



TITLE: Screening and Diagnostic Tools for Autism Spectrum Disorder in Children: A Review of Guidelines

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CONTEXT AND POLICY ISSUES

Autism is a lifelong condition that involves impaired verbal and non-verbal communication, impaired socialization, and repetitive or restricted patterns of behaviour.¹⁻⁴ Autism spectrum disorders (ASD) refer to a range of disorders that include autistic disorder (AD), Asperger's disorder, and pervasive developmental disorder-not otherwise specified (PDD-NOS).³ While those diagnosed with ASD can lead productive lives, others may exhibit severe forms that can have profound effects, not only on the individuals themselves, but on their families.¹⁻⁵

Recognition and diagnosis of autism enables patients and their families to access autism-specific support and resources which, subsequently, can lead to more positive outcomes.^{3,5} The annual costs associated with resources and support in both the United Kingdom and United States exceeds several billion.¹ The reported median global prevalence as of 2007 was 17 per 10,000 for AD and 62 per 10,000 for all pervasive developmental disorders.¹ In Canada, the prevalence of AD as of 2005 was estimated at 13 per 10,000; 2.6 per 10,000 for Asperger's disorder; and 20.8 per 10,000 for PDD-NOS.³ At the present time, there is no consensus as to the cause of ASD nor why there appears to be an increase in its prevalence since the 1980s.³

With an apparent increase in the prevalence and heightened awareness of ASD, there is a need for both accurate screening and diagnosis. Screening refers to the recognition of certain developmental and behavioural signs and symptoms that may be cause for concern to the caregiver or physician while the diagnostic assessment establishes if those concerns can be attributed to either ASD or a different cause.⁵ While there is consensus regarding the need for healthcare professionals to screen and diagnose ASD as early as possible, there is no world-wide consensus on the most effective course of action.³ Interviews, observations, and tools are some of the methods used for screening and diagnosis. This report will review the evidence-based guidelines on the tools used for the recognition and diagnosis of ASD in the pediatric population.

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RESEARCH QUESTION

What are the evidence-based guidelines regarding the available screening or diagnostic tools for the recognition or diagnosis of autism spectrum disorder in children?

KEY MESSAGE

Evidence-based guidelines have recommended the use of the DSM-IV-TR and/or IDC-10 diagnostic criteria for ASD diagnosis. The guidelines were inconsistent in their recommendations regarding the use of ASD screening and diagnostic tools, with three guidelines advocating for tool use in conjunction with clinical judgment and the other one recommending against tool use. The Checklist for Autism in Toddlers (CHAT) tool, along with clinical judgment, was the only screening tool recommended by all three guidelines advocating for tool use. In conjunction with clinical judgment, the Autism Diagnostic Interview-Revised (ADI-R), the Autism Diagnostic Observation Schedule (ADOS)/Autism Diagnostic Observation Schedule – General (ADOS-G), and the Childhood Autism Rating Scale (CARS) were the recommended tools for use when diagnosing ASD in those guidelines advocating their use.

METHODS

Literature Search Strategy

A limited literature search was conducted on key resources including PubMed, The Cochrane Library (2013, Issue 5), University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. Methodological filters were applied to limit retrieval to health technology assessments, systematic reviews, meta-analyses and guidelines. Where possible, retrieval was limited to the human population, under 19 years of age. The search was also limited to English language documents published between January 1, 2008 and June 3, 2013.

Selection Criteria and Methods

One reviewer screened citations and selected studies. In the first level of screening, titles and abstracts were reviewed and potentially relevant articles were retrieved and assessed for inclusion. The final article selection was based on the inclusion criteria presented in Table 1.

Table 1: Selection Criteria

Population	Children ≤19 years in any setting
Intervention	Current tools for the screening and/or diagnosis of autism spectrum disorder (ASD)
Comparator	Any other current tools
Outcomes	Agreement or disagreement between tools Accuracy of tools Efficiency of tools
Study Designs	Guidelines

Exclusion Criteria

Studies were excluded if they did not satisfy the selection criteria, if they were duplicate publications, or were published prior to January 1, 2008. In addition, guidelines were excluded if there was incomplete reporting of methods or if they were superseded by a more recent or more rigorous review or guideline.

Critical Appraisal of Individual Studies

The evidence-based guidelines were assessed using the following domains of the AGREE instrument:⁶ scope and purpose, stakeholder involvement, rigor of development, clarity and presentation, applicability, and editorial independence. A numeric score was not calculated; instead the study strengths and limitations were described narratively.

SUMMARY OF EVIDENCE

Quantity of Research Available

The literature search identified a total of 420 citations. Of these, 390 citations were excluded during the title and abstract screening while 30 full text documents were retrieved based on their potential relevance. Of the 30 potentially relevant articles from the original literature search, none met the inclusion criteria and were subsequently excluded. The grey literature search identified 4 relevant citations.

A PRISMA diagram demonstrating the study selection process is presented in Appendix 1.

Additional references that did not meet the inclusion criteria but may be of potential interest are provided in the Appendix 2. These have not been critically appraised or summarized.

Summary of Study Characteristics

The guidelines included in this report were published in 2008^{3,4}, 2010², and 2011⁵. One guideline was from Canada,³ one from the United States (US),² one from New Zealand (NZ),⁴ and one from the United Kingdom (UK).⁵ The recommendations focused on the screening, assessment, and diagnosis of children,^{2,4} patients aged 0-19⁵ or of very young pediatric populations (0-5 years of age).³ All of the guidelines also focused on routine developmental screening and the evaluation of autism in addition to the aforementioned items.²⁻⁵ The 2010 guidelines from Filipek et al. are a reaffirmation of the earlier 2000, 2003, and 2006 versions.²

Grading of recommendations and levels of evidence

Detailed characteristics on the grading of evidence can be found in Appendix 3.

All of the guidelines were developed by reviewing the relevant original literature and existing evidence-based best practice guidelines.²⁻⁵ Filipek et al.² used distinct classes to assess the quality of the evidence, with Class I through Class III levels indicating the highest to poorest level of evidence, respectively (see Appendix 3 for details).² Grading or strengths of recommendations were provided in the following manner for the US practice parameters: *Standard* providing a high degree, *Guideline* providing a moderate degree, and *Practice Option* providing an uncertain degree of clinical certainty or utility (see Appendix 3 for details).² The NZ

guidelines critically appraised and weighed the body of evidence to further grade the recommendations. The levels of grading were A-C and I whereby a grade of A indicated that the recommendation was supported by good evidence, B by fair evidence, and C by expert opinion only. “I” indicated that no recommendation could be made due to lack of/poor and conflicting evidence.⁴ Nashchen et al.³ did not grade the strength of their recommendations; instead they had committee and subcommittee consensus discussions.

