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Efficacy of Modified Checklist for Autism in Toddlers, Revised, with Follow-up: A systematic review

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Keywords: Autism; CHAT R/F; Neurological disorder.

Abstract

Background: When children with Autism Spectrum Disorder (ASD) are diagnosed early, their behavioral and developmental results improve, making early screening a crucial step in intervention. The Modified Checklist for Autism in Toddlers (M-CHAT) is a widely used screening tool designed to identify early signs of ASD in young children. Its revised version, M-CHAT R/F (Revised with Follow-Up), enhances its accuracy by incorporating follow-up evaluation. Given its extensive use in clinical and research settings, we aimed to evaluate the diagnostic performance and its effectiveness in diverse populations.

Methodology: Studies assessing the diagnostic accuracy of M-CHAT R/F for ASD were included. Observational and validation studies were considered, while case reports, editorials, and studies lacking diagnostic accuracy data were excluded.

Results: In a Chinese cohort of 7,982 toddlers, the tool demonstrated a high Positive Predictive Value (PPV) of 0.91 among high-risk children. A significant improvement in PPV when follow-up interviews were included, particularly in low-risk populations was reported. Research conducted in Iceland, Spain, and France further supported the M-CHAT-R/F's reliability, with varying PPVs across different age groups. Screening of high-risk children showed a higher PPV (0.531) compared to low-risk children (0.138), with follow-up improving screening accuracy.

Conclusion: The M-CHAT-R/F is an effective tool for early detection overall, but in order to improve accuracy and minimize needless concerns, it should be used in conjunction with follow-up evaluations.

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Introduction

The condition known as Autism Spectrum Disorder (ASD) is characterized by limited, repetitive behaviours and difficulties with social communication [1]. When self-withdrawal occurred in schizophrenia patients, the term "autism" was first used to diagnose them. However, it was reinterpreted in the 1940s by Drs. Leo Kanner and Hans Asperger describe a syndrome in children characterized by rigid and repeated routines, as well as difficulty with social interaction and communication [2]. Speech, social interaction, and repetitive or limited actions are the three classic characteristics of ASD. However, it is also associated with a number of physiological and psychological disorders. The signs of ASD typically begin in early childhood, and a child usually gets a diagnosis by the time they are three years old. Early indicators of ASD before this age could include the inability to sustain eye contact and a lack of reaction to one's name [3]. Most symptoms, particularly those related to social and cognitive functioning, continue into adulthood. Over time, though, communication abilities could become more effective, particularly in growing up and development. IQ and intellectual functioning typically remain unchanged over time. India's cultural and socioeconomic variety may have an impact on how the autistic phenotype manifests. In other nations, it has also been demonstrated that socioeconomic factors influence the occurrence of autism. Social communicative deficiencies appear in the framework of cultural norms, especially in those on the Asperger end of the autism spectrum. Therefore, cultural influences may influence the presence and perception of specific symptoms [4]. Along with specialized interventions and accommodations, a robust social support system can enhance the quality of life for those with ASD [5].

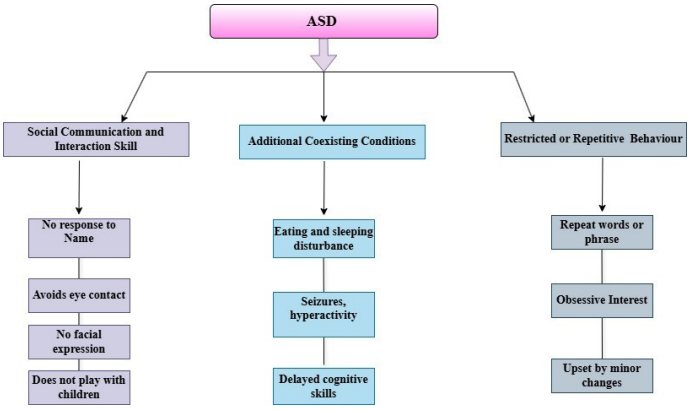

Figure 1: Clinical features of ASD.

