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Testing Two Screening Instruments for Autism Spectrum Disorder in UK Community Child Health Services

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Short title: Screening for ASD

Abbreviations: ASD – autism spectrum disorders; ADI-R – Autism Diagnostic Interview-Revised; ADOS-G – Autism Diagnostic Observation Schedule-Generic; AUC – area under the curve; M-CHAT – Modified Checklist for Autism in Toddlers; NPV = Negative Predictive Value; PPV – positive predictive value; SCQ – Social Communication Questionnaire; Se – sensitivity; Sp – specificity.

Key Words: autism spectrum disorders, screening, diagnosis, accuracy, sensitivity, specificity

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Contributor's Statement: Tony Charman, Gillian Baird, Emily Simonoff, Andrew Pickles, Ajay Sharma and Tony O'Sullivan conceived and designed the study. Susie Chandler, Andrew Pickles and Tony Charman analysed and interpreted the data. Tony Charman drafted the article and Gillian Baird, Emily Simonoff, Andrew Pickles, Abi Davison-Jenkins, Susie Chandler, Ajay Sharma and Tony O'Sullivan revised it critically for important intellectual content. Tony Charman and Susie Chandler had full access to all of the data (including statistical reports and tables) in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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What's Known on This Subject:

- Screening instruments to identify ASD in preschool children have not previously been evaluated in a large referred UK community sample.

What This Study Adds:

- The SCQ and M-CHAT screens performed only moderately well in accurately identifying cases of ASD in children referred to community child health services.

- Screening information in isolation should not be used to decide whether or not to make a referral for specialised ASD assessment.

ABSTRACT

Aim: Test the accuracy of two screening instruments (M-CHAT: Modified Checklist for Autism in Toddlers; SCQ: Social Communication Questionnaire) for autism spectrum disorders (ASD) in UK community child health services. A two-stage screening and in-depth assessment procedure, combined with sampling stratification and statistical weighting, allowed the accuracy of the screens to be estimated in the entire population of referred children.

Methods: All referrals of children aged 18-48 months to community paediatric and speech and language therapy services in two London districts over 12 months. Parents of 808 children were approached; screen data were obtained on 543 children (67.2%). A stratified subsample of 120 children received an in-depth assessment for ICD-10 ASD. Community clinician judgement of likely ASD was available on 98 of the 120 children.

Results: The sensitivity and specificity were 64% (95% confidence intervals 51%, 80%) and 75% (63%, 85%) for the SCQ; and 82% (72%, 92%) and 50% (33%, 64%) for the M-CHAT. The area under the curve (AUC) did not differ between the two screens. Clinician judgement of likely ASD at the initial appointment was as accurate as both screens. The screens did not perform well either to confirm preliminary clinical judgment to refer (in series), nor as an alternative indicator for referral (in parallel).

Interpretation: Whilst screens may provide useful information their accuracy is moderate. Screening information in isolation should not be used to make referral decisions regarding specialised ASD assessment.

[Word count = 235]

INTRODUCTION

Autism spectrum disorders (ASDs) are neurodevelopmental conditions that significantly impact on the individual, their family and society[1,2]. Recent prevalence estimates suggest that around 1% of children and young people have ASD[3,4]. There is an emerging, though still limited, evidence-base for the effectiveness of early social-communication and behavioural interventions[5,6]. Screening instruments have been developed to identify children at a young age[7]. Three have been tested in general population screening studies. The Checklist for Autism in Toddlers (CHAT)[8] was found to have low sensitivity (38%) in a population of 18 month old children. The Early Screening of Autistic Traits (ESAT)[9] had low positive predictive value (PPV) for ASD (25%) at 14 months of age. In two recent studies in populations of 16 to 30 month old children using a 2-stage screen and re-screen design the Modified-CHAT (M-CHAT)[10] and the M-CHAT-Revised with Follow-up (M-CHAT-R/F)[11] were found to have moderate PPV (54% and 48%, respectively). However, in these latter studies as only screen positives were followed-up sensitivity remains to be established.

