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Permalink

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Journal

Journal of Autism and Developmental Disorders, 45(7)

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Publication Date

2015-07-01

DOI

10.1007/s10803-015-2383-z

Peer reviewed



Published in final edited form as:

J Autism Dev Disord. 2015 July ; 45(7): 2187–2199. doi:10.1007/s10803-015-2383-z.

Diary Reports of Concerns in Mothers of Infant Siblings of Children with Autism Across the First Year of Life

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Abstract

We examined the home-based concerns reported by mothers of infant siblings of children with autism across the first year of life. At all three ages measured, mothers of high-risk infants were significantly more likely than mothers of low-risk infants to report language, social communication, and restricted and repetitive behavior concerns but were not more likely to report general, medically-based concerns. At 6 and 9 months of age, maternal concerns were poorly related to infant or family variables. At 12 months of age, there were moderate correlations between maternal concerns and infant behavior, and concerns were associated with the proband's autism symptoms and mothers' concurrent depressive symptoms. These findings highlight the need to examine high-risk infants' development in the family context.

Keywords

high risk infant siblings; parental concerns; autism; home-based measures

Parents are often the first to report concerns about their child's development and therefore serve as the first step in early identification and access to treatment for young children with autism spectrum disorders (ASD). Because of this pivotal role in gating access to treatment, several studies have investigated the clinical utility of parental concerns in predicting diagnostic outcomes. In general, parents of children with ASD report elevated levels of concern beginning in the second year of life (De Giacomo & Fombonne, 1998; Veness et al., 2012). Several studies have investigated the possibility that parents of children with ASD may be particularly sensitive to the early emergence of behavioral symptoms in later-born

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children (Herlihy, Knoch, Vibert, & Fein, 2013; Hess & Landa, 2012; Ozonoff et al., 2009). These studies have demonstrated that while parents of children with ASD report concerns regarding subsequent children's development as early as 6 months of age, these concerns do not begin to predict long-term diagnostic outcomes until the end of the first year of life (Ozonoff et al., 2009).

The poor association between parental concerns and infant behavior early in the first year of life suggests that factors other than infant behavioral symptoms are likely contributing to the increased frequency of parental concern in families with an older diagnosed child. One possibility is that this increase reflects a general hypervigilance regarding infants' development and diagnostic future. Given the nearly 20% recurrence rate reported in prospective longitudinal investigations of infant siblings of children with ASD ('high-risk infants'), this early hypervigilance is not unwarranted and likely serves as motivation for participation in these studies in the first place (Ozonoff, Young, et al., 2011).

In addition to a general hypervigilance, very early parental concerns may reflect other characteristics of the high-risk family context, including the presence of an older diagnosed child and the increased prevalence of depression amongst mothers of children with ASD (Daniels et al., 2008). The fact that the majority of parent reports are collected from mothers is an important consideration to keep in mind, particularly with regards to depression, as the presence of maternal depressive symptoms is associated with over-reporting of a range of child behavioral problems, including the severity of ASD symptoms (Bennett et al., 2012; Fergusson, Lynskey, & Horwood, 1993; Maoz et al., 2014). Thus, it is possible that depressive symptoms amongst mothers of high-risk infants contribute to the increased frequency of concerns in the first year of life, but this has not been explicitly examined.

The goal of the current study is to investigate both infant behavioral symptoms and other family factors hypothesized to influence the concerns of high-risk parents, mothers in particular, over the first year of life. Family factors considered here include maternal depressive symptoms and the symptom severity of the older sibling diagnosed with ASD. These relations are examined utilizing home-based diary measures that capture mothers' day-to-day concerns, rather than laboratory-based parent report. Better understanding both the frequency of everyday concerns and the factors that influence them will yield important insights into the high-risk family context and the subjective experiences of high-risk mothers. The existing data on parental concerns will be reviewed before turning to the specific goals and hypotheses of the current study.

Clinical Utility of Parent Concerns

Both retrospective and prospective investigations have demonstrated the emergence of behavioral symptoms of ASD over the latter half of the first year of life, with many overt symptoms in key domains present by 12 months of age (Osterling & Dawson, 1994; Ozonoff et al., 2010; Werner, Dawson, Osterling, & Dinno, 2000; Zwaigenbaum et al., 2005). Despite these early symptoms, parents typically do not report concerns until the second year of life (Chawarska et al., 2007; De Giacomo & Fombonne, 1998; Herlihy et al., 2013; Hess & Landa, 2012; Veness et al., 2012). Retrospective reports of the age at which

parents first became concerned indicate there may be some benefit of prior experience with an older diagnosed child in detecting early symptoms in later-born children, but the evidence is mixed. Herlihy et al. (2013) found that while parents of firstborn children with ASD reported first becoming concerned around 16 months of age, parents of an older child with ASD reported first becoming concerned about the second child with ASD around 10 months of age. Conversely, Chawarska et al. (2007) found no significant differences in the proportion of infants with diagnosed older siblings whose parents who reported first becoming concerned sometime in the first year of life, between 12 and 18 months, or later than 18 months. The clinical utility of these studies is limited by their retrospective nature; parent reports become less accurate as more time elapses between the time of the child's diagnosis and the time of reporting, and retrospective reports in general are poorly correlated with objective measures of infant symptoms (Ozonoff, Iosif, et al., 2011).