Summary of Critical Appraisal

All of the guidelines²⁻⁵ presented clear overall objectives and specific descriptions of both the clinical questions and the population for whom the guidance was intended. Relevant professionals (including clinicians, nurses, speech and language pathologists, psychologists) and parental groups were included in the development of most guidelines³⁻⁵ but not in the US practice parameters, which did not consult with parental groups.² All guidelines were evidence-based with clearly described methods for guideline formulation.²⁻⁴ Two guidelines^{2,3} did not perform a systematic review of the literature, however the criteria for selecting the evidence was described. Health benefits,³⁻⁵ risks,^{3,5} and side effects^{3,5} were considered when formulating certain recommendations while one² did not contain this information. The recommendations were specific, unambiguous, and clearly presented²⁻⁵ with distinct links between the recommendations and supporting evidence.^{2,3,5} The NICE guidelines discussed the potential organizational barriers,⁵ while cost-implications were considered in two.^{3,5} Some guidelines were editorially independent from the funding source^{2,3} or this relationship was not stated⁴ and, with the exception of the Canadian³ and NZ⁴ guidelines, conflicts of interest were declared.^{2,5} None of the guidelines²⁻⁵ provided any evidence that their guidelines had been piloted among the intended users, however the guidelines from NZ and NICE did provide an impact analysis^{4,5} and one provided implementation tools.⁴ Details of the appraisal of the individual guidelines is presented in Appendix 4.

Summary of Findings

The identified guidelines provided recommendations on the tools available for screening, assessment, and diagnosis for children with ASD.²⁻⁵ An overview of the recommendations is provided in Tables 2 and 3. More detailed reporting of individual guideline recommendations is presented in Appendix 5.

Screening

Three guidelines²⁻⁴ recommended the use of secondary or targeted screening in individuals not attaining critical developmental milestones in the areas of communication and social behavior, for those children whose parents have expressed concerns, and for children with one or more siblings diagnosed with ASD. The NICE guidelines did not recommend the use of screening tools.⁵ Physicians²⁻⁴ and psychologists³ with specific training in ASD screening and diagnosing were the preferred professionals, however, it was noted that the expertise of professionals like public health nurses, nurse practitioners, and early childhood educators should be further utilized and developed for ASD screening purposes.³ The NICE guidelines suggested a core autistic team, consisting of a pediatric or adolescent psychiatrist, a speech and language therapist, and a clinical/educational psychologist, be assembled for ASD diagnosis.⁵ Recommended ASD screening tools from guidelines that supported their use included the Modified Checklist for Autism in Toddlers (M-CHAT)³ in patients 16-30 months of age (to be used in conjunction with the follow-up interview to help increase sensitivity), the Screening Tool

for Autism in Two-Year-Olds (STAT)³ for children 24-36 months of age, and the Autism Screening Questionnaire (ASQ)² in children failing the developmental surveillance procedure. The M-CHAT and STAT tools both reported high sensitivity and specificity for their respective age ranges, with the STAT also showing a high predictive value and effectively differentiating between diagnostic groups functioning at similar levels of development.³ The Checklist for Autism in Toddlers (CHAT) was also recommended⁴ in children failing developmental surveillance procedures² and tentatively recommended as a second level screening tool, particularly with the Denver Modification, for the Canadian population.³ However, Nachshen et al. also indicated the need for more research to elucidate if the CHAT results would maintain high sensitivity and specificity in larger samples with a longer follow-up period.³ The CHAT with the Denver Modification reported strong specificity and sensitivity, however, it may be less sensitive in children with milder forms of ASD and with advanced cognitive ability.³ The NICE guidelines⁵ indicated that screening tools were not essential and discouraged their use to make or rule out a diagnosis of autism as the evidence regarding screening tools was found to be of low quality. In addition, they noted that positive scores with these screening tools could indicate conditions other than autism and that negative scores do not necessarily rule out autism. They did, however, propose their usefulness when gathering developmental and behavioural information.⁵ A detailed list of the screening tools can be found in Table 2.

The need for additional research for better validation was indicated for the following second level screening tools, despite some of these being simultaneously recommended for use: Early Screening for Autistic Traits (ESAT), M-CHAT, Pervasive Developmental Disorder Screening Test-II (PDDST-II), the STAT, and the Social Communication Questionnaire (SCQ).³ The Autism Behaviour Checklist (ASD) and Gilliam Autism Rating Scale (GARS) were not recommended for second level screening as these tools reported low sensitivity.³ Screening tool sensitivities and specificities reported by Nashchen et al.³ can be found in Appendix 6, Table 5, and a list of additional screening tools that were not recommended can be found in Appendix 6, Table 6.

Table 2: Summary of Recommendations for ASD Screening and Corresponding Tools in Children

Recommendations for Screening Tools			
Tools	Type of Tool	Child age	Recommendations
ABC	Interviewer	≥18 months	Not recommended ³
ASQ	Parent- or carer-report	NR	<ul style="list-style-type: none"> Recommended for children failing developmental surveillance procedures² Strength = Guideline^a Recommended, having adequate sensitivity and screening⁴
M-CHAT	Parent-report checklist (23 items)	16-30 months	Use as parent-report tool for second level screening; follow-up interview used in conjunction with tool to increase sensitivity ³
CHAT	Parent-report and behavioural observation	≥18 months	<ul style="list-style-type: none"> Tentatively recommended for second level screening; Denver modification may increase sensitivity with no loss of specificity³ Recommended for children