In samples of young children referred with developmental concerns, where the prevalence of ASD is higher, screens have higher PPV. Snow and Lecavalier[12] found the M-CHAT had a PPV of 79% in 18 to 48 month olds referred for possible ASD. The Social Communication Question (SCQ)[13] has also been tested as a screen in referred samples of 2 to 6 year old children and found to have moderate sensitivity (70%[12] and 60%[14]) and specificity (52%[12] and 70%[14]). In the subsample of children on whom both screens were completed (N=39) both the M-CHAT and SCQ had PPVs around 70%. Eaves and colleagues reported similar PPVs (~65%) for the M-CHAT and SCQ in separate subsamples of children referred to an ASD specialist clinic (age 2-to-3-years and 4-to-6-years, respectively)[15]. Another study of children referred for a clinical assessment between 20 and 40 months of age following positive score

on the ESAT screen reported a PPV of 79%[16]. However, in all of these studies the specificity of both the M-CHAT (used in a one-stage manner) and the SCQ has been low (50% or lower), meaning that reliance on screening information to trigger a referral for specialist assessment could result in many screen 'false negatives'.

The American Academy of Pediatrics (AAP) has recommended routine use of screens (including the CHAT and M-CHAT) at well-child checks[17]. In contrast, the UK NICE guidelines[18] and the UK National Screening Committee[19] concluded that there was insufficient evidence to recommend any ASD specific screening instrument. The threshold set by NICE was for a sensitivity and specificity of at least 80% with a lower confidence interval 70% or greater. In line with this, Al-Qabandi and colleagues[20] have criticised the AAP recommendation for universal screening on the basis of the limited research evidence. There is evidence from both the USA[21] and the UK[22] that in many communities age of diagnosis is highly variable and in some cases unacceptably late. If there were evidence that screening instruments might help identify those at greatest risk of ASD when concerns are first raised, this might aid prompt referral and earlier diagnosis. In some areas the wait for specialist autism assessments is considerable and reducing inaccurate referral via screening could help remove this 'bottleneck' to the benefit of children, parents and local services[23]. However, if the sensitivity of screening instruments is low, there is a cost to children and families in potential delayed assessment and diagnosis, as well as the distress of unnecessary referrals.

The present study aimed to test the accuracy of the most widely studied screening instruments – the M-CHAT and the SCQ – in community child health services in an urban setting in the UK. To test whether ASD screens might improve the accuracy of referrals to specialist ASD diagnostic teams we independently collected screening information on preschool children who had been

referred to community child health and speech and language therapy services. On a stratified subsample we conducted independent diagnostic assessments. In addition, we collected routine clinician judgement at the initial appointment (blinded to screening information) about likely ASD, so that we could compare whether combining clinical judgement with screening information improved the accuracy of referral.

METHOD

Ethical approval: The Guy's Hospital Research Ethics Committee approved the study (03/08/07). Informed consent was obtained from all parents/carers.

A STARD checklist is included as Appendix 1.

The Social Communication Question (SCQ)[13] and the Modified Checklist for Autism in Toddlers (M-CHAT)[11] are questionnaires that ask parents to endorse (Yes/No) symptom descriptions that cover the full range of behaviours described in the classification systems (SCQ 40 items, M-CHAT 23 items). The established cut off on the SCQ for ASD is a score of $\geq$15[13]. The M-CHAT has 2 high/low risk thresholds: scoring on 2 or more of 6 'critical' items and scoring $\geq$3 overall[11].

Screening stage

In the UK when parents or primary care practitioners are concerned about a child's development, the child is referred to community child health services, including paediatrician-led child development teams (CDTs) and speech and language therapy teams (SALTs). If ASD is suspected then it is common for a referral to be made to a more specialist, often multidisciplinary, paediatric-led ASD diagnostic team. Across a 12 month period (September 2004 to September 2005), all parents of children referred to community

services for any developmental problem in 2 inner London NHS Trusts between the ages of 18 and 48 months (mean 32.9, SD 8.0) were approached by the research team, independently of the clinical services.

Following the initial appointment clinicians (paediatricians, speech and language therapists) were asked to complete a checklist of concerns about a possible ASD and/or whether a referral had been initiated for an ASD assessment (both districts had specialist multi-disciplinary ASD diagnostic teams). When clinicians had not completed the checklist the research team accessed the file and recorded whether an ASD concern and/or referral had been noted. The research team independently collected the screening information, which was not available to the community clinicians. The research diagnostic process (described below) was conducted independently of the local community assessments and was blind to the screening information and the community clinical judgement of likely ASD.