Prospective methods reduce some of the limitations with retrospective designs by monitoring infant behavior and parental reports as they occur. Only three prospective studies have examined the relationship between early parent concern and diagnostic outcome, and all have focused on their clinical utility. The first is part of a longitudinal, population-based study that followed infants from 8 months through 4 years of age, when a diagnosis was made (Veness et al., 2012). Parent concerns and standardized parent report measures of infant language and social communication that were collected at 8, 12, and 24 months were analyzed for 114 children (18 with ASD, 16 with Developmental delays, 18 with Specific Language Impairment, and 60 typically developing controls). Parents of children with ASD were significantly more likely to report concerns than the other groups at 24 months of age, but not at either 8 or 12 months. Associations between parental concerns and infant language and social communication skills at each age were not reported, and parental concerns were not included in logistic regression analyses predicting diagnostic classification (only infant measures were included), so the extent to which parental concerns at 24 months predict diagnosis in this population-based sample is not known (Veness et al., 2012).

The other two prospective investigations involved parents of high-risk infants ('high-risk parents'). Ozonoff and colleagues (2009) collected parent concerns through open-ended queries during study visits in the laboratory at 6, 12, and 18 months of age. They found that although high-risk parents report increased levels of concern beginning as early as 6 months of age, these early concerns were poorly related to concurrent infant symptoms and did not help to predict infants who would later be diagnosed with autism. By 12 months of age, the presence of one or more ASD-related concerns (rather than more general developmental concerns) demonstrated moderate sensitivity and specificity in predicting diagnostic outcomes between high-risk infants who were and were not later diagnosed with autism. Hess and Landa (2012) followed a similar group of high-risk infants, collecting parent concerns at 14, 24 and 36 month laboratory visits. They compared high-risk infants who were and were not diagnosed with ASD at 36 months of age (there was no low-risk comparison group). Beginning at 24 months, the presence of one or more concerns was associated with an ASD outcome at 36 months of age. While specificity of parental concern was acceptable, sensitivity was low, with many parents of children demonstrating significant impairments not reporting any concerns.

Together, the existing literature on early parent concerns suggests that concerns are most accurate when reported close to the time the concerning behavior first occurs (rather than retrospectively reporting on infants' early behavior), and that the clinical utility of these concerns improves around 12 months of age in terms of predicting diagnostic outcome. Parents of high-risk infants may be particularly well-positioned to report on autism symptoms as a result of their experience with ASD; they report concerning behaviors earlier than parents without such experience (Herlihy et al., 2013; Ozonoff et al., 2009). However, concerns reported at 6 months of age demonstrate poor association with both concurrent infant behavior and later diagnosis, suggesting that very early parental concerns are influenced by factors other than emerging infant symptoms (Ozonoff et al., 2009).

The Current Study

One explanation for the elevated levels of concerns reported by parents of high-risk infants in the first year of life is that they reflect general parental hypervigilance and anxiety regarding their infants' development (Hess & Landa, 2012; Ozonoff et al., 2009). This hypervigilance is not unwarranted given the elevated recurrence risk for ASD in this population and the high numbers of infants who demonstrate difficulties with language and communication even if not diagnosed (Gamliel, Yirmiya, Jaffe, Manor, & Sigman, 2009; Mitchell et al., 2006; Ozonoff et al., 2014; Ozonoff, Young, et al., 2011).

Here, we investigate the possibility that maternal concerns in the first year of life, particularly those occurring prior to the onset of overt infant symptoms, reflect additional features of the high-risk family context. One of these characteristics is the increased prevalence of depressive symptoms amongst mothers of children with ASD (Bailey, Golden, Roberts, & Ford, 2007; Ingersoll & Hambrick, 2011). The presence of maternal depression symptoms has been associated with an over-reporting of children's concurrent ASD symptoms in recently diagnosed toddlers with ASD (Bennett et al., 2012). Since mothers of high-risk infants by definition have at least one older child with ASD, they may exhibit increased levels of depressive symptoms that are associated with increased levels of concern. Other experiences related to parenting a child with ASD may also play a role, particularly for parents of more severely affected older children. The severity of children's autism symptoms and problem behaviors are positively associated with levels of parenting stress and depression amongst mothers of children with ASD (Estes et al., 2009; Ingersoll & Hambrick, 2011). Thus, parents of more severely affected older children may report higher levels or frequency of concern regarding their infant's development as a result of increased worry or hypervigilance. Parents of more severely affected older children may also be more sensitive to the presence of early behavioral symptoms as a result of their more extensive experience with ASD behaviors.

Better understanding how maternal concerns reflect not just infant behavior but other relevant features of the high-risk family context is important for several reasons. First, it may help to improve procedures for early identification of infants developing symptoms of ASD. It will also enrich our understanding of the high-risk family context itself. There is an emerging literature documenting differences in the dyadic interactions of high-risk mothers and infants in both global ratings of responsivity and directiveness and in specific maternal

behaviors such as gesture use and amount of physical contact (Saint-Georges et al., 2011; Talbot, Nelson, & Tager-Flusberg, 2013; Wan et al., 2012, 2013). These behavioral changes have been hypothesized to reflect both emerging infant symptoms and maternal factors, including increased hypervigilance, but this has not been explicitly studied (Talbot et al., 2013; Wan et al., 2013). Clarifying the extent to which maternal concerns reflect general hypervigilance or other factors associated with high-risk group membership will provide additional direction in investigating the source and implications of changes in maternal behavior patterns.

