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Comparison of Parent Questionnaires, Examiner-Led Assessment and Parents' Concerns at 14

Months of Age as Indicators of Later Diagnosis of Autism

**Abstract**

Parents participating in a prospective longitudinal study of infants with older siblings with autism

completed an autism screening questionnaire and were asked about any concerns relating to their

child's development, and children were administered an interactive assessment conducted by a

researcher at 14 months.  Scores on the parent questionnaire were highest for children later

diagnosed with autism.  Parental concerns and scores from the examiner-led assessment

distinguished children with later developmental difficulties (both autism and other developmental

atypicalities) from those who were developing typically.  Children about whom parents expressed

concern scored higher on both the questionnaire and the interactive assessment than those without

concerns.  There were no significant associations between total or individual item scores from the

questionnaire and interactive assessment.


Keywords: autism, early detection, behavioural signs, assessment, infant siblings

Comparison of Parent Questionnaires, Examiner-Led Assessment and Parents' Concerns at 14

Months of Age as Indicators of Later Diagnosis of Autism

The development of effective instruments to screen for autism in toddlers has been a long-standing aim for researchers and clinicians alike, with the expectation that early identification will lead to earlier diagnosis and intervention, reduce stress and anxiety for parents and promote better outcomes for young children on the autism spectrum (Zwaigenbaum, Bryson, & Garon, 2013). However, attempts to design valid and reliable early parent-report screening tools for autism have had mixed results, with conflicting views about the value of their routine use in a population-wide context. Some official guidelines recommend early screening for autism in primary care settings (Johnson, Myers, & American Academy of Pediatrics Council on Children with Disabilities, 2007; Volkmar et al., 2014), whereas others suggest that existing screening instruments lack sufficient qualities to justify their use in community-wide early years services (e.g. American Academy of Family Physicians, 2016; Siu et al., 2016; UK National Screening Committee, 2012). When used at around 18 months of age screening instruments may be less effective at detecting children who go on to be diagnosed with autism than when used with older toddlers, and different aspects of development have been shown to be informative at different ages (Stenberg et al., 2014; Sturner et al., 2017; Sturner, Howard, Bergmann, Stewart, & Afarian, 2017; Toh, Tan, Lau, & Kiyu, 2017). Sacrey, Bryson and colleagues (2018) describe the range of currently available screeners for autism in pre-schoolers for which evaluations have been conducted.

In addition to the use of screening questionnaires, parents of young children may express explicit concerns about their child's early development. Information about the focus of these concerns in relation to children later diagnosed with autism is often based on retrospective recall following diagnosis. One large-scale study (Zuckerman, Lindly, & Sinche, 2015) found that parents of children later diagnosed with ASD reported first concerns about their child's development at approximately 24 months of age, almost a year earlier than parents of children with either developmental delay or learning disability. However, parents of the children later diagnosed

with autism were more likely to receive a reassuring, passive response from professionals than the more proactive responses relating to the children with non-autistic disabilities.

Prospective longitudinal studies involving young children at elevated likelihood (EL)[1] of autism due to having an older sibling with an autism diagnosis provide an opportunity to elicit and investigate parental concerns relating to children's very early development.  Sacrey et al. (2015) used a semi-structured interview to explore parents' concerns up to six times between 6 months and 24 months of age.  Concerns about sensory and motor skills predicted autism diagnostic outcome as early as 6 months, and concerns about sensory and play skills by 9 months.  Concerns about social development did not predict outcome until 12 months, communication not until 15 months and repetitive behaviours and restricted interests not until 18 months.

Studies report that stereotyped and repetitive behaviour elicited in examiner-led interactive assessments may indicate risk for later autism diagnosis from as early as 12 months of age (e.g. Elison et al., 2014).  Ozonoff and colleagues (2010) suggest that differences between children later diagnosed with autism and their typically developing counterparts may be evident from 12 months of age, based on observational measures of early social behaviour.  Chawarska et al. (2014) investigated the features of early social communication derived from the Autism Diagnostic Observation Schedule – Generic (ADOS-G: Lord et al., 2000), a semi-structured observational measure of autism symptomatology, administered at 18 months.  In this prospective longitudinal study of siblings at EL of autism, different profiles of difficulties and behaviour predicted later diagnosis of ASD, including: poor eye contact plus lack of communicative gestures and giving; poor eye contact with a lack of imaginative play; and repetitive behaviours in combination with a lack of gestures.

Sacrey, Zwaigenbaum et al. (2018) compared items from the Autism Parent Screen for Infants (APSI: Sacrey, Bryson, et al., 2018), a 26-item parent-report questionnaire, with

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[1] We are using the term 'elevated likelihood' in place of the more commonly used term 'high risk' (HR) in response to parental preferences reported in Fletcher-Watson et al. (2017).

corresponding items from the Autism Observation Scale for Infants (AOSI: Bryson, Zwaigenbaum, McDermott, Rombough, & Brian, 2008), a semi-structured examiner-led assessment designed to detect and monitor signs of emerging autism traits.  There was poor agreement between 19 matched items across the two instruments, and items from the parent report at both 12 months and 18 months were generally better than the examiner-based measure in predicting later autism diagnosis.  AOSI total score has been shown to discriminate later ASD outcome at 14 months in another elevated likelihood sibling study (Gammer et al., 2015) and scores from 9 AOSI items at 18 months contributed to the prediction of later ASD diagnosis in the longitudinal prospective sibling study reported by Brian and colleagues (2008).

The Quantitative Checklist for Autism in Toddlers (Q-CHAT: Allison et al., 2008) is a normally-distributed 25-item questionnaire designed to screen for autism in toddlers in the general population.  The utility of the Q-CHAT as a primary screening tool for autism has yet to be demonstrated, although a 10-item version of the Q-CHAT has been reported to show potential utility in highlighting early 'red flags' for autism (Allison, Auyeung, & Baron-Cohen, 2012) and Raza and colleagues (2019) report that this shorter version can predict later ASD diagnosis at 18 and 24 months of age in an EL study context.

The present study involves participants who were recruited as part of a prospective longitudinal study of children at elevated likelihood of autism due to having older siblings with a diagnosis of autism.  Children recruited for such studies are likely to display fewer and less severe symptoms than those recruited on the basis of clinical referral or existing diagnoses (Sacrey et al., 2017) and instruments whose properties may provide greater variance across this type of sample may be more informative than those that have less normally-distributed features.  For this reason, the Q-CHAT was deemed to be appropriate as a parent-report measure of autism symptomatology.  We investigated scores from Q-CHAT and AOSI assessments and also measured the expression of explicit parental concerns about their child's development at 14 months.  We predicted that Q-CHAT and AOSI total scores and the expression of parental concerns would relate to autism

diagnosis at 3 years of age.  We also investigated the additional value of combining results from these three sources of information.