According to a 2009–2017 study, 17% of children between the ages of 3 and 17 have a developmental condition such as autism or attention-deficit disorder. With reported worldwide rates ranging from 0.01% to 4.4%, the estimated prevalence of ASD is 1.0% [6]. East Asia had the highest rates (51/1000), followed by West Asia (3.5/1000) and South Asia (3.1/1000) [7]. However, The prevalence of ASD is still unclear as different countries and continents have different prevalence rates reported by studies. Considering there are few diagnostic and assessment methods available in low-income countries, case counts remain uncertain [8].

ASD is thought to have a complex etiology that includes both genetic and non-genetic components. There are two types of ASD: syndromic and non-syndromic. Usually, monogenic changes or chromosomal abnormalities are associated with syndromic ASD [9] Non-genetic risk factors involve various paternal and maternal contributing factors [9].

Brain function and development have been the main focus of ASD studies for many years. Both postmortem and clinical studies have revealed morphological and cellular CNS diseases, including those in neurons and glial cells. It appears that diseases associated with ASD extend beyond the central nervous system, according to recent studies on immunological responses and gut-brain interaction.

As early as 18 to 24 months, autism can be diagnosed since its distinctive symptoms can be distinguished from those of other developmental delays or disorders. In order to diagnose ASD at the youngest age possible, research has focused extensively on developing efficient screening techniques. This has been in line with initiatives to start therapeutic and educational treatments promptly [10]. Early detection of autism in children leads to better developmental and behavioral outcomes, making early screening a crucial step in intervention. The Modified Checklist for Autism in Toddlers (M-CHAT) is a widely used screening tool designed to identify early signs of ASD in young children. Its revised version, "M-CHAT R/F (Revised with Follow-Up)", enhances its accuracy by incorporating a follow-up evaluation to reduce false positives. Assessing the diagnostic performance of M-CHAT R/F, cultural adaptations, and psychometric qualities is crucial to guaranteeing its efficacy in a variety of communities, given its widespread use in clinical and research contexts. M-CHAT- Revised with Follow-Up (M-CHAT-R/F) is one of the most studied and widely used screening tools for ASD. It is recommended by several national guidelines due to its high sensitivity and ease of administration, particularly for children who are at high risk. 58 different languages and dialects have been translated into it. Tools for screening should be quick, simple, and dependable in order to be used widely and effectively. The M-CHAT-R/F is a two-stage ASD screening tool that has demonstrated adequate sensitivity and specificity [11]. However, the efficacy of M-CHAT-R/F in Chinese Han toddlers has not been thoroughly studied. Its accuracy is dependent on the way parents complete the symptom checklist, similar to other screening questionnaires. Parental underreporting of symptoms may result in an incorrect diagnosis [12]. Given that M-CHAT-R/F is widely used for ASD screening, it is essential to examine its psychometric properties outside of the validation research and use translated versions to evaluate its sensitivity and specificity across a range of groups.

Objective

The primary objective of this systematic review was to evaluate the diagnostic accuracy of M-CHAT R/F in ASD screening.

Methodology

Study design

The present systematic review was performed following "Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines". Studies were included if they assessed the diagnostic performance of M-CHAT R/F as a screening tool for ASD and reported relevant diagnostic accuracy metrics such as sensitivity, specificity, Positive Predictive Value (PPV), and Negative Predictive Value (NPV). Observational studies and validation studies were included, while case reports, editorials, conference abstracts, and studies lacking sufficient diagnostic accuracy data were excluded (Table 1).

Table 1: Eligibility criteria.

Criteria	Description
Population	Children screened using M-CHAT R/F for ASD irrespective of gender, ethnicity, or geographic location.
Intervention	Use of **M-CHAT R/F** as a screening tool for detecting early signs of ASD.
Comparison	Studies with comparison with M-CHAT without follow-up interview
Outcome	Primary: Sensitivity, specificity, Positive Predictive Value (PPV), and Negative Predictive Value (NPV) of M-CHAT R/F. Secondary: Diagnostic accuracy, feasibility, language adaptations, and effectiveness
Study design	Observational and validation studies evaluating the performance of M-CHAT R/F in ASD screening.