The goals of the current study are to describe the frequency and factors associated with the day-to-day concerns of mothers of high-risk infants. This is accomplished through the use of home-based diary to record mothers' concerns on a weekly basis, laboratory-based measures of infant behavior, and standard questionnaire measures of maternal depression and ASD symptoms in the older diagnosed sibling ('proband'). The frequency of maternal concerns and relations between concerns and infant behavior, proband symptoms, and maternal depression are assessed at three points across the first year of life: 6, 9, and 12 months. Based on the existing literature, we hypothesized that mothers of high-risk infants would report ASD-related concerns about their infants significantly more frequently than mothers of infant siblings of typically developing children at all three time points. Additionally, concerns amongst high-risk mothers were expected to positively relate to proband ASD symptoms and maternal depression at all three time points and to infant behavior by 12 months of age.

Methods

Participants

Participants included 89 high-risk infants and 87 low-risk infant siblings of typically developing children ('low-risk infants') and their mothers. Data for these families were collected as part of a larger longitudinal study of infants at risk for autism conducted jointly by Boston University and Boston Children's Hospital/Harvard Medical School. For the larger project, interested families were contacted by the study coordinator, who conducted a detailed telephone eligibility interview. All infants were screened for exclusion criteria (prematurity, extended stays in the neonatal intensive care unit, maternal drug or alcohol use during pregnancy, family history of genetic disorders associated with ASD, and primary languages other than English). Infants were enrolled as high-risk if they had an older sibling ('proband') with a clinical diagnosis of Autism, Asperger Syndrome, or Pervasive Developmental Disorder-Not Otherwise Specified (PDD-NOS), confirmed by the Social Communication Questionnaire (Rutter, Bailey, & Lord, 2003), the Autism Diagnostic Observation Schedule (Lord et al., 2000), or an expert community diagnosis. Infants were enrolled into the low-risk group if they had at least one older sibling who was typically developing and no first-degree relatives diagnosed with an ASD or other neurodevelopmental disorder. The sample had a balanced gender ratio, with 51% of the total sample being male. Twenty-three (13%) infants were from a racial or ethnic minority group. There were no group differences in gender ratio, racial background, or family income (all *p*

values > .24). Descriptive information for these subject characteristics is presented in Table 1. Informed consent was obtained from parents prior to participation.

Measures

Infants were seen in the laboratory several times across the first three years of life, where standardized behavioral and diagnostic and autism symptom assessments were collected.

Mullen Scales of Early Learning—At the 6 and 12 month visit, infants' developmental abilities were assessed using the Mullen Scales of Early Learning (MSEL; Mullen, 1995). The MSEL provides age-equivalent scores for 4 cognitive subscales (expressive and receptive language, visual reception, and fine motor) as well as an overall Cognitive T Score for the 4 cognitive domains. Verbal and non-verbal developmental quotients (VDQ and NVDQ) were calculated from the two verbal (Receptive and Expressive Language) and two non-verbal (Fine Motor, Visual Reception) cognitive subscale scores by averaging the two relevant subscale age equivalents, dividing by the child's chronological age, and multiplying by 100. The use of developmental quotients rather than T scores is frequently utilized with this population in order to minimize floor and ceiling effects (Munson et al., 2008). These two scores were used as measures of verbal and non-verbal abilities at 6 and 12 months of age.

Autism Observation Scale for Infants—The AOSI (Bryson, McDermott, Rombough, Brian, & Zwaigenbaum, 2000) is an 18-item assessment that measures a range of autism-related behaviors (visual attention and tracking, social interest and reciprocity, affect, atypical sensory and motor behaviors, etc.) during a brief semi-structured interaction between a trained examiner and the infant, who is seated on their parent's lap. Individual items are scored from 0 to 2 or 3, with higher scores indicating greater atypicality. The scale yields two final scores: the total number of items endorsed, and the total raw score (out of a possible 50). The AOSI was collected at 9 and 12 months of age. AOSI total raw scores were used here as a measure of autism symptoms.

Autism Diagnostic Observation Schedule (ADOS)—Infants' autism symptoms were assessed at 18, 24, and 36 months using the Autism Diagnostic Observation Schedule (Lord et al., 2000). The ADOS measures children's language, social communication, and restricted or repetitive behaviors during a semi-structured interaction with a trained examiner. Empirically derived cutoffs can be used to classify children as meeting criteria for an ASD. ADOS scores from infants' most recent study visit were used to classify infants into diagnostic outcome groups along with clinical best estimates, when available.

Proband autism symptoms—Proband ASD symptoms were measured during the telephone screen using the Social Communication Questionnaire (SCQ; Rutter et al., 2003). The SCQ is a 40-item parent report screening measure that covers communication, social interactions, and restricted and repetitive behaviors. There are two different versions of the SCQ: a 'current' version for children under the age of 5, and a second 'lifetime' version for children 5 years or older. Total score is out of 39, with higher scores indicating greater impairment.

Maternal depression—The presence of maternal depressive symptoms were measured at 6 and 12 months using the Center for Epidemiologic Studies Depression Scale: Revised (CESDR; Eaton, Smith, Ybarra, Muntaner, & Tien, 2004). The CESD-R is a 20-item questionnaire designed to measure depressive symptomology. A revised version, with two items related to suicidal ideation and self-harm removed, was collected via self-report and used as a continuous measure of current maternal depressive symptoms (rather than as a diagnostic classifier). The CESD-R was collected at 6 and 12 months.