Recommendations for Screening Tools			
Tools	Type of Tool	Child age	Recommendations
			failing developmental surveillance procedures ² Strength = Guideline ^a <ul style="list-style-type: none"> Recommended, having adequate sensitivity and screening⁴
GARS	Parent- or teacher-report (42 items)	3-22 years	Not recommended ³
STAT	Trained Professional	24-36 months	Second level screener to distinguish those with autistic disorder and developmental delays ³
ASD: Recommendations for Screening (and Surveillance ^b)			
<ul style="list-style-type: none"> Primary or universal screening for ASD is not recommended.^{3,4} Developmental surveillance is recommended at all well-baby/child visits from infancy through school-age children and in any aged child where there are concerns regarding behaviour, learning, and social acceptance.²⁻⁴ Secondary or targeted screening for ASD is recommended.^{2,3} Validated screening tools are required for secondary screening.^{2,3} Screening tools are a useful way to gather information on children with an increased risk of autism in a structured way, however, they are not essential and should not be used to make or rule out a diagnosis of autism.⁵ 			

ABC = The Autism Behaviour Checklist; **ASD** = Autism Spectrum Disorders; **ASQ** = Autism Screening Questionnaire; **CHAT** = Checklist for Autism in Toddlers; **GARS** = Gilliam Autism Rating Scale; **KADI** = Krug Asperger's Disorder Index; **M-CHAT** = Modified Checklist for Autism in Toddlers; **NR** = not reported; **STAT** = Screening Tool for Autism in Two-Year-Olds

^a Definitions of the strength of the recommendations (Standard, Guideline, Practice Option), Appendix 3.²

^b Surveillance refers to pre-screening of children for developmental disorder prior to focusing on ASD screening in Filipek et al.²

Of note, there were certain tools that were recommended for assessing childhood development prior to secondary or targeted ASD screening. These included the Ages and Stages, BRIGANCE screens, Child Development Inventories, and Parents' Evaluations of Developmental Status questionnaires (more details in Appendix 6, Table 4).^{2,4} Other tools, such as the Denver Developmental Screening Test-Revised (DDST-II) and the Revised Denver Pre-Screening Developmental Questionnaire (R-DPDQ) were identified but not recommended due to their insensitivity and lack of specificity.²

Diagnosis

Recommended ASD diagnostic tools included the Autism Diagnostic Interview-Revised (ADI-R),^{2,4} the Autism Diagnostic Observation Schedule (ADOS)³/ Autism Diagnostic Observation Schedule – Generic (ADOS-G),^{2,4} the Childhood Autism Rating Scale (CARS),^{2,4} the Gilliam Autism Rating Scale (GARS),^{2,4} the Parent Interview for Autism (PIA),^{2,4} the Pervasive Developmental Disorders Screening Test–Stage 3 (PDDST-II Stage 3),² and the STAT.² According to Nachshen et al., the ADI-R is a valid and reliable tool⁷ for diagnosing ASD and has been reported as having high specificity, sensitivity, and good inter-rater reliability.³ However, it was found to be a less effective tool for children under the age of four with mental ages below 18 months and were non-verbal and in children that did not demonstrate positive symptoms.³ Research indicates that the ADOS has high sensitivity, specificity, test-retest and inter-rater

reliability, and adequate to high internal consistency.³ The ADOS tool, however, was not efficient at discerning ASD from atypical autism (this includes patients who do not meet the criteria for autistic disorder due to their late age of onset, subthreshold symptoms, atypical symptoms, or all of the aforementioned criteria).³ Nachshen et al. highlighted the necessity of using clinical judgment in conjunction with the ADI-R and ADOS tools for ASD diagnosis which remain the gold standard for ASD diagnosis in Canada.³ The Childhood Autism Rating Scale (CARS) can also be used in diagnostic assessments² as it has good inter-rater agreement, test-retest reliability, and internal consistency but revealed limited sensitivity in the assessment of higher functioning children with ASD.³ Additionally, the ADOS-G, GARS, PIA,^{2,4} PDDST-II Stage 3, and STAT were indicated as recommended diagnostic tools as they were found to have moderately sensitivity and good specificity for autism.² NICE does not specifically recommend the use of diagnostic tools but indicates that they may be useful in both gathering developmental and behavioural information and when assessing social, communication, and behavioural skills based on the DSM-IV-TR and/or IDC-10 diagnostic criteria.⁵ Table 3 incorporates a detailed list of diagnostic tools.

Table 3: Summary of Recommendations for ASD Diagnosis and Corresponding Tools in Children

Recommendations for Diagnostic Tools			
Tools	Type of Tool	Child age	Recommendations
ADI-R	Standardized, semi-structured interview for parents and caregivers	Less effective in children under 4 years	<ul style="list-style-type: none"> • In combination with clinical judgment, the ADI-R and ADOS should be used together for ASD diagnosis; current Canadian gold standard for diagnosis.³ • Recommended for its moderate sensitivity and good specificity for autism² • Recommended for its adequate sensitivity and specificity; one of two best tools⁴
ADOS (ADOS-G)	Standardized, semi-structured observation measure (4 modules)	Module used depends on expressive language level and chronological age of child	<ul style="list-style-type: none"> • In combination with clinical judgment, the ADI-R and ADOS should be used together for ASD diagnosis; current Canadian gold standard for diagnosis.³ • Recommended for its moderate sensitivity and good specificity for autism² • Recommended for its adequate sensitivity and specificity; one of two best tools⁴
CARS	Diagnostic observation instruments (15 subscales)	Children ³ (> 24 months) ⁴ and adults	<ul style="list-style-type: none"> • May also be used in diagnostic assessments.³ • Recommended for its moderate sensitivity and good specificity for autism² • Recommended for its adequate sensitivity and specificity⁴

Recommendations for Diagnostic Tools			
Tools	Type of Tool	Child age	Recommendations
GARS	Diagnostic parental interviews	3-22 years	<ul style="list-style-type: none"> Recommended for its moderate sensitivity and good specificity for autism² Recommended for its adequate sensitivity and specificity⁴
PIA	Diagnostic parental interviews	< 3 years of age	<ul style="list-style-type: none"> Recommended for its moderate sensitivity and good specificity for autism² Recommended for its adequate sensitivity and specificity⁴
PDDST-II ^b	Diagnostic parental interviews	Birth to 18 months	Recommended for its moderate sensitivity and good specificity for autism ²
STAT	Trained Professional	24-36 months	Recommended for its moderate sensitivity and good specificity for autism ²
ASD: Recommendations for Diagnosis			
<ul style="list-style-type: none"> DSM-IV-TR and/or IDC-10 diagnostic criteria must be used for clinical diagnosis^{4,5} with all five DSM axes considered during the full diagnostic evaluation.^{2,3} Use caution when applying the DSM-IV-TR symptoms to very young children.³ Clinical judgment, thorough developmental history, and structured behavioural observation are required for diagnosis.²⁻⁴ At least one standardized tool^a is recommended for parents and professionals.^{2,3} Clinical judgment from a trained and experienced professional is critical for interpreting results.^{3,4} Test users should be familiar with the validity, reliability, appropriateness, and limitations when assessing patients and should keep these in mind when forming opinions and listing results.⁴ Consider using an autism specific diagnostic tool to acquire a developmental history focusing on developmental and behavioural histories consistent with DSM-IV-TR and/or IDC-10 diagnostic criteria.⁵ Consider using an autism specific diagnostic tool to assess social, communication, and behaviors focusing on DSM-IV-TR and/or IDC-10 diagnostic criteria.⁵ 			