**Method**

*Participant recruitment and assessment visits*

Children participating in the British Autism Study of Infant Siblings (BASIS: http://www.basisnetwork.org/) were assessed at approximately 8 months, and then at 14, 25 and 38 months.  Participants comprised 113 children (63 male; 50 female) with older siblings with autism (Elevated Likelihood: EL) and 27 children (14 male; 13 female) with at least one older sibling and no history of autism in first-degree relatives (Typical Likelihood: TL).  Three additional EL children were not seen at either the 25- and 38-month visits and were excluded from all analyses presented here.  TL children were born full-term (37 – 42 weeks), except one born prior to 37 weeks, and were recruited via a volunteer database held at the Birkbeck College Centre for Brain and Cognitive Development.  Full details of EL and TL older sibling diagnostic status are shown in the Supplementary Materials.  Participants were administered a range of experimental, behavioural and cognitive tasks and interactive assessments of autistic symptomatology.  Parents completed a range of questionnaires and interviews relating to different aspects of early development.

*Measures*

Cognitive ability was assessed at each visit using the Mullen Scales of Early Learning (MSEL: Mullen, 1995), a standardised measure of early nonverbal reasoning, motor and language skills.  At 25 and 38 months autism symptomatology was assessed using the ADOS-G.  At the 3-year visit parents were interviewed using the Autism Diagnostic Interview – Revised (ADI-R: Lord, Rutter, & Le Couteur, 1994), a detailed interview covering early development and autism diagnostic features.  The Q-CHAT is a 25-item questionnaire with items relating to early social communication and play skills, and restricted, repetitive, stereotyped and sensory behaviours.  Each item has 5 options, based on relative frequency, intensity or typicality, and is scored 0 to 4, with higher scores relating to increased putative autism severity.  All item scores are summed to provide

a total score.  Parents were asked to complete the Q-CHAT prior to the 14-, 25- and 38-month

visits.  The AOSI is an examiner-led interactive assessment with an infant, who is usually sitting on

a caregiver's lap.  Tasks designed to elicit early social communication and play behaviours are

administered, and 19 items relating to autistic symptomatology are scored from 0 to 2 or 3, with

higher scores relating to increased putative autism severity.  Sixteen item scores are summed to

provide a total score.  The AOSI was administered at the 8- and 14-month visits.  At each visit

parents were asked about any concerns relating to the child's health or development.

*Participant diagnostic classification*

Following the final visit experienced researchers (GP, TC ) and members of the testing team

assigned a best estimate research diagnosis of DSM-5 autism (EL-Autism) or non-autism to each

EL child, informed by, but not dependent on, outcomes from the ADOS-G, ADI-R and Mullen

assessments as well as researcher observations from the assessment visits at 2 and 3 years of age.

Non-autistic EL children were classified as typically developing (EL-TD) or 'other' (EL-Other).

Children were assigned to the EL-Other group if they met the following criteria at the 3-year visit:

scoring above the autism spectrum threshold on the ADOS-G, and/or scoring above the autism

spectrum (Risi et al., 2006) threshold on the ADI-R, and/or scoring below –1.5 SD on one or more

of the Mullen *Early Learning Composite*, *Visual Reception*, *Receptive Language* or *Expressive*

*Language* subscales.

*Classifying parental concerns about their children's development*

At each visit parents were asked whether they had any concerns about their child's

development.  Any concerns expressed were recorded verbatim by a researcher.  Responses were

later classified independently by two raters, blind to group status, in relation to eleven pre-specified

categories: *No concerns*; *Medical* (including allergies and asthma); *Sleep*; *Language* (delayed,

unusual, stereotyped); *Social* (relating to children and/or adults); *Stereotyped behaviour* (repetitive,

rigid, unusual); *Behaviour* (overactive, problem); *Motor* (delayed, unusual); *Sensory* (interests,

aversion); *Autism spectrum*; *Other/General*.  Raters assigned a single category most representative

of the description given.  For the 47 cases where at least one rater coded a concern, inter-rater

agreement for classification was moderate (Cohen's $\kappa$=0.572, $p$<.001).  Inter-rater agreement

between each of the raters and GP's independent ratings were higher ($\kappa$=0.755, $N$=44 & $\kappa$=0.717,

$N$=46, both $p$<.001).  Discrepancies between the two blinded raters were resolved by adopting the

category assigned independently by GP.  For the purpose of this analysis, the *Medical*, *Sleep* and

*Other/General* categories – representing 6, 2, and 1 cases respectively – were equated to having no

concerns.

*Intervention trial supplementary analysis*

Fifty-three of the EL participants in this sample took part in a randomized controlled trial

(RCT) of a parent-mediated early intervention programme (Green et al., 2017), with the active

treatment period between the 8- and 14-month visits. Twenty-seven children were in the

intervention arm of the trial, and a further five children took part in a case series pilot of the

intervention (Green et al., 2013).  To investigate whether enrolment in the RCT or receiving the

intervention affected the main outcomes described above for each of the three measures we

conducted several supplementary analyses.

**Results**

*Diagnostic outcomes and participant characterisation*

Following the 3-year visit 17 EL children were identified as having autism (EL-Autism; 15

males: 2 females) as per the procedure described in the Method section above. Sixty-four EL

children were considered to be typically developing (EL-TD; 28 males: 36 females); 32 non-autistic

EL children were classified as not developing typically (EL-Other; 20 males: 12 females).  Of the

children in the EL-Other group, 12 met ADOS-G criteria only, 3 met both ADOS-G and ADI-R

criteria, 1 met ADI-R criteria only, 5 met both ADOS-G and MSEL criteria, 10 met MSEL criteria

only and 1 met ADOS-G, ADI-R and Mullen criteria.  Details of age, MSEL, AOSI, ADOS and

ADI-R scores at each visit are shown in Table 1.  Missing data for Q-CHAT Total, AOSI Total,

MSEL ELC, ADOS-2 CSS and ADI-R Toddler Total scores and ages at assessment were imputed using expectation maximisation procedures in SPSS version 25.