Parent-Reported Diary Concerns—On a weekly basis from 6 through 18 months, parents were given the opportunity to report about their child's development across a range of language and social domains via diaries they completed in the home. Diaries were formatted to include both a binary response and an open-ended query for each item. The item of focus for the current analysis was the final question, which asked whether parents had any concerns about their child and if so, to describe them. The vast majority of diaries were completed by mothers, and thus, are used here as a measure of maternal concern regarding their infant's development.

Diaries could be recorded on physical paper diaries provided by project staff and returned via pre-stamped envelopes, or via an online system set up with an individual ID number and personal password. Mothers' responses to the concern item were coded for content, and placed into 1 of 16 categories. For many of the diaries, the concerns item was left blank. If mothers had answered at least one earlier item (e.g. describing their child's language or play for that week), these blank responses to the concern item were considered 'no concerns'. Diaries returned with responses for all items (including the concerns item) left blank were discarded and not included in these or any other analyses. If a response to the concern item referenced responses given to one of the earlier items (i.e. "yes, what I said about his language", "the weird sound I described before"), the response to that earlier item was coded and included in the final variable. Reported concerns that explicitly mentioned ASD were included in the relevant category of concern (e.g. a concern their child stopped saying 'ball' and they knew language loss was a red flag for autism was coded as a language-related concern).

From these total responses, four concerns subscales of interest were created: Language, Social Communication, Restricted or Repetitive Behaviors (RRB), and General/Medical Concerns. An Autism Concerns subscale was created by summing the Language, Social Communication, and RRB subscales. Descriptive information on each of these categories is provided in Table 2. Ongoing reliability was maintained by having a second coder score 500 diaries (approximately 15%) and assessed using intraclass correlation coefficients (ICC). ICC's were all in the good to excellent range ($ICC_{\text{Language}} = .86$, $ICC_{\text{social}} = .63$, $ICC_{\text{RRB}} = .76$, $ICC_{\text{ASD}} = .83$, $ICC_{\text{General/Medical}} = .84$).

Results

Overview

A total of 3,003 individual diaries were returned (1458 HRA, 1545 LRC). There were no significant differences in the average number of diaries completed by each group, $t(175) = -$.

638, $p = .53$. To facilitate our goal of describing the relationship between maternal diary-reported concerns and concurrent infant and maternal measures, three time periods that overlapped with our standardized measures were selected for analysis: 6-8 months, 9-10 months, and 11-13 months. Scores from all diaries completed during each window were averaged for each of the concerns categories (Language, Social Communication, RRB, Autism, and General/Medical).

Clinical Outcomes

Infants were classified as meeting criteria for ASD if they met ADOS criteria for ASD on their most recent study visit and received clinical judgments of ASD by an expert clinician if the most recent visit was also their final study visit. Seventeen infants met these classification criteria and were included in the ASD group ('ASD'). Thirteen of these infants met both ADOS criteria and received clinical judgments of ASD (10 from 36 month data, 3 from 18 month data). An additional 4 infants met ADOS criteria at their most recent visit (3 at 24, 1 at 18) but have not yet received clinical judgments. Thus, the final ASD group represents preliminary, but not fully confirmed, diagnostic outcomes. High-risk infants who did not meet on the ADOS or who were judged to be typically developing are hereafter referred to as HRA-N. HRA is used when referring to the high-risk group of infants as a whole, including both ASD and HRA-N infants. Information on the number of subjects and the number of diaries contributed to each of these three analysis windows is included in Table 3. There were no significant differences between the groups at any age in the average number of diaries contributed by each group of infants, either by initial risk group or diagnostic group (all p -values $> .05$).

General Analytic Approach

Due to the relatively large number of 'no concerns' reported by all mothers on the diary measures and significant skew in the diary measures as well as several of the behavioral measures, non-parametric analyses were used throughout. Within each age, we conducted two sets of analyses to investigate each of our research questions. First, a series of chi-square tests were used to determine the relative proportion of mothers reporting at least one concern in each of our groups. These analyses were conducted with respect to both initial risk group (LRC, HRA) and clinical outcome (LRC, HRA-N, ASD). For the analyses comparing the three outcome groups, significant omnibus results were followed up with pairwise contrasts between each of the three groups. A Bonferroni-Holm correction was applied to correct for multiple comparisons within age for pairwise Chi-square analyses (Holm, 1979).

The second set of analyses focused exclusively on the HRA group in order to better understand how infant and family factors relate to maternal concerns when they occur in the high-risk context. First, we evaluated whether there were any group-level differences in the infant, maternal, or Proband characteristics of mothers reporting at least one concern (of any type) and those reporting no concerns. These characteristics included infant ASD symptoms (AOSI scores at 9 and 12 months), infant verbal and non-verbal developmental level (MSEL VDQ and NVDQ at 6 and 12 months), maternal depression (CESD-R scores at 6 and 12 months) and proband SCQ scores (collected once at study entry). Second, for mothers who

reported at least one concern, Spearman correlations were used to analyze the associations between the degree of maternal concern (total number reported in each of the four autism-related categories: Language, Social Communication, RRB, and Autism) and infant VDQ, NVDQ, and AOSI scores, maternal CESD-R scores, and proband SCQ scores.

