first words and phrase speech. These results are consistent with previous literature implicating language development (Bickel, Bridgemohan, Sideridis, & Huntingdon, 2015; Fountain, King, & Bearman, 2011), adaptive skills (Mishaal, Ben-Itzchak, & Zachor, 2014) as variables that cue early concerns and facilitate timely detection of at-risk children.

In this study, the development of first words and, to a lesser degree, first phrases appeared to cue parent concerns with more salience relative to other developmental features. While the VABS domains were each significant as single predictors, high scores in these domains only slightly increased the odds of a child being in the Missed versus ASD group. However, children with on-time development of first words were nearly 15 times as likely as children with delayed speech to be in the Missed group. It is notable that many of the adaptive skills at 24 months as measured by the VABS beyond the communication domain are linked to language development. Children are expected to follow simple directions ("share"), respond to verbal cues within familiar routines, say "please," and vocalize to get their needs met. Thus, the finding that Missed children are more likely to have stronger adaptive skills than ASD peers at age four is likely related to the finding that Missed children are also more likely to have on-time speech development.

These findings are also consistent with the plateau trajectory proposed by Ozonoff and colleagues (2011). They posit that in addition to children who demonstrate early onset of symptoms or a regression, a third group of children with ASD show typical social-communication behavior at 6 months that plateaus and does not develop further over the second

year of life. The Missed group, while representing a relatively small subset of the total sample in the present study, may represent this plateau trajectory of ASD symptom expression that early screening time points fail to categorize accurately. We can imagine a child who is speaking "enough," who exhibits an adequate level of daily skills in the home, and who has no obvious repetitive or restrictive behaviors or sensory atypicalities. Such a presentation may not cue parent concerns at 18-24 months, since the child is still within the window of acceptable developmental variability.

Aim Two: Demographic and Family Variables. Previous research suggests that universal screening may diminish disparities related to demographic or family-level factors (Herlihy et al., 2014). We found that among demographic variables tested in this study, neither race/ethnicity nor family income distinguished Missed from ASD children. These findings are consistent with other studies that find no association between race/ or socioeconomic status and age of diagnosis (Daniels & Mandell, 2014). It is possible our findings reflect recent trends towards reduced impact of these variables, perhaps related to growing awareness of autism as well as increased emphasis on early screening, which facilitates entry into the process of obtaining an evaluation and diagnosis. It is also possible that our location in the Northeast interacted with demographic variables in such a way that the relative impact of race/ethnicity and family income were reduced (Rosenberg et al., 2011).

These findings are consistent with Herlihy and colleagues' (2014) conclusion that universal screening practices have the potential to reduce disparities related to race/ethnicity and economic resources. While the results of the current study are not conclusive by themselves, they

underline the potential for universal screening to minimize the impact of other variables that can influence timely diagnosis.

We found that among family-level factors, Missed children were somewhat more likely to have more educated mothers. Previous literature examining contributions of maternal education to early detection suggests the opposite; that is, that children who are detected earlier are more likely to have more educated mothers (Bickel et al., 2015; Mazurek et al., 2014). Our finding is in contrast to large cohort studies both in America and other countries that suggest the contribution of maternal education may fade when other factors such as access to care or services are taken into account (Fountain, King, & Bearman, 2011; Jonsdottir et al., 2010; Mishaal, Ben-Itzchak, & Zachor, 2014).

This may be a finding unique to the sample in the current study. It is important to note that higher maternal education does not necessarily equate to better knowledge of child development or familiarity with ASD symptoms. Parent report measures are vulnerable to disparities in parental knowledge, which has been shown to affect a parent's willingness to broach concerns with pediatricians (Zuckerman et al., 2015). Additionally, personal psychological processes may influence parent reporting, especially for children of high achieving parents. It is possible that mothers that are more educated may have more demands on their time if they work outside the home; this would afford fewer opportunities to observe a child's speech development and overall functioning and may affect accuracy of reporting on behaviors.

Aim Three: Combined Model. When child, demographic, and family variables were considered together, age of first words best distinguished between Missed and ASD children. This finding is consistent with a previous study that examined child-level and family-level

variables and found that for children younger than 36 months, child-level variables such as expressive and receptive language better predicted age of diagnosis than family-level variables (Bickel et al., 2011). The current finding suggests that within the universal screening model, development of first words may carry more weight than other child variables during the 18-24 month time period.

Overall, children in the Missed group appear to be higher functioning in a number of ways compared to early-detected ASD peers. The appearance of intact language skills at age two for children on a plateau trajectory may mask more subtle presentations of ASD symptoms that then become apparent between the ages of two and four, when they can be detected by parents and captured by a screening instrument. For example, delays in the development of phrase speech or failure to gain more words at the expected rate may cue parent concerns between 24-48 months. This particular finding suggests that parental attunement to language development within the universal screening model may facilitate early detection of children in the early onset or regression trajectory who demonstrate slow or delayed speech, but place children on a plateau trajectory at greater risk for being missed by the recommended 18-24 month screening time point.