[TABLE 1 HERE]

*Q-CHAT scores at 14 months*

Q-CHAT total scores were negatively associated with concurrent Mullen ELC score ($r=-.357$, $p<.001$) but not with age at assessment ($r=-.110$, $p=.196$). There were significant between-group differences in Q-CHAT total scores at 14 months ($F(3,136)=4.403$, $p=.005$, partial $\eta^2=.089$). Bonferroni post-hoc tests showed that EL-Autism scores were higher than TL, EL-TD and EL-Other scores ($p=.019$, .005 and .010 respectively). There were no significant differences between the TL, EL-TD and EL-Other groups. Between-group differences were still significant when Mullen ELC scores were controlled for ($F(3,135)=2.850$, $p=.040$, partial $\eta^2=.060$). Mean Q-CHAT total scores by outcome group are shown in Fig. 1. A multivariate ANOVA including all 25 Q-CHAT items showed 9 items with between-group differences: *Response to joint attention* scores were higher in the EL-Autism group than in the three other groups and five items (*Response to name*, *Pointing to request*, *Pointing to share interest*, *Offering comfort* and *Gestures*) had higher scores for the EL-Autism group than for both the TL and EL-TD groups. Full details for individual items are shown in the Supplementary Materials.

[FIGURE 1 HERE]

*AOSI scores at 14 months*

AOSI total scores were negatively associated with concurrent Mullen ELC score ($r=-.429$, $p<.001$) but not with age at assessment ($r=-.090$, $p=.289$). There were significant between-group differences in AOSI total scores at 14 months ($F(3,136)=8.560$, $p<.001$, partial $\eta^2=.159$). Bonferroni post-hoc tests showed that both EL-Other and EL-Autism scores were higher than both TL and EL-TD scores ($p=.009$ and .025 for EL-Other and $p<.001$ and $=.001$ for EL-Autism respectively). There was no significant difference between EL-Other and EL-Autism scores ($p=.912$). Between-group differences remained significant when Mullen ELC scores were

controlled for ($F(3,135)=4.089$, $p=.008$, partial $\eta^2=.083$).  Mean AOSI total scores by outcome

group are shown in Fig. 2.  A multivariate ANOVA including all individual AOSI items showed

three items with between-group differences: *Respond to name* scores were higher in the EL-Autism

group than in the TL and EL-TD groups, *Transitions* scores were higher in the EL-Autism group

than in the EL-TD group and *Eye contact s*cores were higher in the EL-Other group than in the TL

group.  Full details for individual items are shown in the Supplementary Materials.

[FIGURE 2 HERE]

*Parental concerns at 14 months*

Thirty-three parents (23.6%) expressed concerns about their child at 14 months. Three

parents in the TL group (11.1%) and ten parents from each EL outcome group (representing 15.7%,

31.3% and 58.9% for the EL-TD, EL-Other and EL-Autism groups respectively) expressed

concerns.  There were no differences in concurrent Mullen ELC scores or ages at assessment

between the group about whom parents expressed concerns and those about whom parents did not

express concerns ($t=1.780$, $p=.077$).  Concerns were expressed about *Language development* ($n=5$),

*Stereotyped behaviours* ($n=2$), *Motor skills* ($n=5$), *General behaviour problems* ($n=20$) and *Autism*

*Spectrum Disorder* ($n=1$).  The numbers of parents from each group expressing concerns are shown

in Table 2.

[TABLE 2 HERE]

A Pearson $\chi^2$ test for the number of concerns showed significant between-group differences

($\chi^2=17.34$, $df=3$, $p=.001$).  There were significantly more concerns about children in the EL-Autism

group than about those in the TL and EL-TD groups ($\chi^2=11.41$, $p=.001$ and $\chi^2=13.48$, $p<.001$

respectively) and marginally but not significantly more than in the EL-Other group ($\chi^2=3.49$,

$p=.062$).

*Relationships between measures*

There was no association between AOSI total and Q-CHAT total scores ($r=.148$, $p=.081$).

These associations were also investigated within each outcome group, and none of these were

significant.  The results of these within-group tests are presented in the Supplementary Materials.

Children about whom parents had concerns had higher Q-CHAT total scores ($t$=-3.48, $p$=.001,

$d$=0.69) and higher AOSI total scores ($t$=-2.47, $p$=.015, $d$=0.48) than those of parents without

concerns.  Fig. 3 shows a scatterplot of AOSI total and Q-CHAT total scores, with the sample

means for these two measures, domain of parental concern and EL-Autism group indicated.  To

investigate whether looking at all three measures in combination was informative, we considered

three criteria: 1) scoring above the mean for the Q-CHAT; 2) scoring above the mean for the AOSI;

3) the presence of parental concern.  All 17 children in the EL-Autism group met at least one of

these criteria.  Twelve of these children met at least two criteria.  Across the other outcome groups

the numbers and percentages of children meeting at least one and at least two criteria in each group

was as follows: TL: 18 (66.7%) & 6 (22.2%); EL-TD: 39 (60.9%) & 16 (25%); EL-Other: 27

(84.4%) & 14 (43.8%).

Scores from individual items relating to the same or similar concepts from the AOSI and the

Q-CHAT were compared.  None of the eleven comparisons tested showed significant associations

(with significance set to $p$<.01 to account for multiple comparisons).  Details of these comparisons

are shown in the Supplementary Materials.

*Intervention trial supplementary analysis*

For Q-CHAT total and AOSI total scores we conducted univariate ANOVAs to test for main

effects of RCT participation or receiving intervention, with binary variables representing

participation in the RCT and receiving intervention as the independent variables.  We then repeated

the univariate ANOVAs with diagnostic outcome group as the independent variable and the RCT

and intervention variables as covariates.  There were no main effects of either RCT or intervention

variable on Q-CHAT or AOSI total scores (all $F$<1.8).  Controlling for RCT participation and

receiving intervention, between-group differences remained significant for both Q-CHAT and

AOSI total scores ($F$(3,134)=4.447, $p$=.005, partial $\eta^2$=.091 and $F$(3,134)=8.366, $p$<.001, partial

$\eta^2$=.158 respectively).  For the expression of parent concerns, we conducted Pearson $\chi^2$ tests for the

number of concerns across RCT participation and intervention groups. In both cases there were no significant differences (RCT: $\chi^2$=2.07, $df$=1, $p$=.150; intervention: $\chi^2$=1.36, $df$=1, $p$=.244). Follow-up analyses were done by first excluding participants who took part in the RCT and then those who received intervention. In each case the pattern of results reported for the main findings above were the same (i.e. there were significantly more concerns reported by parents of children later diagnosed with autism than those in the TL and EL-TD groups, but no significant differences between the EL-Autism and EL-Other groups, despite relatively large differences in proportions of expressed concerns – not in RCT: 54.5% vs 23.5%; no intervention: 50.0% vs 30.4%). Full details are reported in the Supplementary Materials.