6-8 Month Data

Analyses comparing the proportion of mothers reporting concerns in the two risk groups revealed several significant differences. Significantly more HRA mothers than LRC mothers reported Language, Social Communication, RRB, and Autism concerns. Analyses comparing the proportion of mothers reporting concerns in each of the three outcome groups revealed significantly more HRA-N mothers than LRC mothers reported Social Communication and Autism Concerns. There were no significant contrasts involving the ASD group. There were no significant differences in the number of mothers reporting General/Medical Concerns for either the risk or outcome group analyses. These results are summarized in Table 4 (HRA vs. LRC comparisons) and Tables 5 and 6 (LRC, HRA-N, and ASD comparisons). Tables include the percentage of mothers in each group reporting concerns and relevant odds ratios, which represent the probability of a mother in a specific group reporting a concern in a given subscale relative to the probability of a mother in a comparison group reporting a concern of the same type (e.g. at 6 months, HRA mothers are 4.27 times more likely to report an Autism concern than LRC mothers).

Turning to the analyses focusing on HRA mothers reporting concerns ($n = 38$), analyses at 6 months revealed no significant findings. There were no significant differences on any of the infant, maternal, or proband variables between mothers reporting at least one concern and those reporting no concerns (VDQ Mean difference = 3.98, $p = .34$; NVDQ Mean difference = 1.96, $p = .67$; CESD-R Mean difference = -3.33, $p = .22$; SCQ Mean difference = -.32, $p = .88$). Similarly, none of the Spearman correlations between the number of maternal concerns and infant VDQ and NVDQ, maternal CESD-R, or proband SCQ scores, were significant for any of the 4 autism related concern categories.

9-10 Month Data

Comparisons of the proportion of mothers reporting concerns were identical to the 6-8 month analyses for both the risk and outcome group analyses. HRA mothers were significantly more likely than LRC mothers to report Language, Social Communication, RRB and Autism concerns (Table 4). Likewise, HRA-N mothers were significantly more likely than LRC mothers to report Social Communication and Autism concerns than LRC mothers. There were no significant group differences involving the ASD group, nor were there any significant group differences involving the General/Medical concerns category (Tables 5 and 6).

Several significant findings emerged from our analyses focusing more specifically on HRA mothers. First, there were no significant differences between mothers who reported at least one concern ($n = 19$) and those reporting no concerns for infant AOSI or Proband SCQ scores (AOSI Mean difference = .38, $p = .73$; SCQ Mean difference = -.07, $p = .94$). However, the correlational analyses on the subset of HRA mothers who had reported at least

one concern revealed significant positive associations between HRA infants' AOSI total scores and mothers' Language ($r_s = .57, p = .01$), RRB ($r_s = .50, p = .03$) and Autism concerns ($r_s = .69, p = .001$). A positive correlation between ASD concerns and proband SCQ score was observed at the trend level $r_s = .33, p = .08, n = 28$.

11-13 Month Data

Analyses comparing the proportion of mothers reporting concerns in the two risk groups revealed an identical pattern of results to those obtained from the 6-8 and 9-10 month analyses. HRA mothers were significantly more likely to report concerns in the Language, Social Communication, RRB, and Autism categories than LRC mothers. There were no group differences for General/Medical concerns (Table 4). Comparisons of the proportion of mothers reporting concerns across the three outcome groups revealed significant differences for the following pairs: ASD > LRC for Language Concerns, HRA-N > LRC for RRB Concerns, and HRA-N > LRC and ASD > LRC for Autism Concerns (Tables 5 and 6). None of the contrasts between ASD and HRA-N were significant.

Turning to the analyses examining differences between HRA mothers who report concerns ($n = 34$) and those reporting no concerns, we find several significant differences between the groups. First, mothers reporting at least one concern reported significantly more depressive symptoms than mothers reporting no such concerns (Concerns: Mean = 14.41, SD = 10.7; No Concerns: Mean = 7.88, SD = 9.0), $t(44) = -2.11, p = .04$. There were no significant group differences between these two groups for any of the infant or proband measures (AOSI scores: Mean difference = $-.58, p = .39$; VDQ: Mean difference = 2.0, $p = .70$; NVDQ: Mean difference = $.65, p = .88$; proband SCQ: Mean difference = $.95, p = .67$).

The correlational analyses revealed a significant association between mothers' ASD Concerns and Proband SCQ at 12 months ($r_s = .56, p = .004, n = 25$). This association remained significant after controlling for infants' concurrent ASD symptoms (AOSI total score; $r = .65, p = .001, n = 22$). Within the group of HRA mothers who had reported at least one concern (34 HRA infants), Spearman correlations were used to analyze the associations between each of the 4 ASD-related concerns subscales and infants' AOSI, VDQ, and NVDQ scores. There were significant negative associations between ASD Concerns and VDQ ($r_s = -.37, p = .03$), and NVDQ ($r_s = -.34, p = .048$) and trend-level positive associations between AOSI scores and ASD Concerns ($r_s = .33, p = .06$) and RRB Concerns ($r_s = .30, p = .08$) and between Language concerns and VDQ ($r_s = -.33, p = .06$).

Discussion

The goals of this study were to describe the frequency of concerns amongst mothers of high-risk infant siblings of children with ASD in the everyday setting of the home at 6, 9, and 12 months of age, and to analyze associations between these home-based concerns mothers report and both infant and family factors hypothesized to influence them.

We found that across all three ages measured, mothers of high-risk infants were significantly more likely than mothers of low-risk infants to report concerns about language, social communication, and restricted and repetitive behaviors, but were not more likely to report

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general, medically-based concerns. These findings mirror those obtained from laboratory-based parental reports of concern at 6 and 12 months, and extend this work by demonstrating that high-risk parents' concerns reported at home extend throughout the 6-13 month period (Ozonoff et al., 2009).