ADI-R = Autism Diagnostic Interview-Revised; **ADOS** = Autism Diagnostic Observation Schedule; **ADOS-G** = Autism Diagnostic Observation Schedule – Generic; **ASD** = Autism Spectrum Disorders; **CARS** = Childhood Autism Rating Scale; **DSM** = Diagnostic and Statistical Manual of Mental Disorders; **(DSM)-IV-TR** = Diagnostic and Statistical Manual of Mental Disorders; **GARS** = Gilliam Autism Rating Scale; **ICD-10** = International Classification of Diseases; **PDDST-II** = The Pervasive Developmental Disorders Screening Test–Stage 3; **PIA** = The Parent Interview for Autism; **NR** = not reported; **STAT** = Screening Tool for Autism in Two-Year-Olds

^a Standardized, norm referenced parent-report measure or behavioural observation measure.

^b Stage 3 - Autism Clinic Severity Screener (ACSS)

Limitations

Of the four guidelines that were identified in this review, one was Canadian and, consequently, limits generalizability to the Canadian population.³ Even though other guidelines were from Commonwealth countries^{4,5} and the US,² their generalizability may still not be as relevant to Canadians. Two of the four identified guidelines were not based on a systematic review of the

evidence,^{2,3} hence there exists the possibility that potentially relevant information was not included in the development of these guidelines.

Nachshen et al.³ did not assess the level of evidence or grade the recommendations thus potentially leading to a misrepresentation of their importance. The NICE guidelines were formed using GRADE to assess the identified evidence, however, there was no grading of their recommendations.⁵ Additionally, the recommendations from Filipek et al.² and NZ⁴ were based on a grading of “Guideline” (moderate clinical certainty)² or “B” (supporting evidence rated as fair), respectively.⁴ Neither of these ratings represents the highest level of evidence in their respective grading assessments, indicating that the recommendations may not be based on the best possible evidence.

Parental opinions were sought in all of the guidelines³⁻⁵ with the exception of those from the US.² These were developed solely with expert consensus when examining the evidence² which may have led to the formation of recommendations without considering the opinions of those closest to and constantly observing the patient. Exclusion of parental input may result in the loss of some of the valid and intricate details associated with the disorder that could help shape some aspects of the guideline not always observed by clinicians.

Three of the four guidelines assessed and recommended tools, along with clinical judgment, for both ASD screening and diagnosing,²⁻⁴ whereas NICE contrasted the importance of these tools.⁵ NICE suggested that the screening and diagnostic tools should only be used to gather the developmental, behavioural, and social information but it was the clinical judgment that was paramount when screening and diagnosing ASD.⁵

CONCLUSIONS AND IMPLICATIONS FOR DECISION OR POLICY MAKING

Screening and diagnostic tools for ASD and their subsequent use in children suspected of having ASD were examined in four guidelines. While older guidance from the American Academy of Pediatrics recommends specific ASD screening of all infants at 18 to 24 months,⁸ none of the more recent identified guidelines recommended this practice. All of these guidelines highlighted the importance of regular developmental screening during well-baby/child visits and to further assess children who did not meet developmental milestones with regard to social and communication skills and behavior, regressed in social or communication ability, or had a sibling with ASD. However, there were inconsistencies in the importance of screening and diagnostic tools in conjunction with clinical judgment, with three guidelines expressing the need for these tools²⁻⁴ and the other indicating that they were not necessary.⁵

The screening tools identified to be used in combination with clinical judgment in the three guidelines advocating for their use were the following:

- ASQ^{2,4}
- CHAT,^{2,4} (with Denver modification)³
- M-CHAT³
- STAT.³

The diagnostic tools identified to be used concurrently with clinical judgment in the three advocate guidelines were the following:

- ADI-R,^{2,4}
- ADOS/ADOS-G^{2,4}
- ADI-R/ADOS combination (Canadian gold standard)³
- CARS²⁻⁴
- GARS^{2,4}
- PIA^{2,4}
- PDDST-II²
- STAT²

Diagnostic assessment using the DSM-IV-TR and/or IDC-10 diagnostic criteria was also unanimously advocated in all of the guidelines, and all guidelines indicated that ASD screening and diagnosis was best performed by trained physicians and psychologists.

Numerous guidelines identified the need for further research in the development of new screening tools with increased sensitivity and specificity,^{2,3} particularly for use in children under the age of one and by a wide range of physicians.² In addition, more research was indicated for more time-efficient screening tools and for innovative research into tools that would identify atypical variants of ASD (including those with milder symptoms, higher cognitive ability,^{2,3} and Asperger's disorder.²)