Strengths and limitations of the current study. The current study offered a unique opportunity to examine how early universal screening for ASD intersects with child, family, and demographic variables. The inclusion of both objective variables, variables measured at the time of diagnosis, and variables derived from parent report allowed thorough examination of the factors that may best predict early detection of children with ASD.

The primary limitation of the study was the inability to confirm screen-negatives at 36-48 months. That is, it was not possible to confirm that children did not have ASD after passing the initial screening time point. As Kleinman and colleagues (2008) note, participation in the study was voluntary and parents with concerns may have avoided returning the 36-48 month screener. Alternatively, they may have under-reported or misidentified symptoms, resulting in a failure to detect risk. Another limitation was the small sample size of the Missed group, which limits the accuracy of the estimates and generalizability of the findings. The gender and racial/ethnic makeup of the sample were relatively homogeneous, which limited exploration of the contributions of these variables. However, there were no differences between groups in gender or racial/ethnic distributions.

Additionally, the current study was limited by the response bias inherent to the nature of the study procedures. Parents who filled out and mailed back a 36-48 month screener may have had concerns or been more motivated than other parents with a child equally at-risk. In addition, parents may have had concerns and already received diagnoses or services elsewhere, and so were not motivated to participate further. This resulted in a potentially biased picture of children who make up the Missed group.

Implications and future directions. Overall, the relatively low ratio of Missed children to early-detected ASD children suggests that the 18-24 month early screening time point captures a majority of at-risk children. However, current study findings suggest that different trajectories of ASD interact with early ASD screening in ways that have important implications for clinical practice. Children who develop language within an acceptable window may be at greater risk for going undetected by early screening that relies on parent report alone, as the presence of some

language may mask a plateau of development or other subtle symptoms. Children may warrant closer monitoring for appropriate gains in language skills. This result underlines the need for active pediatrician surveillance in early screening; reliance on parent report alone may miss children who demonstrate a plateau trajectory.

The current findings also highlight the importance of multiple screening time points, as one screening alone may not capture all trajectories of ASD. It is notable that within this study, 81% of the sample was detected at the 18-24 month time point. This indicates that the advantages of detecting most children early in development outweigh the risk of waiting to screen for the first time at 36-48 months in order to capture children who may be in a plateau trajectory.

Some trends in the current study suggest areas for further exploration. The Bonferroni correction used in the current analysis is conservative and may have increased the chance of false negatives. Though not significant at our corrected alpha level, Missed children had fewer symptoms of ASD as measured by the CARS and were less likely to have parent-reported regression concerns. These trends are consistent with previous literature suggesting ASD symptoms (Mandell, Novak, & Zubritsky, 2005; Mazurek et al., 2014) and regression (Jonsdottir et al., 2010; Shattuck et al., 2009) may cue parent concerns and facilitate earlier detection of ASD. Ideally, future analyses would consider these variables in a larger sample using less conservative methods to correct for multiple comparisons.

Additionally, birth order showed a trend towards distinguishing Missed from ASD children such that Missed children were more likely to be first-born, consistent with previous literature suggesting that children with older siblings are diagnosed earlier (Bickel et al., 2015; Fountain, King, & Bearman, 2011; Frenette, 2010; Mishaal, Ben-Itzchak, & Zachor, 2014). The

current trend suggests that within a universal screening model, parent report may be vulnerable to inaccuracy for first-born children. This may be due to unfamiliarity with child development or fewer opportunities to compare to typically developing siblings or peers. This finding warrants further exploration, as it has potential implications for clinical implementation of early screening measures. First-born children may warrant greater surveillance by pediatricians and other clinical professionals administering early screeners, even in the absence of parental concerns.

Appendix

Table 1. Participant Characteristics

	Missed				ASD			
Variable	N	M	SD	Range	N	M	SD	Range
Cognitive								
MSEL Expressive Language	23	73.42	22.72	33-109	104	55.85	25.83	10-130
MSEL Receptive Language	23	56.17	31.10	10-98	103	51.06	26.20	10-98
MSEL Visual Reception	23	49.30	33.52	10-96	105	46.79	24.68	10-96
MSEL Fine Motor	23	64.74	30.06	10-99	103	55.05	24.02	10-99
Adaptive								
VABS Communication Skills	25	88.76	18.40	57-129	110	67.82	19.15	40-121
VABS Socialization Skills	25	74.44	7.67	58-87	110	64.01	12.12	48-104
VABS Daily Living Skills	25	75.64	11.83	55-103	110	60.78	12.73	38-100
VABS Motor Skills	25	82.68	14.67	60-119	110	70.60	16.83	38-110
ASD Symptoms								
CARS Total Score	25	28.44	4.39	19.5-37.0	108	32.21	5.67	20.5-45.5
ADOS CSS	24	6.04	2.25	2-10	109	7.20	1.93	1-10
Developmental								
Age of 1st Parent Concern (months)	25	17.12	8.24	0-36	107	14.61	6.23	0-34
Age of 1st Words (% On Time, months)	84.0%	13.75	4.97	7-30	26.4%	24.01	10.95	6-53
Age of 1st phrases (% On Time, months)	48.0%	25.96	8.34	12-42	11.8%	35.55	11.60	15-96
Regression Concerns (% Present)	20.0%	-	-	-	49.1%	-	-	-
Demographics								
Gender (% Male)	88.0%	-	-	-	85.4%	-	-	-
Ethnicity (% White)	91.4%	-	-	-	81.8%	-	-	-
Household Income (tens of thousands)	24	8.46	2.70	2-11	100	7.66	2.96	1-11
Family								
Birth Order (% 1st Born)	76%	-	-	-	57.2%	-	-	-
Maternal Age (years)	25	30.88	5.18	22-47	106	32.39	5.66	19-45
Years of Maternal Education	25	16.84	3.09	12-20	106	14.70	2.93	11-20