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Closer examination of maternal concerns in each of the three clinical outcome groups reveal that at 6 and 9 months, group differences are observed primarily in the high-risk non-diagnosed group, who differ significantly from the low-risk group in the number of mothers reporting both social communication and overall ASD-related concerns at both ages. At 12 months, significantly more mothers of non-diagnosed high-risk infants than low-risk infants report restricted and repetitive behaviors and ASD-related concerns; significantly more mothers of diagnosed high-risk infants than mothers of low-risk infants report language and autism-related concerns. At no age do more mothers of infants later classified as ASD report concerns than mothers of non-diagnosed high-risk infants.

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The fact that maternal concerns were not significantly more frequent amongst mothers of infants later diagnosed with ASD, even at 12 months, is consistent with the existing literature on laboratory-based concerns in high-risk samples. Ozonoff and colleagues (2009) reported that presence of at least one parental concern at 12 months of age helped somewhat in predicting diagnostic outcome but overall, 12-month concerns were not a robust predictor of later classification. Likewise, Hess and Landa (2012) reported that parent concerns distinguished high-risk diagnosed from non-diagnosed infants beginning at 24, but not 14 months. The data presented here suggest similarly limited predictive value for mothers' concerns occurring in the first year of life. Instead, our findings suggest that the very early concerns of high-risk mothers reflect factors relating to high-risk group membership beyond emerging infant symptoms of ASD.

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At 6 months, nearly one-third of high-risk mothers reported at least one autism-related concern about their infant, yet these concerns were not significantly associated with any of the variables considered here. Thus, it seems likely that maternal concerns at this age reflect broad effects of risk status, including knowledge of their infant's increased risk and corresponding hypervigilance and anxiety regarding their development. As noted previously, this hypervigilance is not unwarranted given both the high recurrence risk for ASD and the frequency of language and communication difficulties across the entire high-risk population (Gamliel et al., 2009; Ozonoff et al., 2014; Ozonoff, Young, et al., 2011).

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At 9 and 12 months, moderate correlations between maternal concerns and concurrent infant behavior were observed across the high-risk group as a whole. While mothers of infants later diagnosed with ASD were not more likely to report concerns than mothers of high-risk infants not ultimately diagnosed, this is not unexpected given the heterogeneity of early behavioral symptoms which emerge over this period for both groups of infants (Ozonoff et al., 2014). Indeed, differentiating high-risk infants who will ultimately be diagnosed with ASD from those with either other clinical outcomes or no developmental issues remains a central challenge for the field. Parent report measures involving ratings of specific behaviors (e.g. frequency of gesture use or vocalizations, enjoyment of social games like peek-a-boo) likely have more clinical utility than qualitative reports of concern (Rowberry et al., 2014).

Of interest to the present investigation, maternal concerns at 12 months were associated not only with concurrent infant behavior but also with concurrent maternal depression and the severity of the proband's autism symptoms. This is in contrast to previous analyses of laboratory-based concerns which found no association between parental concerns and proband severity (Ozonoff et al., 2009). The association between maternal concerns and proband severity for these home based measures suggest that the kinds of concerns mothers report on home-based diary measures may be qualitatively different than the kinds of concerns than those reported in a laboratory or clinic setting (Hess & Landa, 2012; Ozonoff et al., 2009). The association between proband ASD symptoms and maternal concerns about later-born infants warrants further inquiry. One possibility is that this relationship reflects increasing parental worry as a direct consequence of the older child's severity – mothers of more severely affected children over-report concerns about the infant. Another possibility is that the relationship between proband severity and maternal concern indirectly reflects parenting stress, to the extent that reported severity of diagnosed child serves a proxy for parenting stress. This latter possibility is supported by reports of significant positive associations between self-reported parenting stress and children's concurrent ASD symptomatology and problem behaviors (Estes et al., 2009; Ingersoll & Hambrick, 2011). It is important to note that our measure of proband symptom severity was collected upon study entry when infants were 6 months of age. The fact that maternal concerns at 6 months were not significantly correlated with this proband measure suggest the relationship between concerns and proband severity is more complicated than simply reflecting direct effects of the older diagnosed child's symptoms on mothers' concurrent concerns. Although speculative, it may be that mothers of more severely affected older children report increased concerns later in the first year of life as symptoms are more easily detectable at this age and thus, the possibility of diagnosis may be particularly salient.

The relationship between mothers' concerns and concurrent depressive symptoms is similarly intriguing. We found that maternal concerns at 12-months were associated with mothers' concurrent depressive symptoms, such that mothers with more concerns also reported high levels of depressive symptoms. Prior research has reported children's concurrent ASD symptoms are both directly and indirectly related to concurrent maternal depression, but we found no significant association between maternal depressive symptoms and either infant or proband symptoms (Bennett et al., 2012; Ingersoll & Hambrick, 2011). It is unclear from the present study whether increased depressive symptoms lead to over-reporting of concerning behaviors, mothers' perception of concerning behaviors increases depressive symptoms, or the influence of these factors is bi-directional. Additionally, the influence of maternal depression on concurrent concerns may be underestimated as the return rate of our diary measures was quite low and mothers experiencing relatively more depressive symptoms or parenting stress may be even less likely to complete such a measure. A full understanding of the relationship between maternal depression, infant behavior, and maternal concerns is limited by the small sample size and measures available for this analysis. Future studies with larger samples and more extensive indices of maternal depression will be needed to answer these questions. Finally, it is important to note that extent to which increased early concern characterizes families of high-risk infant siblings

who do not choose to enroll in prospective, longitudinal investigations may differ significantly from families that seek out participation.