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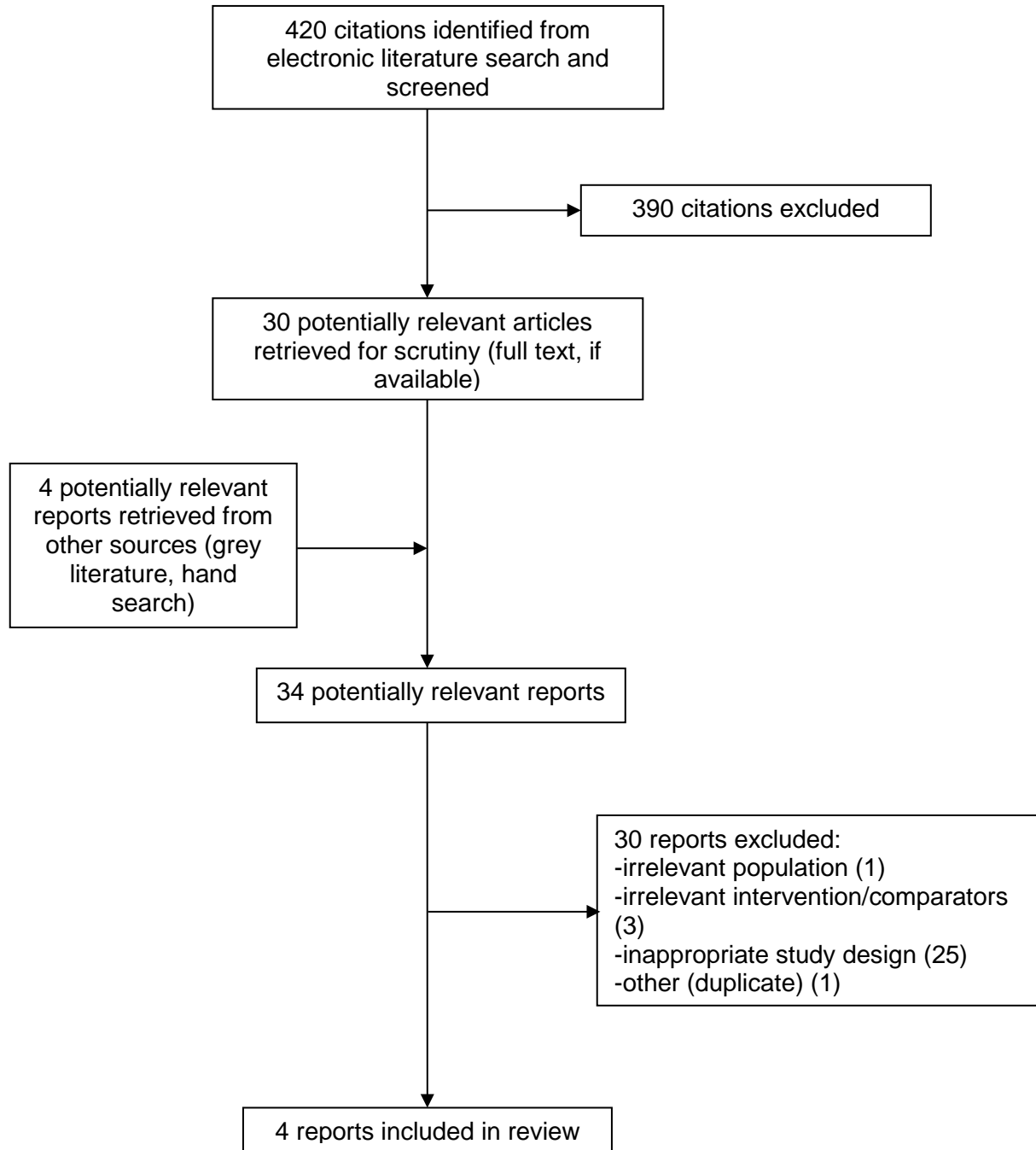
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APPENDIX 1: Selection of Included Studies



APPENDIX 2: Additional Articles of Potential Interest

Best Practice Guidelines – Methodology Uncertain

1. Missouri Autism Guidelines Initiative. Autism spectrum disorders: Missouri best practice guidelines for screening, diagnosis, and assessment [Internet]. Jefferson City: Missouri Department of Mental Health; 2010. [cited 2013 Jun 12]. Available from: <http://www.autismguidelines.dmh.mo.gov/pdf/Guidelines.pdf>
See: Screening Tools - Table 2.2, pg.26-27; Appendix-D14, pg.143-143.
Components of Diagnostic Evaluation – Table 3.2, pg. 57; Tools Appendix F, pg, 149.
Summary of Best Practice Recommendations – Appendix A, pg. 134 – 137.

Systematic Reviews – Diagnostic Procedures

2. Falkmer T, Anderson K, Falkmer M, Horlin C. Diagnostic procedures in autism spectrum disorders: a systematic literature review. *Eur Child Adolesc Psychiatry*. 2013 Jun;22(6):329-40.
[PubMed: PM23322184](#)

Comparison Studies

3. Wiggins LD, Piazza V, Robins DL. Comparison of a broad-based screen versus disorder-specific screen in detecting young children with an autism spectrum disorder. *Autism*. 2012 Dec 21.
[PubMed: PM23262658](#)

APPENDIX 3: Grading of Recommendations and Levels of Evidence

Guideline, Year, Country	Level of evidence	Grading/Strength of Recommendation
Nachshen et al. ³ for the Miriam Foundation, 2008 Canada	N/A	N/A
New Zealand autism spectrum disorder guideline, ⁴ 2008 New Zealand	<ol style="list-style-type: none"> 1. Critical appraisal of individual studies: <ul style="list-style-type: none"> • Used checklist to assign overall level of evidence (study met most or all, some, or few or none of criteria) 2. Weighing body of evidence and development of graded recommendations: <ul style="list-style-type: none"> • For each clinical question the following were performed: <ul style="list-style-type: none"> ○ Evidence (including evidence tables) were considered ○ Decision on quality made 	<p>A – recommendation supported by GOOD evidence (including a number of valid, acceptable, and clinically relevant studies)</p> <p>B – recommendation supported by FAIR evidence (mostly valid studies which may cause uncertainty from issues surrounding relevance, applicability, consistency, and volume; results not likely to be overturned)</p> <p>C – recommendation supported by EXPERT OPINION only (in the form of consensus guidelines, and published and unpublished expert opinion)</p> <p>I – no recommendation can be made due to insufficient evidence (poor quality, conflicting or lacking, and determination of benefits/harms cannot be deciphered)</p>
Filipek et al., ² 2010 USA	<p>Class I – Must contains a - d:</p> <ol style="list-style-type: none"> a. Prospective study of a well-defined cohort b. Adequate sample size with statistical power to validate conclusion or identifies subgroups for which testing does or does not generate significant information c. Interpretation of evaluation blinded to outcome d. Satisfactory description of evaluation technologies (i.e. MRI, etc.) 	<p>Standard - high degree of clinical certainty (usually requiring ≥ 1 Class I study directly assessing clinical question or overwhelming Class II evidence (whereby RCTs are not included))</p> <p>Guideline – moderate clinical certainty (≥ 1 Class II studies or strong consensus of Class III evidence)</p> <p>Practice Option – uncertain clinical utility (inconclusive or conflicting)</p>