Study selection

The literature search was conducted in PubMed, Google Scholar, Scopus, and PsycINFO. The search strategy incorporated "Medical Subject Headings (MeSH) terms" and relevant keywords, such as "M-CHAT R/F" OR "Modified Checklist for Autism in Toddlers Revised", "Autism Spectrum Disorder screening" OR "ASD early detection", "M-CHAT validity" OR "M-CHAT reliability", and "Autism diagnostic tools". Boolean operators (AND, OR, NOT) were applied to refine the search.

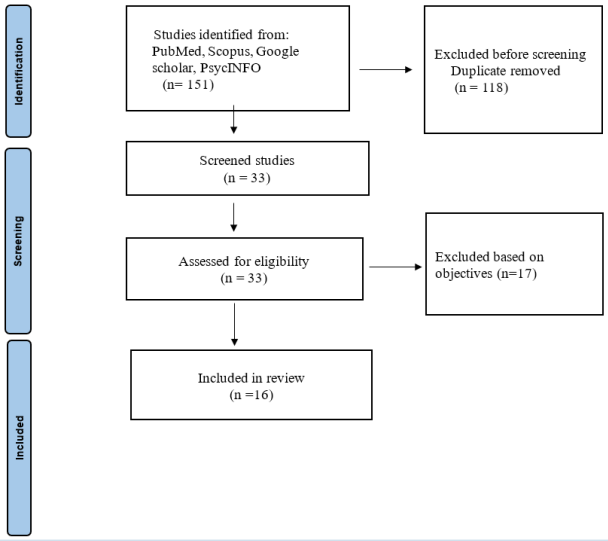

Figure 2: Flowchart of study selection.

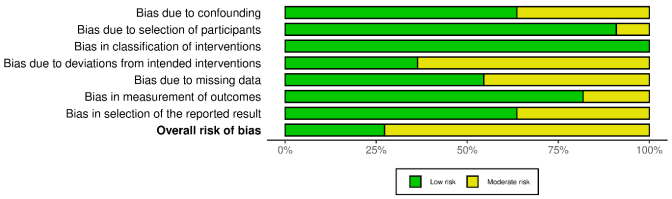

Figure 3: Distribution of risk of bias judgment.

Table 2: Patient characteristics.

Study	Sample Size	Mean age with SD	Male	Female	Study location
Guo C et al 2019 [16]	4391	22.69±4.05	4391	-	US
Robins DL et al 2008 [15]	16071	26.23+5.45 months	175	88	China
Kleinman JM et al 2008 [17]	3793	24.79+3.06	2003	1743	US
Jonsdottir SL et al 2022 [18]	1586	31.66+1.72	801	20	Iceland
Magán-Maganto M et al 2020 [19]	3529	18.22+0.72	1805	1621	Spain
Ozgur Oner et al 2020 [20]	6712	26.75+5.76	3179	2990	Turkey
Bradbury K et al 2020 [13]	175	22.81+3.98	101	72	US
Christopher et al 2021 [14]	290	32.8+7.7	218		US
Jung-Mei Tsai 2019 [21]	317	24.3+4.4	167	150	Taiwan
Sophie Baduel et al 2017 [22]	1250	24 months old age group	663	587	France
Modibo Sangare et al 2019 [23]	947	7.64+3.85	139	834	West Africa