The in-depth measures consisted of the Autism Diagnostic Interview-Revised (ADI-R)[24] and the Autism Diagnostic Observation Schedule-Generic (ADOS-G)[25] as the core assessments of autism. In addition, IQ was assessed using the Mullen Scales of Early Learning Scales (MSEL)[26], language using the Preschool Language Scale (PLS)[27], and adaptive behaviour using the Vineland Adaptive Behaviour Scales (VABS)[28].

The ADI-R is an investigator-led parent interview that has an established cut-off for childhood autism[24] and a recommended cut off for broader ASD[29]. The ADOS-G is a structured, play-based experimenter-child observation that generates an algorithm score with established cut-offs both for ASD[25]. In the current study 58 children completed Module 1 (for non-verbal children and children with single words) and 62 Module 2 (for children with phrase speech).

Diagnostic stage

The research team scored the assessments and made an initial clinical diagnosis. The principal clinical investigators (GB, ES, TC) reviewed comprehensive clinical material on every case, including ADI and ADOS summary, clinical vignette and psychometric results. A consensus clinical diagnosis of ICD-10[30] childhood autism or other ASD (other pervasive developmental disorder, pervasive developmental disorder-unspecified, atypical autism) was made on the basis of all sources of information. Due to the relatively young age of children at assessment and the modest sample size of the childhood autism and 'other ASDs' subgroups, the subgroups were merged into one ASD diagnosis group for analysis.

Analysis

All reported frequencies and means are unweighted. All other statistics, such as proportions and percentages, are target population estimates calculated using inverse probability weighting to take account of the differences in sampling proportions and the selective participation in in-depth assessment across the sample stratification (see *Sample stratification and selection* below). Confidence intervals and standard errors were calculated using the linearisation version of the robust parameter covariance matrix as implemented by the *svy* procedures of Stata[31]. A receiver-operator-characteristic (ROC) Area-Under-the-Curve (AUC) analysis was performed to assess and compare the discriminant power of the screens/clinician judgement in distinguishing ASD cases from non-ASD cases[32,33]. Confidence intervals for weighted AUC estimates, and tests were obtained by bootstrap resampling ROC procedures of Stata 9[31].

--- Figure 1 about here ---

RESULTS

A total of 347 referrals to child health services and 461 referrals to speech and language therapy services were received. Of these 808, 722 gave primary reasons for referral as language difficulties 398 (55%), social communication difficulties 138 (19%), behaviour 82 (11%), general development 48 (7%) and medical or other problems 56 (8%); for 86 children no reason for referral was recorded.

Parents of all 808 referrals (556 boys, 237 girls, 15 missing) were approached (initially by post; followed-up by a telephone call) to complete the screening pack containing the SCQ and M-CHAT. The presentation of the two screens was counterbalanced in the questionnaire pack across the sample. A total of 543 screens were completed (67.2%), 276 by post and 267 by telephone. Characteristics of participants for whom screening data were achieved are shown in Table 1.

--- Table 1 about here ---

Clinician checklist information was available on 369 out of 543 (68%) children for whom screening information was available (233 completed by clinicians, 132 by research team, 4 cases information missing). In 101 cases (19%) concern about possible ASD and/or referral to the specialist team was noted at the initial appointment. Initial clinical appointments took place sometimes before (N=132) but more often after (N=298) the screens were completed (mean (SD) lag=1.2 (3.4) months, range -13.4 months to 17.2 months, appointment date missing on 131 cases).

Sample stratification and selection

For in-depth assessment we sampled children from across all cells of consistency and inconsistency of measures. The sample was thus stratified not only by service (equal proportions: CDT vs. SALT) and referral to ASD diagnostic team (2 levels: Yes

vs. No) but also by SCQ score (four levels: low score <8; moderately low score 8-14; moderately high score 15-21; high score ≥22) and MCHAT (binary: high vs. low risk). The sampling fraction for each stratum was then used as an inverse probability weight such that the weighted selected sample was then representative of the whole screened sample. Of 181 families selected, 61 were not seen (21 opted out, 40 were not contactable) and 120 children (100 boys, 20 girls) received in-depth assessment (66.3%) (see Figure 1). There was no evidence that children selected for in-depth assessment who did not participate further were more likely to be screen positive vs. screen negative ($\chi^2(1) = 0.46$, p=.50). Mean age at the time of assessment was 51.6 months (SD = 8.8, range 32 to 73) as the direct assessments only begun once the screening stage of the study was completed.

