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[Diagnostic Test Accuracy Review]

Diagnostic tests for autism spectrum disorder (ASD) in preschool children

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ABSTRACT

Background

Autism spectrum disorder (ASD) is a behaviourally diagnosed condition. It is defined by impairments in social communication or the presence of restricted or repetitive behaviours, or both. Diagnosis is made according to existing classification systems. In recent years, especially following publication of the *Diagnostic and Statistical Manual of Mental Disorders - Fifth Edition (DSM-5; APA 2013)*, children are given the diagnosis of ASD, rather than subclassifications of the spectrum such as autistic disorder, Asperger syndrome, or pervasive developmental disorder - not otherwise specified. Tests to diagnose ASD have been developed using parent or carer interview, child observation, or a combination of both.

Objectives

Primary objectives

1. To identify which diagnostic tools, including updated versions, most accurately diagnose ASD in preschool children when compared with multi-disciplinary team clinical judgement.
2. To identify how the best of the interview tools compare with CARS, then how CARS compares with ADOS.
 - a. Which ASD diagnostic tool - among ADOS, ADI-R, CARS, DISCO, GARS, and 3di - has the best diagnostic test accuracy?
 - b. Is the diagnostic test accuracy of any one test sufficient for that test to be suitable as a sole assessment tool for preschool children?
 - c. Is there any combination of tests that, if offered in sequence, would provide suitable diagnostic test accuracy and enhance test efficiency?
 - d. If data are available, does the combination of an interview tool with a structured observation test have better diagnostic test accuracy (i.e. fewer false-positives and fewer false-negatives) than either test alone?

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As only one interview tool was identified, we modified the first three aims to a single aim (Differences between protocol and review): This Review evaluated diagnostic tests in terms of sensitivity and specificity. Specificity is the most important factor for diagnosis; however, both sensitivity and specificity are of interest in this Review because there is an inherent trade-off between these two factors.

Secondary objectives

1. To determine whether any diagnostic test has greater diagnostic test accuracy for age-specific subgroups within the preschool age range.

Search methods

In July 2016, we searched CENTRAL, MEDLINE, Embase, PsycINFO, 10 other databases, and the reference lists of all included publications.

Selection criteria

Publications had to:

1. report diagnostic test accuracy for any of the following six included diagnostic tools: Autism Diagnostic Interview - Revised (ADI-R), Gilliam Autism Rating Scale (GARS), Diagnostic Interview for Social and Communication Disorder (DISCO), Developmental, Dimensional, and Diagnostic Interview (3di), Autism Diagnostic Observation Schedule - Generic (ADOS), and Childhood Autism Rating Scale (CARS);
2. include children of preschool age (under six years of age) suspected of having an ASD; and
3. have a multi-disciplinary assessment, or similar, as the reference standard.

Eligible studies included cohort, cross-sectional, randomised test accuracy, and case-control studies. The target condition was ASD.

Data collection and analysis

Two review authors independently assessed all studies for inclusion and extracted data using standardised forms. A third review author settled disagreements. We assessed methodological quality using the QUADAS-2 instrument (Quality Assessment of Studies of Diagnostic Accuracy - Revised). We conducted separate univariate random-effects logistical regressions for sensitivity and specificity for CARS and ADI-R. We conducted meta-analyses of pairs of sensitivity and specificity using bivariate random-effects methods for ADOS.

Main results

In this Review, we included 21 sets of analyses reporting different tools or cohorts of children from 13 publications, many with high risk of bias or potential conflicts of interest or a combination of both. Overall, the prevalence of ASD for children in the included analyses was 74%.

For versions and modules of ADOS, there were 12 analyses with 1625 children. Sensitivity of ADOS ranged from 0.76 to 0.98, and specificity ranged from 0.20 to 1.00. The summary sensitivity was 0.94 (95% confidence interval (CI) 0.89 to 0.97), and the summary specificity was 0.80 (95% CI 0.68 to 0.88).

For CARS, there were four analyses with 641 children. Sensitivity of CARS ranged from 0.66 to 0.89, and specificity ranged from 0.21 to 1.00. The summary sensitivity for CARS was 0.80 (95% CI 0.61 to 0.91), and the summary specificity was 0.88 (95% CI 0.64 to 0.96).

For ADI-R, there were five analyses with 634 children. Sensitivity for ADI-R ranged from 0.19 to 0.75, and specificity ranged from 0.63 to 1.00. The summary sensitivity for the ADI-R was 0.52 (95% CI 0.32 to 0.71), and the summary specificity was 0.84 (95% CI 0.61 to 0.95).

Studies that compared tests were few and too small to allow clear conclusions.