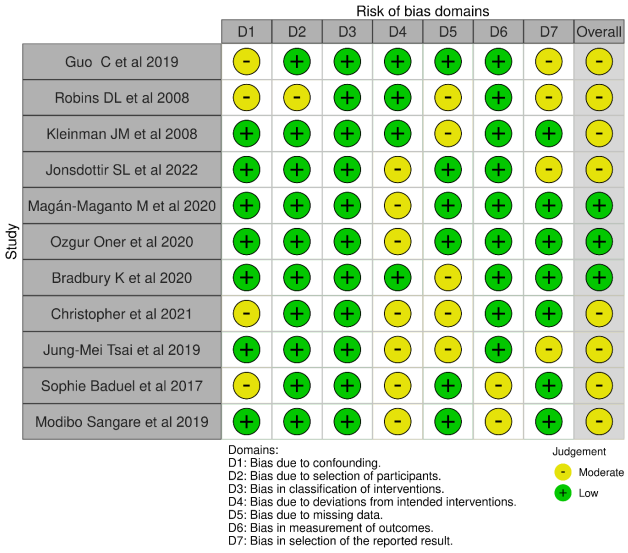

Figure 4: Traffic plot representation of risk assessment.

Assessment of quality of study

The domains considered were as per ROBINS-I tool, as follows: "risk of bias due to confounding (D1), bias due to selection of participants (D2), bias in classification of interventions (D3), bias due deviation from intended interventions (D4), and bias due to missing data (D5), risk of bias arising from the measurement of outcome (D6) and risk of bias in the selection of reported result (D7)" Figure 3 & 4.

Result

Patient characteristics

The included studies exhibit significant variation in sample sizes, ranging from small cohorts, such as Braddhur et al. (175 participants) [13] and Christopher et al. (290 participants) [14], to large-scale studies (16,071 participants) [15] and Guo et al (4,391 participants) [16]. The mean age of participants reported from the youngest cohort (18.22±0.72 years) and to the oldest (31.66±1.72 years) (Table 2).

Outcome analysis

The outcome analysis of the reviewed studies is summarised in Table 3. Guo et al validated M-CHAT-R/F among 7982 toddlers in the Chinese population of age group 16-30 months. Of the 1,140 children who tested positive for M-CHAT-R/F at first, 575 were recommended for the follow-up. 67.5% of them stopped screening positive. Based on the clinician's observations, 33 of them were referred for additional assessment. Of the 565 who missed follow-up, 335 from hospitals completed diagnostic evaluation. Among children who initially screened positive for M-CHAT-R, 17.7% had developmental concerns. Of the 77 high-risk children who completed an evaluation, 70 were diagnosed with developmental, resulting in a Positive Predictive Value (PPV) of 0.91. These findings highlight its efficiency in early ASD detection [16].

3,793 children aged 16 to 30 months were evaluated by the M-CHAT in the Jamie et al. study; those who tested positive were given diagnostic evaluation, and 1,416 children aged 42 to 54 months were rescreened to compare the PPV at two-time points. The initial screening had a low PPV in the low-risk sample (0.11) but was higher in the high-risk sample (0.60). When combined with the follow-up interview, PPV improved significantly to 0.65 in the low-risk group and 0.76 in the high-risk group, resulting in an overall PPV of 0.74. This highlights the importance of follow-up interviews in enhancing screening accuracy, particularly in low-risk populations. On reassessment, the initial screening at time 1 had a PPV of 0.38, which improved to 0.59 when combined with the follow-up interview [17].

In order to verify the M-CHAT-R/F in an Icelandic population, Srigdhar et al. screened 1,586 children at 30 months with a minimum follow-up of two years. Of the 29 diagnoses for ASD, 18 were accurately classified as true positives and 11 were confirmed as false negatives [18].

Table 3: Outcome analysis.

Study	Positive predictive value	Negative predictive value	Sensitivity	95%CI (Sensitivity)	Specificity	95%CI (Specificity)
Guo C, et al 2019 [16]	6.9	100	96.3	89.7-99.2	86.4	85.7-87.2S
Robins DL, et al 2008 [15]	0.509	0.997	0.66	0.58-0.75	0.995	0.99-0.99
Jonsdottir SL, et al 2022 [18]	0.72	0.97	0.95	0.85-1.00	0.84	0.73-0.95
Magán-Maganto M, et al 2020 [19]	0.47(0.25-0.71	0.99	0.82	0.48-0.97	0.99	0.99-0.99
Ozgur Oner, et al 2020 [20]	0.26	1	100	-	0.67	-
Christopher K, et al 2021 [14]	0.79	0.40	0.90	-	0.22	-
Tsai JM, et al 2019 [21]	0.53	0.99	0.86	0.65-0.97	0.94	0.91-0.97
Baduel S, et al 2017 [22]	0.60	0.99	0.67	0.41-0.86	0.94	0.92-0.95
Modibo Sangare et al 2019 [23]	1	0.87	0.50	0.08-0.91	1	0.77-1