Within the sample of 120 children seen for in-depth assessment, 55 met criteria for a consensus ICD-10 clinical diagnosis of ASD. Of the 65 children who did not meet criteria for an ASD diagnosis 16 had an intellectual disability (IQ<70), 11 a language delay, 4 hyperkinetic disorder, 4 oppositional defiant disorder, 1 each cerebral palsy, medical disorder (Holt-Oram Syndrome, a congenital syndrome affecting upper limbs and heart) and 28 did not meet criteria for any of the clinical conditions that were assessed as part of the ASD-focused assessment. Because the assessments did not comprehensively test for all possible psychiatric or medical disorders we consider possible diagnoses (or lack of them) in this group uncertain. However, in many of these children there had been an earlier developmental concern (e.g. speech delay or unclear speech) that prompted the initial referral that had resolved or was below clinical threshold for a developmental disorder by the time of the research assessment. Characteristics of the children seen for assessment are shown in Table 2. Some children were not able to complete the direct assessments and others fell below the test basal required to calculate standardised scores. Ns for each assessment are shown in the Table.

--- Table 2 about here ---

The area under the curve (AUC), sensitivity (Se), specificity (Sp), positive predictive value (PPV) and negative predictive value (NPV) of the two screens in predicting consensus diagnosis ASD versus non-ASD status are shown in Table 3. The area under the curve (AUC) did not differ (p=.47) between the SCQ (70%) and M-CHAT screens (66%). The sensitivity and specificity for the SCQ were 64% and 75% and for the M-CHAT 82% and 50%, respectively. For clinical judgement alone the AUC was 77% which did not differ from the SCQ (p=.27) nor the M-CHAT (p=.11), sensitivity was 85% and specificity 69%. When the screened sample was split by median age (<=33 months vs. > 33 months) the M-CHAT had the highest sensitivity for younger children (93% with accompanying low specificity of 42%) and clinical judgement had the highest sensitivity for older children (97% with a specificity of 72%).

--- Table 3 about here ---

Clinician judgement of a likely ASD was then combined with screen positive results on the two screens in two ways (see Table 3). First, they were considered in series and the sensitivity and specificity calculated for children who were *both* screen positive *and* for whom clinicians had indicated a possible ASD. Sensitivity was reduced (clinician and SCQ 51%; clinician and M-CHAT 69%) but specificity increased (clinician and SCQ 87%; clinician and M-CHAT 82%). Next, they were considered in parallel and the sensitivity and specificity calculated for children who were *either* screen positive *or* for whom clinicians had indicated a possible ASD. Sensitivity was greatly increased (clinician or SCQ 98%; clinician or M-CHAT 98%) but specificity was low (clinician or SCQ 47%; clinician or M-CHAT 27%).

DISCUSSION

Both the SCQ and the M-CHAT performed only moderately well at identifying cases who went on to meet diagnostic criteria for ASD. The M-CHAT had higher sensitivity than the SCQ but lower specificity. Based on their performance in this study, reliance on either of the screening instruments in isolation would lead to considerable under-identification of children likely to go on to receive an ASD diagnosis (that is, an unacceptable rate of screen 'false negatives', especially the SCQ) and also considerable over-identification of children who would be unlikely to go on to receive an ASD diagnosis (that is, an unacceptable rate of screen 'false positives', especially the M-CHAT). Initial clinician judgement about likely ASD was as accurate as each of the two screening instruments. Further the screens did not perform well either to confirm preliminary clinical judgement to refer (in series) or as an alternative indicator for referral (in parallel). As would be expected, if *both* clinical judgement *and* a positive screen result was required to trigger a referral, sensitivity was unacceptably low (leading to under identification of cases), whilst if referral was based on *either* a clinical judgement of likely ASD *or* a screen positive result specificity was unacceptably low (leading to many non-ASD cases being referred on). Finally, in younger children (=<33 months) the M-CHAT had the highest sensitivity and in older children (>33 months) clinical judgement had the highest sensitivity; but the current study lack power to robustly test whether the screens worked differently in children of different ages.