[FIGURE 3 HERE]

## Discussion

This is the first study to investigate the relative utility of three different concurrent sources of information about later autism diagnosis in children in the early part of their second year of life. Q-CHAT total scores at 14 months were significantly higher for the children later diagnosed with autism, AOSI total scores distinguished children with autism from those who were developing typically, but not from those with apparent non-autism developmental difficulties. Parents of children subsequently diagnosed with autism were more likely to report concerns about their child's development than parents of children with no apparent later developmental difficulties and almost twice as likely to report concerns compared to parents of children who subsequently had developmental difficulties but not autism, although this difference was not statistically significant due to the relatively modest sample. The expression of parental concerns at 14 months was associated both with higher Q-CHAT and AOSI total scores.

Individual items from the two instruments that were higher in the group later diagnosed with autism were mostly related to social communication and interaction skills, particularly *Response to joint attention, Gestures*, *Pointing to request*, *Pointing to share interest*, *Offering comfort* and *Response to name* from the Q-CHAT and *Respond to name* from the AOSI. In contrast, the

concerns expressed by seven of the ten parents whose children were subsequently diagnosed with autism were about broad behavioural issues rather than about aspects of social interaction, language or communication.  Examples of these behavioural concerns include "Headbutting when upset, or if you take him away from something he wants to do – can hurt himself too", "…definitely going through the terrible two's – throws things all the time and has no sense of danger" and "… gets very upset when he can't see his mum".  Only five of all parents expressed concerns about unusual or delayed language and just two were concerned about unusual, repetitive or stereotyped behaviour. The one child whose parent was explicitly concerned about autism subsequently appeared to be developing typically.  However, whilst parents did not *explicitly* identify concerns about social communication and interaction it does appear that they were able *implicitly* to recognise differences in their children's early social communication skills when endorsing scores on relevant items on the Q-CHAT.

Our findings regarding the Q-CHAT broadly correspond to those reported by Sacrey, Bryson et al. (2018) in relation to their use of the 26-item APSI parent-report questionnaire at 12 months.  They found that APSI total scores were higher in children with ASD outcomes in their EL sample compared to both EL non-ASD and TL groups, and all seven individual items that exclusively distinguished the ASD group from the other two groups were reflective of social communication and interaction skills (i.e. *Respond to name*, *Anticipatory social response*, *Eye contact*, *Reciprocal social smile*, *Reactivity*, *Cuddle with you*, and *Share interests with others*). Furthermore, the six items from our study that distinguished children subsequently diagnosed with autism from those in the TL and EL-TD groups all appear in the short version of the Q-CHAT presented by Allison, Auyeung and Baron-Cohen (2012) that includes the ten items found to have the highest positive predictive values.  The *Respond to name* item was the strongest indicator of autism outcome from the AOSI in our study – a finding that has been reported in other EL studies where the AOSI has been used between 12 and 18 months (e.g. Gammer, et al., 2015; Sacrey, Zwaigenbaum, et al., 2018) and which confirms the importance of measuring this behaviour in

toddlers for whom autism is being considered.  Overall, our findings from the AOSI showing differences in early emerging autism symptomatology at 14 months confirm findings from previous studies about early behavioural manifestations of autism being detectable from soon after the child's first birthday using semi-structured examiner-led instruments (e.g. Brian, et al., 2008; Elison, et al., 2014; Gammer, et al., 2015; Ozonoff, et al., 2010).

With regard to the expression of parental concerns, our findings are not directly comparable with those reported by Sacrey et al. (2015) in that they had a much larger sample of children later diagnosed with autism, their data were based on a semi-structured interview with pre-determined aspects of development and concerns about more than one area were potentially counted for each participant at each time point.  However, there is a partial concordance with our findings: Sacrey and colleagues (2015) report that at both 12 and 15 months the overall number of concerns were higher for the children later diagnosed with ASD than in both of the non-ASD comparison groups, and around 30% of parents of children in the ASD group expressed concerns about general behavioural problems.  In contrast to our findings Sacrey et al. (2015) report that both sensory and communication issues distinguished the ASD outcome group from the non-ASD groups at every time point between six and 24 months.

Measures pertaining to similar constructs ascertained via different methods – direct interactive assessment with a child versus parental interview, for example – often have poor agreement, even when two measures have identical items (e.g. Sacrey, Zwaigenbaum, et al., 2018). Even though instruments such as the AOSI and the ADOS are designed to elicit behaviours known to be symptomatic of autism, children who display these in their everyday behaviour may not exhibit them within a relatively brief assessment.  Their parents, however, may be fully aware of, and report, the presence of these behaviours, such as mannerisms, echolalic speech, unusual interests, and so on.  Alternatively, in relation to specific aspects of early social communication skills such as responding to joint attention, many parents may not be aware of this as a behaviour of interest and therefore may not report the presence or absence of this behaviour reliably, yet within

the context of an examiner-administered semi-structured assessment this may be a target behaviour with a relatively observable response.  It is not unexpected, therefore, that items from our two instruments relating to identical or overlapping concepts did not correlate, and that the three measures reported here showed differences in terms of their ability to discriminate later autism diagnostic status.

*Limitations*

The primary limitation of this study is that data are drawn from a prospective longitudinal study of young children at elevated likelihood of autism diagnosis, and therefore the findings may not generalise to a community-based context (Sacrey, et al., 2017).  One consequence of the study design is that the majority of parents have an older child with autism, which is likely to influence responses to questions about their child's early development as well as their perception of and attitude towards putative problem behaviours and difficulties in their young child.  Even though parents who have older children with autism are inevitably better informed about the emerging signs of autism than most parents of young children, it is not clear to what extent or in what direction the reporting of concerns will be affected – they may be 'hypervigilant' to every potential manifestation associated with autism, or their 'calibration' of behaviours in comparison to potential typical development may be such that they have a tendency to under-report autistic-like behavioural symptoms.  A second consequence of the study design is that even the children assigned a diagnosis of autism at 3 years were relatively low in terms of their autism symptomatology, particularly in relation to their scores on the ADOS: the EL-Autism group ADOS-2 Calibrated Severity Score mean of 3.8 is lower than the lower cut-off score of 4 that corresponds to an ADOS-2 classification of autism spectrum.  In spite of this relatively low severity, however, the instrument scores and expression of concerns still distinguish the children with autism from their non-autistic counterparts to some extent.  We might assume that were it possible to recruit a sample of children with more profound levels of autism severity, these measures would distinguish children with autism more

strongly.  A final limitation relating to the study design is the relatively small sample, which contains just 17 children diagnosed with autism.