Guideline, Year, Country	Level of evidence	Grading/Strength of Recommendation
	<p>Class II – Must have a or b:</p> <ul style="list-style-type: none"> a. Retrospective study of well-defined cohort or meets Class I a,b or d criteria b. Prospective or retrospective study which lacks adequate sample size, methodology, appropriate inclusion/exclusion criteria descriptions, and patient characteristics <p>Class III – Must have a or b:</p> <ul style="list-style-type: none"> a. Small cohort or case report b. Relevant expert consensus, survey, or opinion. 	<p>opinion and/or evidence)</p>
<p>NICE,⁵ 2011 UK</p>	<p>Initial grading of the evidence used to form the recommendations was based on the initial study quality design and used the GRADE approach:</p> <p>High – RCTs</p> <p>Low – Controlled observational studies</p> <p>Very Low – uncontrolled observational studies</p> <p>In addition, checklists were used to quality rate the studies using:</p> <p>QUADAS – for diagnostic accuracy and predictive accuracy studies</p> <p>CASP – for cohort studies used in epidemiological or descriptive studies</p> <p>NICE checklist – for qualitative studies</p> <p>* One exception to this was the assessment of uncontrolled observational studies which were all graded as very low quality</p>	<p>NR</p>

CASP = Critical Appraisal Skills Programme; **GRADE** = Grading of Recommendations Assessment, Development and Evaluation; **N/A** = not applicable; **NR** = not reported; **NICE** = National Institute for Health and Clinical Excellence; **RCT** = randomized controlled trials; **QUADAS** = quality assessment tool for diagnostic accuracy studies

APPENDIX 4: Summary of Critical Appraisal Using AGREE Instrument⁶

Guideline, Year, Country, Indication	Strengths	Limitations
<p>Nachshen et al.³ for the Miriam Foundation, Canadian Best Practice Guidelines 2008 Quebec, Canada Screening, Assessment and Diagnosis of Autism Spectrum Disorders in Young Children</p>	<ul style="list-style-type: none"> • Clearly defined objectives and clinical questions • Comprehensive literature search and search of existing guidelines • Expert, Scientific, Parental, and Clinician Subcommittees consulted • Recommendations are evidence-based and are directly linked to evidence • External independent reviewers evaluated the third draft • Major outcomes were considered (sensitivity and specificity) 	<ul style="list-style-type: none"> • Systematic review of original literature not performed • No grading of evidence or recommendations; only committee and subcommittee discussion • Barriers to implementation NR • Tools for dissemination NR
<p>New Zealand autism spectrum disorder guideline⁴ 2008 New Zealand Screening, assessment, and diagnosis of ASD</p>	<ul style="list-style-type: none"> • Clearly defined objectives and clinical questions • Comprehensive literature search and search of existing guidelines • Expert consensus for recommendation formation • Graded recommendations • Potential benefits of guideline implementation provided • Internal and external review • Guideline validation provided 	<ul style="list-style-type: none"> • Major outcomes were not considered • Potential harms of guideline recommendation implementation NR • Barriers to implementation NR
<p>Filipek et al.² Reaffirmation 2010 United States Practice</p>	<ul style="list-style-type: none"> • Clearly defined objectives and clinical questions • Comprehensive literature search • Experts consulted • Every 3 years, author and member of QSS/TTA conduct 	<ul style="list-style-type: none"> • Methodology was only available on National Guidelines Clearinghouse website • Systematic review of original literature not performed • Parental views and preferences were not sought

Guideline, Year, Country, Indication	Strengths	Limitations
parameter: screening and diagnosis of autism	literature search using original parameters to determine the need for guideline updating <ul style="list-style-type: none"> • Recommendations are evidence-based and are directly linked to evidence • Rreaffirmation dates of this guideline were July 10, 2010, October 28, 2006, and October 18, 2003 • Internal and external review 	<ul style="list-style-type: none"> • Barriers to implementation NR • Tools for dissemination NR • Unsure if external review independent • Guideline validation NR
NICE ⁵ 2011 United Kingdom Autism: recognition, referral and diagnosis of children and young people on the autism spectrum	<ul style="list-style-type: none"> • Clearly defined objectives and clinical questions • Systematic review of evidence • Experts, physicians, parents, psychologists engaged in development of guidelines • Recommendations are evidence-based • Major outcomes were considered (sensitivity and specificity) • Potential benefits and harms of guideline recommendation implementation provided 	<ul style="list-style-type: none"> • Barriers to implementation NR • Tools for dissemination NR

NICE = National Institute for Health and Clinical Excellence; **NR** = not reported; **QSS** = The Quality Standards Subcommittee; **TTA** = The Therapeutics and Technology Assessment Subcommittee

APPENDIX 5: Guidelines and Recommendations on Screening and Diagnosis for ASD

Guideline, Country, Indication	Recommendations
<p>Nachshen et al.³ for the Miriam Foundation</p> <p>2008</p> <p>Quebec, Canada</p> <p>Screening, Assessment and Diagnosis of Autism Spectrum Disorders in Young Children: Canadian Best Practice Guidelines</p>	<p>Screening:</p> <ul style="list-style-type: none"> • “Universal (Primary) screening for ASDs is not currently recommended.” pg. 17 • “Targeted (Secondary) screening for ASDs is recommended and requires the use of empirically validated screening tools.” pg. 17 <p>Practice:</p> <ul style="list-style-type: none"> ○ “The M-CHAT is an appropriate parent-report tool for use in second-level screening due to its ease of administration (may be given to parents in the physician waiting room) <ul style="list-style-type: none"> ▪ It is recommended that the follow-up interview is administered in conjunction with the parent-report questionnaire to increase sensitivity.” pg. 34 ○ “The CHAT is the most researched screening tool and may be tentatively recommended for second level screening. <ul style="list-style-type: none"> ▪ The Denver modification is tentatively recommended to increase sensitivity without a loss to specificity. In this scoring criteria, parents can endorse one of two critical items, pretend play AND / OR protodeclarative pointing.” pg. 34 ○ “The STAT is recommended as a second-level screener for use by professionals trained in its administration in distinguishing autistic disorder from other developmental delays.” pg. 34 ○ “The use of the ABC and GARS is not recommended.” pg. 35 ○ “There is a need to develop and utilize the expertise of other professionals (public health nurses, early childhood educators) for the purpose of screening children for ASDs.” pg. 35 <p>Diagnosis:</p> <ul style="list-style-type: none"> • “The clinical diagnosis must be in accordance with the DSM-IV-TR and/or ICD-10 diagnostic criteria.” pg. 17 <p>Practice:</p> <ul style="list-style-type: none"> ○ “Diagnoses of ASDs must be made in reference to the criteria outlined in the DSMIV-TR or the ICD-10.” pg. 47