Whilst screens may provide useful information to aid the decision to refer for a specialised ASD assessment their accuracy is moderate and does not meet the criterion set of 80% sensitivity and specificity used in the recently published UK NICE guidance[18] and recommended in general for screens for developmental disabilities[34]. In children about whom a developmental concern has been

raised, ASD screening in isolation should not be used to make a referral for specialised ASD assessment; neither should they be combined with clinical opinion about likely ASD either to confirm this opinion (which leads to a rise in missed cases) nor as an alternative to clinical opinion (which leads to over-inclusion). The current findings do not support the AAP recommendation that ASD screening instruments should be used at universal well-child checks[17], and are in line with more cautionary opinion[20]. It might be that the two-stage screen and re-screen procedure recently reported for the M-CHAT/M-CHAT-R[10,11] provides a model for a more accurate screening procedure. However, in these studies the rate of initial (first stage) screen positives were 9%[10] and 7%[11] which would place considerable demand on services required to conduct the follow-up screening, as well as careful explanation to parents as to what the initial test result meant. Even if such service provision was available this would only be justified if the sensitivity was high. However, a recent very large population study (N=52,026) using the M-CHAT in a single-stage manner, and that included population follow-up to identify all known cases of ASD, found that only one third of ASD cases were screen-positive on the initial M-CHAT administration at 18 months of age[35].

Competing motivations lie behind the increasing interest in early screening for ASD. On the one hand, there is a concern to identify ASD as soon as possible in young children, in order to provide support to the family and access to appropriate interventions and services. On the other hand, waiting lists for multidisciplinary assessment for ASD and other complex developmental disorders are under pressure in many countries so there is a desire to reduce the referral of children who may not require this specialist service[23]. This needs to be balanced with the relative costs and benefits of false positives and false negatives. Broadly these costs fall on

different parties: false positives may lead to unneeded specialised assessment and parental concern; whereas false negatives may lead to under-identification and late diagnosis and intervention.

In many ways the moderate performance of the screens to accurately identify ASD is perhaps not surprising. ASD is a developmental disorder whose presentation, perhaps particularly in young children, can wax and wane over time. It also commonly co-occurs with other developmental disorders such as language delay/disorder[36] and intellectual disability[37] and at a later age with child psychiatric disorders[38] – making differential diagnosis challenging. Population studies indicate that a significant number of children may display characteristics of ASD at a preschool age but go undiagnosed and although their trajectory of symptoms into mid-childhood is less severe than children who receive a diagnosis; they have elevated rates of educational and behavioural problems[39].

Another important consideration is whether developing accurate screens *specifically* for ASD is either a desirable or a realistic goal. At an early age emerging symptoms of ASD overlap with those seen in other groups of children who would also benefit from a more comprehensive assessment and intervention, such as children with general developmental delay, language impairment, and those with early emerging emotional and behavioural difficulties. Some of the interventions that such children require, and the support and advice to be provided to parents, are based on similar principles. Few studies have directly compared general developmental screeners versus ASD-specific screens and such studies should be undertaken to further inform child healthcare policy and practice (for rare exceptions see[40,41]). More generally, the services and advice that parents of children with a range of neurodevelopmental disabilities

(that affect general development, language and communication, and commonly motor and other aspects of adaptive functioning) require are best-served by professional teams that have expertise not only in ASD but in a range of neurodevelopmental conditions.

The extent to which these results are applicable to other populations is unclear. The two health districts in which the study was conducted are inner London areas in the UK with high levels of social and economic deprivation, individuals from ethnic minorities and families where English is an additional language. From personal knowledge, both districts had also worked for many years to train their work force about early signs of ASD. However, the sensitivity and specificity levels on the SCQ and M-CHAT in this study are comparable to those found in referred preschool samples in very different communities in the USA, Australia and the Netherlands[12,14,15,16]. No previous study has achieved screening data on such a large community clinic sample, none has directly compared two different screening instruments, and none has systematically also captured referring clinician judgement about possible ASD.