Our additional analyses relating to the children who took part in the early intervention trial described in Green et al. (2017) demonstrate that neither participation in the trial nor being in receipt of the intervention had a significant impact on the pattern of findings relating to the sample as a whole.  Given that the active intervention phase of the trial ended shortly before the children were assessed at 14 months, it is not unlikely that the scores on either the AOSI or the Q-CHAT, or the expression of concerns about a child's development, would have been influenced to some extent by participation in the intervention programme.  Indeed, Green et al. (2017) report non-significant benefits in AOSI scores at this visit for the children in the intervention arm of the trial, although no claims for effects relating to longer term diagnostic outcome are made.  It is beyond the scope of this report to further analyse potential treatment effects relating to the trial.

We do not have alternative measures of either parent-reported or examiner-observed autistic symptomatology at 14 months (the M-CHAT or the Toddler Module of the ADOS, for example) with which to make direct comparisons with our findings from the Q-CHAT and the AOSI.  The measures investigated here show high levels of variance, so in conjunction with the highly heterogenous nature of autism, these findings can only be interpreted at the group level and are not readily interpretable for individual children.  Professionals considering the likelihood of autism diagnosis for a young child should be cautious when presented with information from a single source, whether that be a semi-structured assessment, parental questionnaire or the expression of parental concerns.

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*Table 1.* Age, Mullen Early Learning Composite, Autism Diagnostic Observation Schedule and

Autism Diagnostic Interview – Revised scores at 14 and 38 months: mean (SD) and between-group

differences

| | TL[1] (*n*=27) | EL-TD[2] (*n*=64) | EL-Other[3] (*n*=32) | EL-Aut[4] (*n*=17) | |
|---|---|---|---|---|---|
| Age at 14-month visit | 15.0 (0.90) | 14.8 (0.94) | 14.9 (0.95) | 14.8 (0.95) | $F(3,136)=0.417$, $p=.741$, partial $\eta^2=0.009$ |
| Age at 38-month visit | 38.7 (1.56) | 38.9 (1.44) | 38.7 (1.87) | 38.6 (1.66) | $F(3,136)=0.299$, $p=.826$, partial $\eta^2=0.007$ |
| Mullen ELC* at 14 months | 102.6[a,b] (14.43) | 98.2[c] (12.48) | 91.5[a] (15.84) | 85.5[b,c] (12.81) | $F(3,136)=7.053$, $p<.001$, partial $\eta^2=0.135$ |
| Mullen ELC* at 38 months | 118.5[a,b] (15.13) | 114.4[c,d] (15.80) | 87.4[a,c] (25.59) | 86.0[b,d] (27.77) | $F(3,136)=22.130$, $p<.001$, partial $\eta^2=0.328$ |
| ADOS-2 CSS[§] at 38 months | 2.0[a,b] (1.54) | 1.3[c,d] (0.54) | 4.1[a,c] (2.31) | 3.8[b,d] (3.32) | $F(3,136)=22.24$, $p<.001$, partial $\eta^2=0.329$ |
| ADI-R[†] Toddler Total at 38 months | 1.0[a,b] (1.38) | 1.8[c,d] (2.27) | 4.0[a,c,e] (5.26) | 16.2[b,d,e] (6.65) | $F(3,136)=72.522$, $p<.001$, partial $\eta^2=0.615$ |

[1] Typical Likelihood
[2] Elevated Likelihood – Typical Development
[3] Elevated Likelihood – Other
[4] Elevated Likelihood – Autism
* Early Learning Composite;
§ Autism Diagnostic Observation Schedule – Second edition Calibrated Severity Score (NB ADOS-2 CSS scores were calculated using ADOS-G item scores);
† Autism Diagnostic Interview – Revised;
Superscript letters indicate between-group differences at *p*<.05

*Table 2*. Numbers of parents expressing concerns at 14 months

| | TL[1] (*n*=27) | EL-TD[2] (*n*=64) | EL-Other[3] (*n*=32) | EL-Autism[4] (*n*=17) | All (*n*=140) |
|---|---|---|---|---|---|
| No concern | 24 | 54 | 22 | 7 | 107 |
| Language development | 0 | 2 | 2 | 1 | 5 |
| Stereotyped behaviour | 0 | 1 | 0 | 1 | 2 |
| Motor skills | 1 | 1 | 2 | 1 | 5 |
| Behaviour | 2 | 5 | 6 | 7 | 20 |
| ASD | 0 | 1 | 0 | 0 | 1 |
| Total concerns (%) | 3 (11.1%) | 10 (15.7%) | 10 (31.3%) | 10 (58.9%) | 33 (23.6%) |

[1] Typical Likelihood
[2] Elevated Likelihood – Typical Development
[3] Elevated Likelihood – Other
[4] Elevated Likelihood – Autism

Figure Captions

*Figure 1*.  Mean Q-CHAT total score by outcome group

*Figure 2*.  Mean AOSI total score by outcome group

*Figure 3*. Scatterplot of Q-CHAT total x AOSI total score, showing domain of parental concern and EL-Autism group