Note: MSEL=Mullen Scales of Early Learning, VABS=Vineland Adaptive Behavior Scale, CARS=Childhood Autism Rating Scale, ADOS=Autism Diagnostic Observation Schedule. Means and standard deviations

calculated from MSEL developmental quotient (DQ) scores (*M* = 100, *SD* = 15); DAS-II, VABS and VABS-II standard scores (*M* = 100, *SD* = 15); ADOS calibrated severity scores (CSS) (non-spectrum = 1–3, ASD = 4–5, AD = 6–10); and CARS total scores (ASD cut-off = 25.5).

Table 2. Child Variables predicting whether a child was in the Missed Group

Predictor	Wald's χ^2	*df*	*p*	Odds Ratio (e^{β})	95% CI of odds ratio
Cognitive					
MSEL Expressive Language	7.866	1	.005	1.028	1.008-1.048
MSEL Receptive Language	.671	1	.413	1.007	.990-1.024
MSEL Visual Reception	.173	1	.678	1.004	.987-1.021
MSEL Fine Motor	2.696	1	.101	1.016	.997-1.035
Adaptive					
VABS Communication Skills	**16.966**	**1**	**<.001**	**1.052**	**1.027-1.078**
VABS Socialization Skills	**12.826**	**1**	**<.001**	**1.073**	**1.032-1.115**
VABS Motor Skills	**9.352**	**1**	**.002**	**1.042**	**1.015-1.070**
VABS Daily Living Skills	**18.683**	**1**	**<.001**	**1.085**	**1.046-1.127**
ASD Symptoms					
CARS Total Score	8.517	1	.004	0.875	.800-.957
ADOS CSS	5.844	1	.016	0.755	.602-.948
Developmental					
Age of 1st Parent Concern	2.785	1	.095	1.059	.990-1.132
Age of 1st Words	**20.936**	**1**	**<.001**	**14.664**	**4.642-46.325**
Age of 1st phrases	**14.710**	**1**	**<.001**	**6.76**	**2.543-17.892**
Regression Concerns	7.231	1	.007	4.235	1.479-12.128

Note: MSEL=Mullen Scales of Early Learning, VABS=Vineland Adaptive Behavior Scale, CARS=Childhood Autism Rating Scale, ADOS=Autism Diagnostic Observation Schedule. Each row represents a separate bivariate comparison with ASD as the referent group. Significance levels were corrected for multiple comparisons. Significant OR (p<.002) indicated in boldface.

Table 3. Demographic and Family Variables predicting whether a child was in the Missed Group

Predictor	Wald's χ^2	*df*	*p*	Odds Ratio (e^{β})	95% CI of odds ratio
Demographic					
Gender	.109	1	.742	.801	.215-2.992
Ethnicity	1.456	1	.228	.391	.085-1.796
Household Income	1.437	1	.231	1.105	.938-1.302
Family					
Birth Order	8.150	1	.004	4.245	1.573-11.452
Maternal Age	1.272	1	.225	.952	.878-1.031
Maternal Education	**9.171**	**1**	**.002**	**1.252**	**1.082-1.448**

Note: MSEL=Mullen Scales of Early Learning, VABS=Vineland Adaptive Behavior Scale, CARS=Childhood Autism Rating Scale, ADOS=Autism Diagnostic Observation Schedule. Each row represents a separate bivariate comparison with ASD as the referent group. Significance levels corrected for multiple comparisons. Significant OR ($p<.002$) indicated in boldface.

Table 4. Combined model predicting whether a child was in the Missed Group

	Wald's χ^2	*df*	*p*	Odds Ratio (e^{β})	95% CI for Odds Ratio
Child					
Age of 1st word	**10.136**	**1**	**.001**	**11.652**	**2.57-52.832**
Age of 1st phrase	.191	1	.662	1.389	.319-6.051
Regression concerns	6.745	1	.009	6.913	1.607-29.735
CARS total	.098	1	.754	.968	.788-1.188
MSEL expressive language	1.679	1	.195	.978	.947-1.011
VABS Combined	3.951	1	.047	1.091	1.001-1.089
VABS motor skills	.178	1	.673	.989	.940-1.041
Family					
Maternal education	1.070	1	.301	1.129	.897-1.421
Birth order	2.173	1	.140	2.836	.798-11.345

Note: MSEL=Mullen Scales of Early Learning, VABS=Vineland Adaptive Behavior Scale, CARS=Childhood Autism Rating Scale. Model Wald χ^2 =50.665, N= *df* =8, *p* <.001. Significant (p<.002) OR values indicated in boldface.

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