Conclusions

We found that both when used in isolation, and also when combined with clinician judgement, neither the SCQ nor the M-CHAT performed sufficiently well to be recommended for universal adoption within UK community paediatric services. As with much clinical practice, clinical judgement in combination with information gained from administering specific tests and assessments including information from ASD screening instruments, as well as the presence of parental concerns[42] and the impact the developmental problems are having on the child and family, should inform the decision to refer for more specialised assessment rather than reliance on the result of a screening instrument in isolation.

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Table 1 Characteristics of participants screened

N	543
N (%) boys[1]	388 (71.5)
Mean (SD; range) age (months)	35.2 (8.3; 18 to 56)
N (%) parent reported child ethnicity[2]	
Black	259 (48.6%)
White	184 (34.5%)
Asian	15 (2.8%)
Other	43 (8.1%)
Mixed race	32 (6.0%)
N (%) language spoken at home[3]	
English only	311 (58.9%)
English plus an additional language	173 (32.8%)
Additional language only	44 (8.3%)
N (%) maternal highest qualifications[4]	
No formal qualifications	89 (17.2%)
Vocational qualifications	100 (19.4%)
GCSE	107 (20.7%)

[2] N = 10 missing
[3] N = 15 missing
[4] N = 27 missing

A levels	73 (14.1%)
Degree or above	147 (28.5%)

Table 2 Characteristics of the participants directly assessed

	Non-ASD		ASD	
	N	Mean (SE)	N	Mean (SE)
Mullen ELC (SS)	60	84.4 (2.6)	22	68.3 (3.3)
PLS TLS (SS)	61	82.4 (2.5)	24	72.2 (3.9)
VABS ABC (SS)	64	78.3 (1.7)	48	61.5 (1.7)
ADOS-Social	65	2.60 (0.27)	55	8.56 (0.45)
ADOS-Comm	65	1.91 (0.17)	55	4.35 (0.31)
ADI-Social	65	4.42 (0.45)	54	15.2 (0.81)
ADI-Verbal	58	4.31 (0.42)	26	12.1 (0.83)
ADI-Non verbal	7	3.71 (1.32)	28	9.79 (0.57)
ADI-Repetitive	65	1.74 (0.24)	54	4.89 (0.31)

Key: Mullen ELC – Mullen Early Learning Composite, PLS TLS = Preschool Language Scale Total Language Scale, VABS ABC = Vineland Adaptive Behavior Scale Adaptive Behavior Composite, ADOS = Autism Diagnostic Observation Schedule, ADI = Autism Diagnostic Interview.

Table 3 AUC, Sensitivity, specificity, PPV and NPV of the SCQ, M-CHAT and clinical judgement in isolation and combined (weighted values)

	AUC	**Sensitivity**	**Specificity**	**PPV**	**NPV**

	Weighted value (95% CI)	*Weighted value (95% CI)*	*Weighted value (95% CI)*	*Weighted value (95% CI)*	*Weighted value (95% CI)*
SCQ	70% (59% to 80%)	64% (51% to 78%)	75% (63% to 85%)	60% (48% to 73%)	78% (65% to 88%)
M-CHAT	66% (55% to 76%)	82% (72% to 92%)	50% (33% to 64%)	49% (33% to 62%)	82% (67% to 92%)
Clinical judgement	77% (68% to 87%)	85% (76% to 94%)	69% (52% to 81%)	73% (61% to 82%)	83% (68% to 93%)
SCQ plus clinical judgement	69% (60% to 78%)	51% (37% to 63%)	87% (75% to 94%)	79% (64% to 91%)	65% (51% to 78%)
M-CHAT plus clinical judgement	76% (66% to 85%)	69% (54% to 80%)	82% (68% to 90%)	79% (64% to 89%)	73% (58% to 84%)
SCQ or clinical judgement	73% (51% to 95%)	98% (95% to 100%)	47% (27% to 65%)	65% (54% to 75%)	97% (85% to 100%)
M-CHAT or clinical judgement	63% (54% to 72%)	98% (94% to 100%)	27% (11% to 49%)	57% (44% to 68%)	94% (67% to 100%)

Key: SCQ = Social Communication Questionnaire, M-CHAT = Modified Checklist for Autism in Toddlers, AUC = Area Under the Curve, PPV = Positive Predictive Value, NPV = Negative Predictive Value

Figure 1 Stratum selection and participation