M-CHAT-R/F screening of children aged 14–22 months in Spain revealed that 97 out of the 106 children who tested positive needed a follow-up assessment, with 22.7% remaining positive, 55.7% screening negative, and 21.6% being unavailable. Alternate neurodevelopmental diagnoses were made for most of the 10 cases that were found to be false positives. Even though two of the cases had language impairments, only three instances lacked a DSM-5 neurodevelopmental diagnosis, underscoring the importance of careful monitoring and evaluation [19]. Ozgur Oner et al showed that 9.8% of positive cases at the initial stage were in the low-risk group among the 16-36 age group, whereas 39.7% of positive cases were reported on follow-up interviews [20].

The screening of 187 high-risk children of 18-24 months was conducted by Bradbury et al using M-CHAT R/F compared with findings in the low-risk group. At the first screening, the high-risk sample's PPV for ASD was considerably greater than the LR sample's, with values of 0.531 for HR and 0.138 for low-risk. The PPV values for the high-risk and low-risk samples were similar by follow-up, with 0.607 and 0.488, respectively. Furthermore, the low-risk sample showed a substantial increase at Follow-Up for ASD, whereas the HR sample's PPV was constant between the initial evaluation and assessment on follow-up [13].

M-CHAT-R/F was found to be high AUC among the age group of 18-30 months with 0.706 and slightly low in 18-48 months with 0.650. Whereas the AUC was decreased to 0.613 in the 31-48 months of age group [14]. Further, the validation study showed that the M-CHAT-R/F-T was successful in identifying toddlers at risk for ASD with a high false-positive rate (0.47) and a strong PPV (0.91) for diagnosing ASD in the 16–30-month age group. These results reinforce the utility of the M-CHAT-R/F-T in early identification efforts [21].

Comparison of M-CHAT R/F to original versions

Among children of the age group 24-month-old from the French population, Sophie Baduel aimed to validate the M-CHAT. In the low-risk cohort, 12 out of 1227 children were diagnosed with ASD, yielding a PPV of 0.60 at 36 months. Initially, the screening positive cases were 79%. Twenty individuals tested positive at follow-up, and 12 of those cases received an ASD diagnosis. The validity of the M-CHAT both by itself and in combination with follow-up has been further examined. With the M-CHAT, the NPV was 0.99 and the PPV was 0.14. However, when paired with the subsequent interview, the PPV increased to 0.60, while the NPV remained at 0.99 [22].

Colby et al initially compared the utility of M-CHAT with M-CHAT-F by screening 18989 toddlers. Screen-positive children with M-CHAT underwent the M-CHAT/F and those who remained positive after the follow-up received a diagnostic evaluation. 54% of children who tested positive on the M-CHAT and M-CHAT/F had ASD, and 98% of them had developmental issues. M-CHAT detects almost all screen-positive patients with a score cutoff of ≥3. Furthermore, a practical clinical cutoff of ≥7 enables physicians to skip the M-CHAT/F and move straight on to evaluation and intervention [24]. In line with this, Robbins et al compared M-CHAT R/F with M-CHAT-F, and the initial screen-positive rate showed a significant decline, decreasing from 9.15% to 7.17%. However, the PPV of the two-stage screening process remained comparable between versions, with no significant difference (P=.492). In the comparison, the M-CHAT-R/F

demonstrated a significantly higher detection rate, with 67 cases per 10,000 being identified, whereas the original M-CHAT/F detected 45 cases per 10,000, and the difference was statistically significant [15].