Figure 1. Top
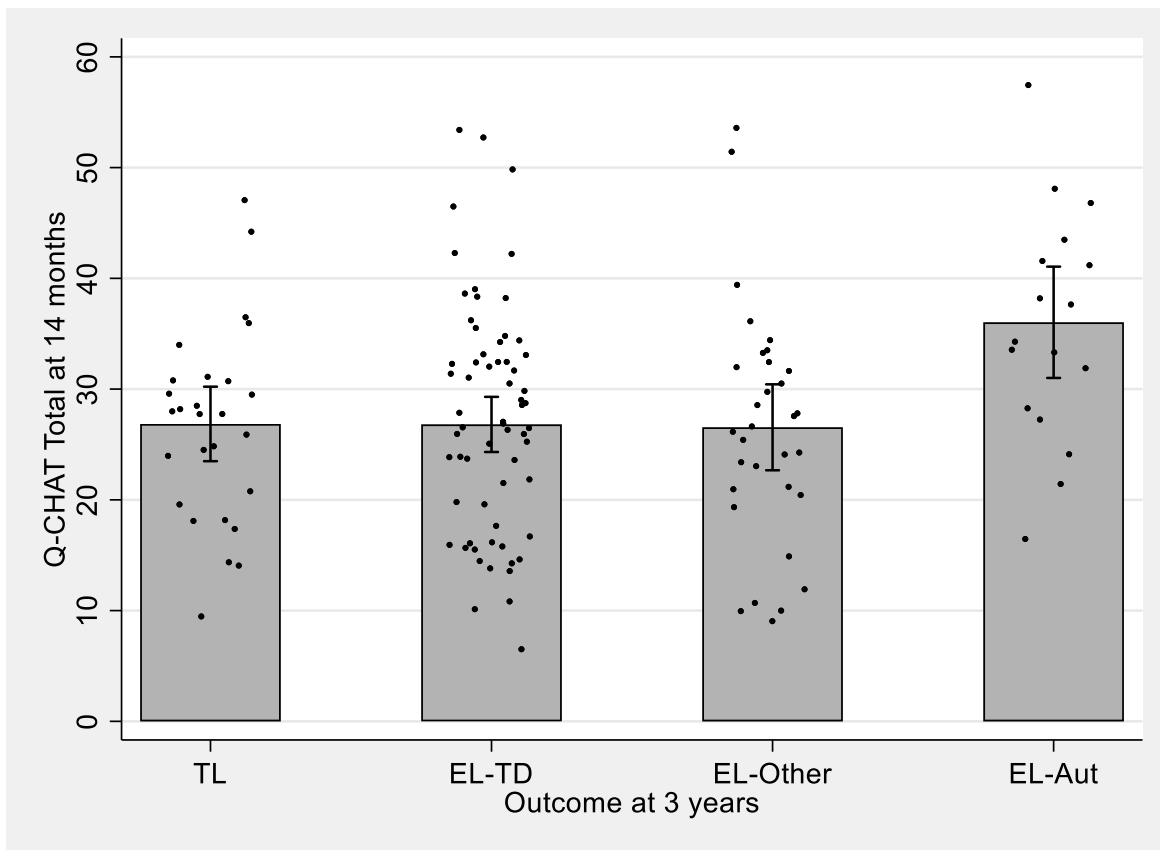


Key:
Q-CHAT: Quantitative Checklist for Autism in Toddlers
TL: Typical Likelihood
EL-TD: Elevated Likelihood – Typical Development
EL-Other: Elevated Likelihood – Other
EL-Aut: Elevated Likelihood – Autism

Figure 2. Top
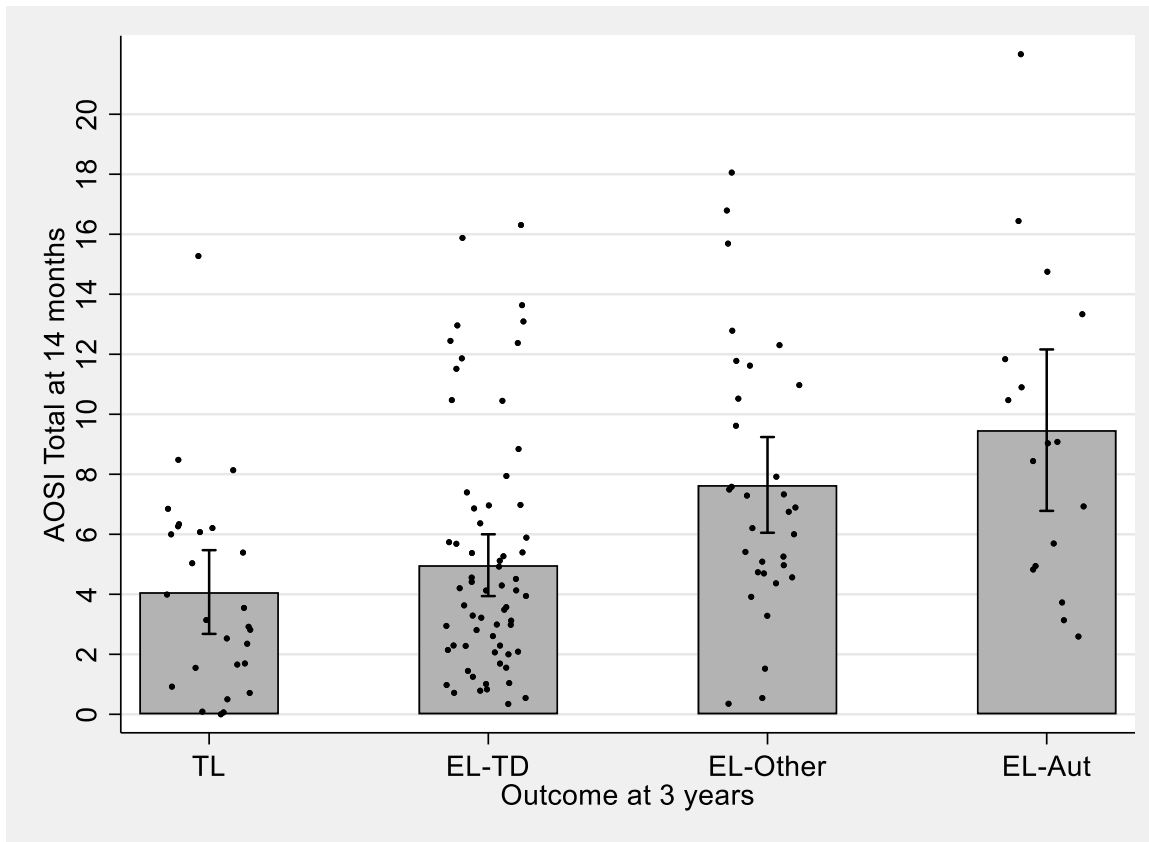


Key:
AOSI: Autism Observation Scale for Infants
TL: Typical Likelihood
EL-TD: Elevated Likelihood – Typical Development
EL-Other: Elevated Likelihood – Other
EL-Aut: Elevated Likelihood – Autism