Guideline, Country, Indication	Recommendations
	<ul style="list-style-type: none"> ○ “All five DSM axes should be considered in the full diagnostic evaluation of the individual. Although the traditional global functional assessment may not be applicable to very young children with disabilities, an effort must be made to assess the child’s general level of functioning in order to paint a more complete picture of the child and provide information relevant to treatment planning.” pg. 47 ○ “Caution should be used when applying the symptoms outlined in the DSM-IV-TR / ICD-10 to very young children.” pg. 47 ● “The diagnosis should be made on the basis of a thorough developmental history and structured behavioural observation, in conjunction with clinical judgment. The use of at least one standardized, norm-referenced parent report measure and at least one standardized, norm-referenced behavioural observation measure is recommended.” pg. 17 <p>Practice:</p> <ul style="list-style-type: none"> ○ “The combined use of the ADI-R and ADOS, in combination with clinical judgment is, at this time, the gold standard for the diagnosis of ASDs; however, a lack of ADI-R, ADOS data should not prevent a child from receiving much needed services if a diagnostician with sufficient expertise conducts the assessment.” pg. 50 ○ “The CARS may also be used in diagnostic assessments.” pg. 50 ○ “Clinical judgment, which requires significant training and experience, is critical when interpreting results of standardized measures and differentiating between the types of ASDs.” pg. 50 ○ “Whether or not empirically-validated assessment tools are used in the diagnostic process, a formal behavioural observation process and a parental interview, including a thorough developmental history, should be conducted and documented.” pg. 50 <p>Policy: “The ADOS and ADI-R should be advanced as the standard assessment protocol in assessment clinics across Canada.” pg. 50</p>

Guideline, Country, Indication	Recommendations
	<ul style="list-style-type: none"> • “The assessment of cognitive and developmental level is central to the diagnosis of ASDs.” pg. 17 <p>Practice:</p> <ul style="list-style-type: none"> ○ “Although cognitive assessments are not required for the diagnosis of an ASD, a thorough developmental assessment should be undertaken during or following the assessment process to determine the presence of an intellectual disability and to document the child’s strengths and weaknesses. This is particularly useful for intervention purposes, as the type of intervention and its success may depend on the presence and severity of cognitive delay.” pg. 53 ○ “The developmental assessment must be conducted with the use of standardized, norm-referenced instruments.” pg. 53 <p>Policy: “It is necessary to include funding for cognitive testing in the diagnostic assessment.” pg. 53</p>
<p>New Zealand autism spectrum disorder guideline⁴</p> <p>2008</p> <p>New Zealand</p>	<p>Developmental Screening^a:</p> <p>“Sensitive and specific developmental screening instruments include: (GRADE A)</p> <ul style="list-style-type: none"> • Ages and Stages Questionnaire (ASQ) • BRIGANCE Screens • Child Development Inventories (CDI) • Parents’ Evaluations of Developmental Status (PEDS).” pg. 290 Appendix 5 <p>ASD Screening Tools:</p> <p>“Autism-specific screening tools that have adequate sensitivity and specificity include: (GRADE B)</p> <ul style="list-style-type: none"> • Checklist for Autism in Toddlers (CHAT) • Autism Screening Questionnaire (ASQ).” Pg. 290, Appendix 5 <p>ASD Diagnostic Tools:</p> <p>“Diagnostic tools for autism that have been shown to have adequate sensitivity and specificity include the following: (GRADE B)</p> <ul style="list-style-type: none"> • Gilliam Autism Rating Scale (GARS). This is a checklist, DSM-IV based, with an age range of 3–22 years, giving a global rating of autism symptomatology. • Parent Interview for Autism (PIA). This is a structured interview with 118 items that takes 45 minutes to deliver.

Guideline, Country, Indication	Recommendations
	<ul style="list-style-type: none"> • Autism Diagnostic Interview – Revised (ADI-R). This is currently one of the two best available reference points for diagnosis of ASD. It is a comprehensive structured parent interview which takes one hour to deliver, with specific training and validation procedures. • Childhood Autism Rating Scale (CARS). This is a structured interview and observations with 15 items, designed for children > 24 months, which takes 30–45 minutes to deliver. • Autism Diagnostic Observation Schedule – Generic (ADOS-G). This is currently one of the two best available reference points for diagnosis. It is a semi-structured observational assessment in four modules. It gives DSM-IV and ICD-10 diagnoses with definitive cutoff scores and takes 30 to 45 minutes to deliver.” pg. 290, Appendix 5 • “The Denver II tool cannot be recommended.” (GRADE B) pg. 290, Appendix 5
<p>Filipek et al.² Reaffirmation 2010 United States Practice parameter: screening and diagnosis of autism</p>	<p>Developmental Screening^a and ASD Screening:</p> <ul style="list-style-type: none"> • “Developmental surveillance should be performed at all well-child visits from infancy through school-age, and at any age thereafter if concerns are raised about social acceptance, learning, or behavior.” pg. 5 • “Recommended developmental screening tools include the Ages and Stages Questionnaire, the BRIGANCE(R) Screens, the Child Development Inventories, and the Parents’ Evaluations of Developmental Status.”^a pg. 5 or NGC website • “Because of the lack of sensitivity and specificity, the Denver-II (DDST-II) and the Revised Denver Pre-Screening Developmental Questionnaire (R-DPDQ) are not recommended for appropriate primary-care developmental surveillance.” pg. 5 or NGC website • “Screening specifically for autism should be performed on all children failing routine developmental surveillance procedures using one of the validated instruments—the CHAT or the Autism Screening Questionnaire.” pg. 5 or NGC website <p>Diagnosis:</p> <ul style="list-style-type: none"> • “The diagnosis of autism should include the use of a diagnostic instrument with at least moderate sensitivity and good specificity for autism. Sufficient time should be planned for standardized