In two studies that included analyses for both ADI-R and ADOS, tests scored similarly for sensitivity, but ADOS scored higher for specificity. In two studies that included analyses for ADI-R, ADOS, and CARS, ADOS had the highest sensitivity and CARS the highest specificity.

In one study that explored individual and additive sensitivity and specificity of ADOS and ADI-R, combining the two tests did not increase the sensitivity nor the specificity of ADOS used alone.

Performance for all tests was lower when we excluded studies at high risk of bias.

Authors' conclusions

We observed substantial variation in sensitivity and specificity of all tests, which was likely attributable to methodological differences and variations in the clinical characteristics of populations recruited.

When we compared summary statistics for ADOS, CARS, and ADI-R, we found that ADOS was most sensitive. All tools performed similarly for specificity. In lower prevalence populations, the risk of falsely identifying children who do not have ASD would be higher.

Now available are new versions of tools that require diagnostic test accuracy assessment, ideally in clinically relevant situations, with methods at low risk of bias and in children of varying abilities.

PLAIN LANGUAGE SUMMARY

How accurate are diagnostic tools for autism spectrum disorder in preschool children?

Review question

How accurate are tools for diagnosing autism spectrum disorder (ASD) in preschool children?

Why is accurate ASD diagnosis important?

Not diagnosing ASD in children when it is present (false-negative result) means children with ASD may miss receiving early intervention and families may miss receiving timely support and education. An incorrect diagnosis of ASD (false-positive result) may cause family stress, lead to unnecessary investigations and treatments, and place greater strain on already limited service resources.

What is the aim of this Review?

To find out which of the commonly used tools is most accurate for diagnosing ASD in preschool children. Cochrane researchers reviewed 13 published articles to answer this question.

What was studied in the Review?

Six tests were reviewed: Four gathered information about children's behaviours from interviews with parents or carers (Autism Diagnostic Interview-Revised (ADI-R), Gilliam Autism Rating Scale (GARS), Diagnostic Interview for Social and Communication Disorder (DISCO), and Developmental, Dimensional, and Diagnostic Interview (3di)); one required that a trained professional observe a child's behaviour on specific tasks (Autism Diagnostic Observation Schedule (ADOS)); and one combined observation of the child with interview of parents or carers (Childhood Autism Rating Scale (CARS)).

What are the main results of the Review?

The Review included 21 relevant sets of analyses conducted on a total of 2900 children. Results were available for only three tools: ADOS (Modules 1 and 2), CARS, and ADI-R. If instruments were applied to 1000 children, 740 of whom had ASD, then 696, 592, and 385 children would be correctly identified by ADOS, CARS, and ADI-R, respectively, whereas 52, 31, and 42 children without ASD would be incorrectly classified as having ASD. Of 260 children without ASD, 208, 229, and 218 would be correctly classified by ADOS, CARS, and ADI-R, respectively, whereas 44, 148, and 355 children with ASD would be incorrectly classified as not having ASD.

See [Figure 1](#).

One publication looked at using ADI-R together with ADOS and found that use of both tools together was no more accurate than use of ADOS alone.

How reliable are the results of analyses in this Review?

Using a variety of best-estimate clinical approaches led to diagnosis in children. This method is commonly used in research but does not always replicate the multi-disciplinary assessment recommended for clinical diagnosis.

Problems with how some studies were conducted and the presence of conflicts of interest in some publications may result in ADOS, CARS, and ADI-R appearing more accurate than they really are. Also, if these tools are used in populations with a lower prevalence of ASD, a higher proportion of children who do not have ASD are likely to receive an ASD diagnosis.

The numbers shown above represent average values across analyses. However, as individual estimates varied, we cannot be sure that ADOS will always produce these results. Numbers of children included in studies conducted to date, including studies comparing the accuracy of different tools, are insufficient to evoke confidence in these results.

Who do results of the Review apply to?

Studies included were carried out in Australia, Canada, India, the Netherlands, United Kingdom, and United States. Studies included children younger than six years of age, or children with a mean age less than six years, with language difficulties, developmental delay, intellectual disability, or a mental health problem, presenting to a clinical service or enrolling in a research study.

What are the implications of this Review?

Current findings suggest that ADOS is best for not missing children who have ASD and is similar to CARS and ADI-R in not falsely diagnosing ASD in a child who does not have ASD. ADOS has acceptable accuracy in populations with a high prevalence of ASD. However, overdiagnosis is likely if the tool is used in populations with a lower prevalence of ASD. This finding supports current recommended practice for ASD diagnostic tools to be used as part of a multi-disciplinary assessment, rather than as stand-alone diagnostic instruments.

How up-to-date is this Review?

This Review was up-to-date as of July 2016.