Figure 3. Top
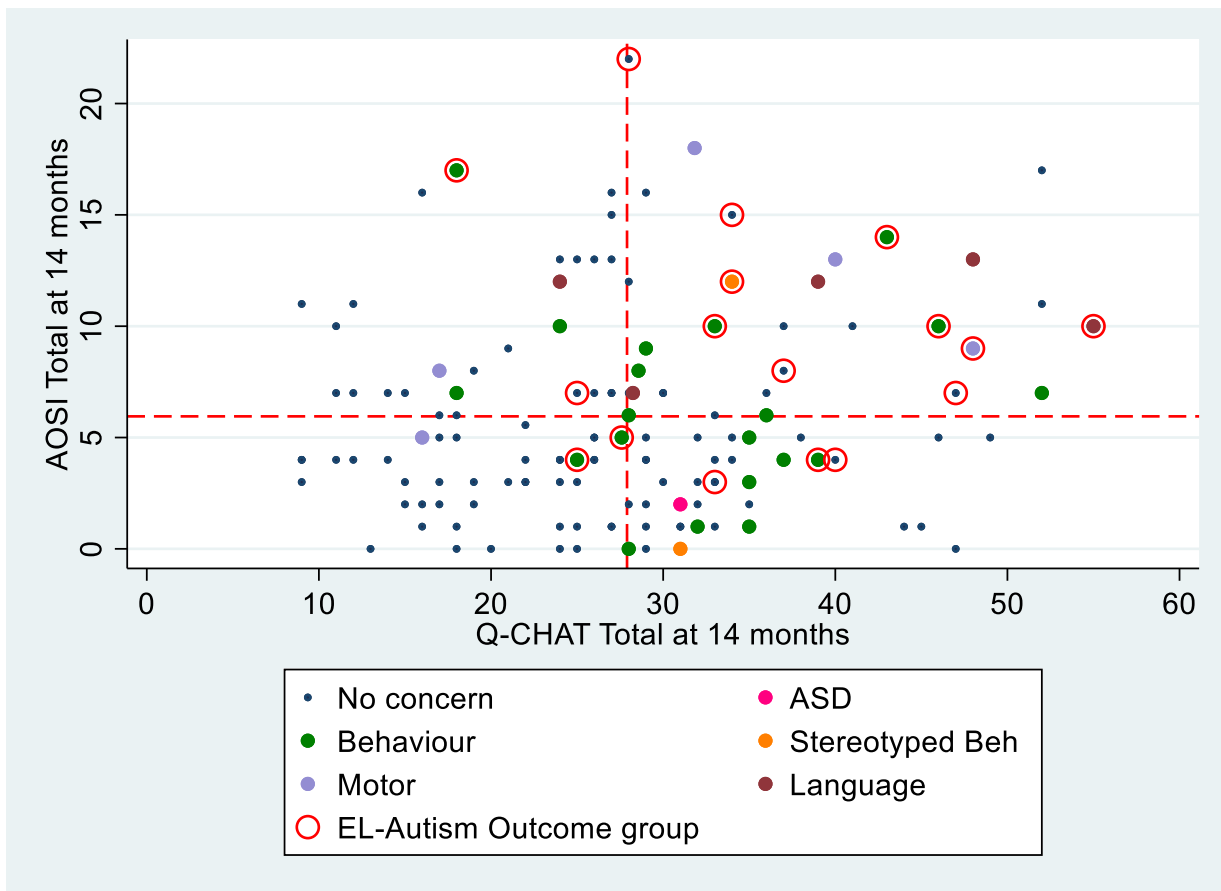


Red dotted lines show mean scores for AOSI (5.95) and Q-CHAT (27.9)
Key:
AOSI: Autism Observation Scale for Infants
Q-CHAT: Quantitative Checklist for Autism in Toddlers

Diagnostic status of participants' older siblings

For all 113 children with an older sibling with a community clinical diagnosis of ASD (hereafter probands) parents completed the Development and Well-Being Assessment (DAWBA: Goodman, Ford, Richards, Gatward, & Meltzer, 2000) and/or the Social Communication Questionnaire (SCQ: Rutter, Bailey, & Lord, 2003).  Eighty-nine probands met criteria on both the DAWBA and SCQ.  Seven children scored below threshold on the SCQ and one was missing the SCQ, but no exclusions were made due to meeting threshold on the DAWBA and expert opinion. For 16 probands, confirmation of local clinical diagnosis was only available via the SCQ. Screening for possible ASD in the older siblings of the typical likelihood (TL) infants was undertaken using the SCQ, with no child scoring above the instrument cut-off for ASD ($\geq$15).  For one TL child the SCQ was missing. Medical history review confirmed a lack of ASD within first-degree relatives.

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SM Table 1.

Individual Q-CHAT* Items and contribution to between-group differences. Items with p<.05 shown in bold

| Item | $F(3,132)$ | $p$ | Partial $\eta^2$ | Post-hoc differences |
|---|---|---|---|---|
| **Response to Name** | **3.06** | **.031** | **0.065** | **EL-Aut > TL & EL-TD ($p$=.029 & $p$=.048)** |
| Eye Contact | 1.54 | .208 | 0.034 | |
| Lining Up Objects | 1.01 | .130 | 0.042 | |
| **Intelligibility** | **2.72** | **.047** | **0.058** | NB – no individual comparisons significant at p<.05 |
| **Pointing to Request** | **5.09** | **.002** | **0.104** | **EL-Aut > TL & EL-TD ($p$=.002 & $p$=.012)** |
| **Pointing to Share Interest** | **4.44** | **.005** | **0.092** | **EL-Aut > TL & EL-TD ($p$=.003 & $p$=.019)** |
| Staring at Spinning Objects | 1.22 | .306 | 0.027 | |
| Number of Words | 2.58 | .056 | 0.055 | |
| **Pretend Play** | **3.29** | **.023** | **0.070** | **EL-Aut > TL ($p$=.021)** |
| **Response to Joint Attention** | **4.41** | **.005** | **0.091** | **EL-Aut > TL, EL-TD & EL-Other ($p$=.007, $p$=.032 & $p$=.009)** |
| **Unusual Sensory Interests** | **3.42** | **.019** | **0.072** | **TL > EL-TD & EL-Other ($p$=.039 & $p$=.027)** |
| Use of Other's Hand as a Tool | 1.53 | .209 | 0.034 | |
| Tiptoe Walking | 2.21 | .090 | 0.048 | |
| Flexibility | 0.64 | .594 | 0.014 | |
| **Offering Comfort** | **3.29** | **.023** | **0.070** | **EL-Aut > TL & EL-TD ($p$=.022 & $p$=.037)** |
| Repetitive Behaviour | 1.52 | .211 | 0.033 | |
| Typicality of First Words | 0.98 | .404 | 0.022 | |
| **Echolalia** | **3.44** | **.019** | **0.072** | **EL-Other > EL-Aut ($p$=.047)** |
| **Gestures** | **5.16** | **.002** | **0.105** | **EL-Aut > TL & EL-TD ($p$=.001 & $p$=.014)** |
| Mannerisms | 0.27 | .850 | 0.006 | |
| Social Referencing | 1.04 | .376 | 0.023 | |
| Intense Interest in Objects | 1.18 | .321 | 0.026 | |
| Repetitive Use of Objects | 0.36 | .781 | 0.008 | |
| Oversensitivity to Noise | 1.16 | .328 | 0.026 | |
| Staring at Nothing | 0.70 | .553 | 0.016 | |

* Quantitative Checklist for Autism in Toddlers

SM Table 2.