Despite these limitations, the findings presented here offer important insight into the high-risk family context. First, it is clear that a large number of high-risk mothers are concerned about their infants' development and that these concerns reflect both infant symptoms as well as maternal and sibling variables. Diagnostically, care needs to be taken to disentangle relevant maternal concerns from those reflecting sources other than infant behavior. These findings also highlight the need to consider how some of these same family factors, particularly maternal concerns and depressive symptoms, may influence early parent-child dyadic interactions. Importantly, these maternal characteristics may serve as both additional risk and protective factors for high-risk infants in early development. For example, Talbot et al. (2013) reported that mothers of non-diagnosed high-risk infants used significantly more gestures than mothers of low-risk infants and that this increase was attenuated amongst mothers of later-diagnosed high-risk infants. They hypothesized that the increase in maternal gesture use reflected the same hypervigilance and awareness of risk implicated here. This increase use of gesture may help to scaffold language development, an area of relative difficulty for both diagnosed and non-diagnosed high-risk infants (Mitchell et al., 2006; Ozonoff et al., 2014; Talbot et al., 2013). Conversely, the presence of depressive symptoms may be associated with reduced maternal language use to high-risk infants, as has been reported for mothers with depression outside of the high-risk autism context (Pan, Rowe, Singer, & Snow, 2005; Rowe, Pan, & Ayoub, 2005). Understanding how maternal concerns and other features of the high-risk family context play a role in both the early identification and developmental course of infant siblings of children with autism is an important avenue for future research.

Acknowledgments

We are extremely grateful to the many children and families who have participated in this study, and to the project staff and interns who have assisted in the data collection, especially Karen Chenausky. This work was supported by grants from the NIH (R01-DC010290 and R21 DC 08637), Autism Speaks, and the Simons Foundation (137186). A portion of the work presented in this manuscript was presented as part of the first author's doctoral dissertation.

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Table 1

Participant Characteristics, by Family Risk Group

	Family Risk Group	
	LRC	HRA
Sex (% Male)	51.2%	48.9%
Race (% Non-White, Non-Hispanic)	15.1%	10.2%
Family Income (% making less than \$65,000)	30.2%	26.1%
Average number of diaries returned (Mean, SD)	17.8 (15.7)	16.2 (16.8)

Note: LRC = Low-Risk Control, HRA = High-Risk Autism

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Table 2

Home-Based Diary Concerns Categories

Autism Concerns			
Language	Social Communication	Restricted or Repetitive Behaviors	General/Medical
<ul style="list-style-type: none"> • babbling • words • language loss • odd sounds 	<ul style="list-style-type: none"> • eye contact • gestures • social interactions 	<ul style="list-style-type: none"> • sensory issues, including excessive mouthing • repetitive motor behaviors, including self-injury • rigid or circumscribed interests of play routines 	<ul style="list-style-type: none"> • teething • feeding • sleeping • motor milestones • general illness, gastrointestinal issues • temperament (aggression, activity level)

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Table 3

Number of Diaries Completed at Each Age, by Outcome Group

Age		Outcome Group		
		LRC	HRA-N	ASD
6 Months	Number of Diaries (mean, SD)	2.21 (.82)	2.42 (.73)	2.5 (.67)
	Number of Subjects	<i>n</i> = 81	<i>n</i> = 57	<i>n</i> = 12
9 Months	Number of Diaries (mean, SD)	1.74 (.44)	1.77 (.42)	1.67 (.49)
	Number of Subjects	<i>n</i> = 65	<i>n</i> = 44	<i>n</i> = 15
12 Months	Number of Diaries (mean, SD)	2.40 (.79)	2.36 (.79)	2.21 (.80)
	Number of Subjects	<i>n</i> = 53	<i>n</i> = 42	<i>n</i> = 14

LRC = Low-Risk Control, HRA-N = High-Risk Non-Outcome, ASD = High-Risk Autism Outcome

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Table 4

Chi-Square Results and Proportion of Parents Reporting Concerns by Concern Type, Age, and Family Risk Group

Concern Type	6 Months			9 months			Contrasts <i>df</i> =1 <i>N</i> =109
	Contrasts <i>df</i> =1 <i>N</i> =150	Odds Ratio	Percent Reporting Concerns	Contrasts <i>df</i> =1 <i>N</i> =124	Odds Ratio	Percent Reporting Concerns	
Language	$\chi^2 = 7.41$	HRA vs. LRC	HRA = 23.2%	$\chi^2 = 7.99$	HRA vs. LRC	HRA = 18.6%	$\chi^2 = 12.59$
	<i>p</i> = .010	OR = 3.77	LRC = 7.4%	<i>p</i> = .007	OR = 7.22	LRC = 3.1%	<i>p</i> = .000
Social Communication	$\chi^2 = 8.35$	HRA vs. LRC	HRA = 13%	$\chi^2 = 8.17$	HRA vs. LRC	HRA = 11.9%	$\chi^2 = 6.58$
	<i>p</i> = .006	OR = 12.0	LRC = 6.7%	<i>p</i> = .005	-	LRC = 0%	<i>p</i> = .017
RRB	$\chi^2 = 6.13$	HRA vs. LRC	HRA = 13.05%	$\chi^2 = 5.67$	HRA vs. LRC	HRA = 15.3%	$\chi^2 = 6.53$
	<i>p</i> = .024	OR = 5.9	LRC = 2.5%	<i>p</i> = .025	OR = 5.7	LRC = 3.1%	<i>p</i> = .016
Medical	$\chi^2 = 1.90$	HRA vs. LRC	HRA = 49.3%	$\chi^2 = .998$	HRA vs. LRC	HRA = 37.3%	$\chi^2 = .02$
	<i>p</i> = .19	OR = .63	LRC = 60.5%	<i>p</i> = .37	OR = .70	LRC = 46.2%	<i>p</i> = 1.0
Autism	$\chi^2 = 12.17$	HRA vs. LRC	HRA 34.8%	$\chi^2 = 13.90$	HRA vs. LRC	HRA 32.2%	$\chi^2 = 17.56$
	<i>p</i> = .001	OR = 4.27	LRC = 11.1%	<i>p</i> = .000	OR = 7.24	LRC = 6.2%	<i>p</i> = .000