Guideline, Country, Indication	Recommendations
	<p>parent interviews regarding current concerns and behavioral history related to autism, and direct, structured observation of social and communicative behavior and play.” pg. 8 or NGC website</p> <ul style="list-style-type: none"> • “Recommended instruments include: <ul style="list-style-type: none"> ○ <i>Diagnostic parental interviews</i> - GARS, PIA, PDDST-II Stage 3, ADI-R ○ <i>Diagnostic observation instruments</i> – CARS, STAT, ADOS-G.” pg. 8 or NGC website
<p>NICE⁵ 2011 United Kingdom Autism: recognition, referral and diagnosis of children and young people on the autism spectrum</p>	<p>Screening: Recommendation 25: “Be aware that tools to identify children and young people with an increased likelihood of autism may be useful in gathering information about signs and symptoms of autism in a structured way but are not essential and should not be used to make or rule out a diagnosis of autism. Also be aware that:</p> <ul style="list-style-type: none"> • a positive score on tools to identify an increased likelihood of autism may support a decision to refer but can also be for reasons other than autism • a negative score does not rule out autism.” pg. 76 <p>Diagnosis: Recommendation 49: “Use information from all sources, together with clinical judgment, to diagnose autism based on ICD-10 or DSM-IV criteria.” pg.113</p> <p>Recommendation 50. “Do not rely on any autism-specific diagnostic tool alone to diagnose autism.” pg.113</p>

ABC = The Autism Behaviour Checklist; **ADOS** = Autism Diagnostic Observation Schedule; **ADI-R** = Autism Diagnostic Interview-Revised; **ASD** = Autism Spectrum Disorders; **CARS** = Childhood Autism Rating Scale; **CHAT** = Checklist for Autism in Toddlers; **DSM** = Diagnostic and Statistical Manual of Mental Disorders; **(DSM)-IV-TR** = Diagnostic and Statistical Manual of Mental Disorders; **GARS** = Gilliam Autism Rating Scale, **ICD-10** = International Classification of Diseases; **M-CHAT** = Modified Checklist for Autism in Toddlers; **NGC** = National Guideline Clearinghouse; **NICE** = National Institute for Health and Clinical Excellence; **PDDST-II** = The Pervasive Developmental Disorders Screening Test–Stage 3; **PIA** = The Parent Interview for Autism; **STAT** = Screening Tool for Autism in Two-Year-Olds

^a Developmental screening tools found in Table 1, Appendix 2

APPENDIX 6: ADDITIONAL TABLES

Table 4: Recommendations for Various Developmental Screening Tools Prior to Actual ASD Screening^{2,4}

Tools	Recommendations
ASQ	Recommended for use; ^b Strength - Guideline ^a
BRIGANCE(R) Screens	Recommended for use; ^b Strength - Guideline ^a
CDI	Recommended for use; ^b Strength - Guideline ^a
DDST-II	Not recommended for primary-care developmental surveillance; Strength - Guideline ^a
PEDS	Recommended for use; ^b Strength - Guideline ^a
R-DPDQ	Not recommended for primary-care developmental surveillance; Strength - Guideline ^a

ASQ = Ages and Stages; **CDI** = Child Development Inventories; **DDST-II** = (formerly the) Denver Developmental Screening Test-Revised; **PEDS** = Parents' Evaluations of Developmental Status; **R-DPDQ** = The Revised Denver Pre-Screening Developmental Questionnaire

^a Definitions of the strength of the recommendations (Standard, Guideline, Practice Option), Appendix 3.²

^b Sensitive and specific developmental screening instrument⁴

Table 5: ASD Screening Tool Sensitivity and Specificity Ranges Reported by Nachshen et al.³

Tools	Sensitivity range	Specificity range
ABC	0.38 – 0.71	0.70 – 0.97
CHAT	0.18 – 0.65, 0.75- 0.85 ^a	0.98 – 1.0, 0.92 - 1.0 ^a
GARS	0.48 ^b	NR
M-CHAT	0.77 - 0.97	0.27 - 0.99
PDDST II	0.73 - 0.92	0.49 - 0.91
STAT	0.83 – 0.92	0.85 – 0.86
SCQ	0.79 – 0.96	0.54 – 0.80

ABC = The Autism Behaviour Checklist; **CHAT** = Checklist for Autism in Toddlers; **GARS** = Gilliam Autism Rating Scale; **M-CHAT** = Modified Checklist for Autism in Toddlers; **NR** = not reported; **PDDST II** = Pervasive Developmental Disorder Screening Test-II; **STAT** = Screening Tool for Autism in Two-Year-Olds; **SCQ** = Social Communication Questionnaire

^a CHAT with Denver Modification.

^b No range reported.

Table 6: Other^a Recognized Screening and Diagnostic Tools^{4,5}

Screening Tools		
Tools	Type of Tool	Child age
3di ⁴	Computerized assessment for ASDs	NR
AQ ⁴	Self-administered	For those suspected of having Asperger's syndrome or High Functioning Autism
CAST ⁴	Parent-completed screening test ⁴	5–11 years
DBC-ES ⁵	Parent or carer instrument (17 items)	18-48 months
DISCO ⁴	Clinician-administered schedule	All ages

Screening Tools		
Tools	Type of Tool	Child age
GADS ⁴	Scale for use by parents and professionals for assessing Asperger's syndrome ⁴	3–22 years
KADI ⁴	Scale for use by professionals assessing Asperger's syndrome	6–22 years
SCQ ⁵	Parent questionnaire (40 items)	> 4 years with mental age >2 years
Diagnostic Tools		
Tools	Type of Tool	Child age
ASAS ⁴	Checklist for parents	Primary school children
ASDI ⁴	Clinical-administered	Children and adults suspected of having Asperger's syndrome or High Functioning Autism

3di = Developmental, Diagnostic and Dimensional Interview; **ASAS** = Australian Scale for Asperger's syndrome; **ASDI** = Asperger Syndrome Diagnostic Interview; **AQ** = Autism Spectrum Quotient; **CAST** = Childhood Asperger Syndrome Test; **DBC-ES** = Developmental Behavior Checklist – Autism – Early Screen; **DISCO** = Diagnostic Interview for Social and Communication Disorders; **GADS** = Gilliam Asperger's Disorder Scale; **KADI** = Krug Asperger's Disorder Index; **NR** = not reported; **SCQ** = Social Communication Questionnaire

^a Recommendations were not provided for these tools.