Individual AOSI* Items and contribution to between-group differences. Items with p<.05 shown in bold

| Item | $F_{(3,136)}$ | $p$ | Partial $\eta^2$ | Post-hoc differences |
|---|---|---|---|---|
| Visual Tracking | 1.58 | .197 | 0.034 | |
| Disengagement of Attention | 0.61 | .609 | 0.013 | |
| **Respond to Name** | **8.12** | **<.001** | **0.152** | **EL-Aut > TL, EL-TD & EL-Other (*p*=.001, <.001 & =.049, resp.)** |
| Differential Responses to Facial Expressions | 1.27 | .288 | 0.027 | |
| Anticipatory Responses (to Peekaboo) | 1.34 | .264 | 0.029 | |
| Imitation of Actions | 0.47 | .705 | 0.010 | |
| Social Babbling | 2.19 | .092 | 0.046 | |
| **Eye Contact** | **3.83** | **<.001** | **0.078** | **EL-Other > TL (*p*=.011)** |
| Reciprocal Social Smile | 2.29 | .081 | 0.048 | |
| Coordination of Eye Gaze & Action | 2.17 | .094 | 0.046 | |
| Reactivity | 1.54 | .208 | 0.033 | |
| Social Interest & Shared Affect | 2.06 | .108 | 0.044 | |
| **Transitions** | **3.66** | **.014** | **0.075** | **EL-Aut > EL-TD (*p*=.009)** |
| Motor Control & Behaviour | 1.32 | .272 | 0.028 | |
| Atypical Motor Behaviours | 2.57 | .057 | 0.054 | |
| Atypical Sensory Behaviours | 2.04 | .112 | 0.043 | |

*Autism Observation Scale for Infants

SM Table 3

**Results of within-group correlations between Q-CHAT[1] total and AOSI[2] total scores**

| Group | Pearson's *r* | *p* | *n* |
|---|---|---|---|
| Typical Likelihood | -.039 | .845 | 27 |
| Elevated Likelihood – Typically Developing | .139 | .274 | 64 |
| Elevated Likelihood – Other | .157 | .390 | 32 |
| Elevated Likelihood – Autism | -.165 | .528 | 17 |

Key:
1 Quantitative Checklist for Autism in Toddlers
2 Autism Observation Scale for Infants

SM Table 4

**Correlations between individual items from the Q-CHAT and AOSI measuring similar constructs**
(All *n*=136)

| Q-CHAT[1] item | AOSI[2] item | Spearman's rho | *p* |
|---|---|---|---|
| Response to name | Orientation to name | .089 | .303 |
| Eye contact | Eye contact | -.083 | .335 |
| Flexibility | Transitions | .113 | .190 |
| Response to joint attention | Disengagement of attention | -.042 | .630 |
| Social referencing | Social referencing | .010 | .909 |
| Staring at spinning objects | Atypical sensory behaviours | -.033 | .704 |
| Unusual sensory interests | Atypical sensory behaviours | .017 | .848 |
| Oversensitivity to noise | Atypical sensory behaviours | .080 | .353 |
| Staring at nothing | Atypical sensory behaviours | .197 | .022 |
| Mannerisms | Atypical motor behaviours | -.004 | .963 |
| Repetitive behaviour | Atypical motor behaviours | -.005 | .957 |

Key:
1 Quantitative Checklist for Autism in Toddlers
2 Autism Observation Scale for Infants

Intervention trial supplementary analyses

SM Table 5

**Numbers of children participating in Randomised Control Trial (RCT)**

|  |  | In RCT | Not in RCT | Total |
|---|---|---|---|---|
| Outcome at 3 yrs | TL[1] | 0 | 27 | 27 |
|  | EL-TD[2] | 32 | 32 | 64 |
|  | EL-Other[3] | 15 | 17 | 32 |
|  | EL-Autism[4] | 6 | 11 | 17 |
|  | Total | 53 | 87 | 140 |

Key:

[1] Typical Likelihood

[2] Elevated Likelihood – Typical Development

[3] Elevated Likelihood – Other

[4] Elevated Likelihood – Autism

SM Table 6

**Numbers and percentages of concerns expressed at 14 months by participation in Randomised Control Trial (RCT)**

| RCT participation | TL[1] Not RCT | EL-TD[2] In RCT | EL-TD[2] Not RCT | EL-Other[3] In RCT | EL-Other[3] Not RCT | EL-Autism[4] In RCT | EL-Autism[4] Not RCT | Total In RCT | Total Not RCT |
|---|---|---|---|---|---|---|---|---|---|
| No Concern | 24 | 26 | 28 | 9 | 13 | 2 | 5 | 37 | 70 |
| Concern | 3 | 6 | 4 | 6 | 4 | 4 | 6 | 16 | 17 |
| Percentage concerns | 11.1 | 18.3 | 12.5 | 40.0 | 23.5 | 66.7 | 54.5 | 30.2 | 19.5 |

Key:

1 Typical Likelihood

[2] Elevated Likelihood – Typical Development

[3] Elevated Likelihood – Other

[4] Elevated Likelihood – Autism

SM Table 7

**Numbers of children in Randomised Control Trial (RCT) Intervention group or case series**

| | | Intervention | No intervention | Total |
|---|---|---|---|---|
| Outcome at 3 yrs | TL[1] | 0 | 27 | 27 |
| | EL-TD[2] | 18 | 46 | 64 |
| | EL-Other[3] | 9 | 23 | 32 |
| | EL-Autism[4] | 5 | 12 | 17 |
| | Total | 32 | 108 | 140 |

Key:
1 Typical Likelihood
[2] Elevated Likelihood – Typical Development
[3] Elevated Likelihood – Other
[4] Elevated Likelihood – Autism

SM Table 8

**Numbers and percentages of concerns expressed at 14 months by participation in Randomised Control Trial (RCT) / case series intervention**

| | TL[1] | EL-TD[2] | | EL-Other[3] | | EL-Autism[4] | | Total | |
|---|---|---|---|---|---|---|---|---|---|
| Intervention | No | Yes | No | Yes | No | Yes | No | Yes | No |
| No Concern | 24 | 15 | 39 | 6 | 16 | 1 | 6 | 22 | 85 |
| Concern | 3 | 3 | 7 | 3 | 7 | 4 | 6 | 10 | 23 |
| Percentage concerns | 11.1 | 16.7 | 15.2 | 33.3 | 30.4 | 80.0 | 50.0 | 30.2 | 21.3 |

Key:
[1] Typical Likelihood
[2] Elevated Likelihood – Typical Development
[3] Elevated Likelihood – Other
[4] Elevated Likelihood – Autism