Note: Bonferroni-Holm corrections were applied within age. Significant Chi-square results are bolded. RRB = Restrictive, Repetitive Behaviors; OR = Odds Ratio.

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Table 5

Proportion of Parents Reporting Concerns by Concern Type, Age, and Outcome Group

Concern Type	Age			
	Group	6 Months	9 Months	12 Months
Language	ASD	16.7%	13.3%	13.3%
	HRA-N	24.6%	20.5%	38.6%
	LRC	7.4%	3.1%	6.2%
Social Communication	ASD	0%	6.7%	21.4%
	HRA-N	15.8%	13.6%	14.3%
	LRC	1.2%	0%	1.9%
RRB	ASD	8.3%	0%	7.1%
	HRA-N	14.0%	20.5%	23.8%
	LRC	2.5%	3.1%	3.8%
Medical	ASD	50%	60.0%	35.7%
	HRA-N	49.1%	29.5%	45.2%
	LRC	60.5%	46.2%	41.5%
Autism	ASD	25%	13.3%	57.1%
	HRA-N	36.8%	38.6%	45.2%
	LRC	11.1%	6.2%	11.3%

Note: RRB = Restrictive, Repetitive Behaviors, LRC = Low Risk Control, HRA-N = High-Risk Non-Outcome, ASD = High-Risk Autism Outcome

Table 6

Chi-Square Results by Concern Type, Age, and Outcome Group

Concern Type	Contrast Pairs	6 Months			9 months			12 months		
		Omnibus <i>df</i> =2 <i>N</i> =150	Contrast χ^2, p	Odds Ratio	Omnibus <i>df</i> =2 <i>N</i> =124	Contrast χ^2, p	Odds Ratio	Omnibus <i>df</i> =2 <i>N</i> =109	Contrast χ^2, p	Odds Ratio
Language	HRA-N vs. LRC	$\chi^2 = 7.91$ <i>p</i> = .019	7.94, .007	4.07	$\chi^2 = 8.60$ <i>p</i> = .014	8.73, .007	8.10	$\chi^2 = 17.57$ <i>p</i> = .000	7.395, .011	4.90
	ASD vs. LRC		1.14, .274	2.50		2.70, .158	4.85		18.53, .000	16.33
	ASD vs. HRA-N		.347, .718	0.61		.374, .712	0.60		3.733, .055	3.30
Social Communication	HRA-N vs. LRC	$\chi^2 = 12.32$ <i>p</i> = .002	10.55, .002	15.00	$\chi^2 = 9.19$ <i>p</i> = .010	9.38, .003	-	$\chi^2 = 7.22$ <i>p</i> = .027	5.28, .042	8.67
	ASD vs. LRC		.150, 1.0	0		4.39, .187	-		7.534, .026	14.18
	ASD vs. HRA-N		2.18, .342	0		.52, .666	0.45		.397, .676	1.63
RRB	HRA-N vs. LRC	$\chi^2 = 6.61$ <i>p</i> = .037	6.66, .016	6.45	$\chi^2 = 11.46$ <i>p</i> = .003	8.73, .007	8.10	$\chi^2 = 9.31$ <i>p</i> = .010	8.52, .005	8.00
	ASD vs. LRC		1.15, .343	3.60		.473, 1.0	0		2.94, .511	2.00
	ASD vs. HRA-N		.284, 1.0	0.56		3.62, .095	0		1.85, .258	0.25
Medical	HRA-N vs. LRC	$\chi^2 = 1.90$ <i>p</i> = .39	1.75, .224	0.63	$\chi^2 = 5.26$ <i>p</i> = .072	3.03, .11	0.49	$\chi^2 = 4.11$ <i>p</i> = .81	.133, .84	1.16
	ASD vs. LRC		.476, .540	0.65		.935, .40	1.75		.155, .767	0.67
	ASD vs. HRA-N		.003, 1.0	1.04		4.44, .062	3.60		.389, .756	0.672
Autism	HRA-N vs. LRC	$\chi^2 = 13.0$ <i>p</i> = .002	13.02, .001	4.67	$\chi^2 = 18.63$ <i>p</i> = .000	17.80, .000	9.60	$\chi^2 = 18.26$ <i>p</i> = .000	13.90, .000	6.47
	ASD vs. LRC		1.74, .183	2.67		.906, .313	2.35		14.07, .001	10.44
	ASD vs. HRA-N		.613, .521	0.57		3.28, .110	0.27		.596, .44	1.61

Note: Bonferroni-holm corrections were applied within age. Significant results are bolded. LRC = Low Risk Control, HRA-N = High-Risk Non-Outcome, ASD = High-Risk Autism Outcome, RRB = Restrictive, Repetitive Behaviors; Odds Ratio.