Further on comparison study among the Iceland population, true positive cases were 6.83±3.66 and false positive cases were 5.86±2.55 in M-CHAT-R, whereas M-CHAT R/F had 6.00±3.61 and FP of 4.29±2.87, indicating relatively lower FP cases. The M-CHAT-R's internal consistency was insufficient (α=0.677), and excluding foil items relating to motors had little effect. The removal of two items relating to hearing, however, raised reliability to a respectable level (α=0.745). Following the follow-up interview, the M-CHAT-R/F showed good internal consistency (α=0.831), emphasizing the value of follow-up in enhancing screening reliability [18].

Discussion

The M-CHAT-R successfully distinguished children at risk for ASD from children who are usually developing. M-CHAT-R/F with follow-up evaluation as part of its updated format, accuracy is increased by reducing false positives while preserving high sensitivity for ASD detection. A validation study by Robbins et al [15] showed a lower positive rate at the initial stage compared to Guo et al [16] This suggests that the false positive rate is relatively higher in China compared to the US. However, screening in marginalized populations or developing nations indicates that social, educational, and cultural factors may have an impact on variations in positive rates. A lack of health literacy, medical resources, or parenting expertise may cause people to mistake the questionnaire's actual purpose [25]. Guo et al. reported that as it takes more time for caregivers with lower incomes or educational levels to complete questionnaires on their own, they frequently prefer verbal instructions over written ones. These parents needed additional support with developmental evaluations and screening [16]. M-CHAT-R/F's sensitivity was noticeably higher than that of the physician's clinical judgment. However, ASD detection rates were significantly increased when both approaches were used together, demonstrating that routine developmental surveillance and standardized screening improve early ASD identification.

Children without an ASD diagnosis had a higher level of impairment in the high-risk group, most likely due to prior developmental problems. Nonetheless, ASD diagnoses from high- and low-risk groups shared comparable clinical and demographic traits in the Jamie et al study. Despite differences in PPV and screening outcomes between high- and low-risk samples, the M-CHAT effectively identified similar ASD cases across both groups. Prior to the follow-up interview, the M-CHAT's low PPV in unselected populations was its primary drawback. Particularly for cases with fewer failed items, the telephone interview is crucial to reducing needless referrals [17]. A higher cutoff may be considered by pediatricians screening low-risk populations in an effort to increase PPV, although performing thus carries the risk of missing cases. In comparison to the low-risk sample, the high-risk sample showed greater PPV for ASD, which was noticeably greater at the initial screen but became comparable at follow-up. The high-risk sample's PPV remained the same during the first screening and follow-up for ASD. In contrast, the PPV for the low-risk sample increased at follow-up for both ASD and any developmental delay, suggesting improved predictive accuracy over time in this group [13].

A PPV of 0.60 was found when the M-CHAT and the follow-up were combined, indicating that over 60% of children who tested positive on both tests were diagnosed with ASD. The M-CHAT, on the other hand, had a PPV of 0.14 when used alone, which indicates that only around 10% who tested positive were eventually diagnosed with ASD. The screening with M-CHAT alone is not advised for screening in a low-risk, general population because of its unacceptable low PPV. The follow-up is used to collect more data on a child's risk status, which improves the test's overall performance and assists in reducing pointless referrals and parental concerns [22].

Overall, the sensitivity and specificity of M-CHAT R/F vary across studies due to differences in methodology and sample populations, which limits its clinical applicability. Despite this variability, M-CHAT(-R/F) remains a valuable screening tool for identifying children at risk for ASD. However, in High-Risk (HR) samples where multiple developmental disorders are present, specificity tends to decrease, even though sensitivity remains consistently high across groups. This emphasizes the importance of thorough assessments for precise differential diagnosis. Additionally, the tool remains in use for screening up to 48 months, but with reduced sensitivity in older children, even though it was validated among children in the age group of 16 and 30 months. Comparing sensitivity across ASD screening studies is challenging due to variations in study execution. Key differences include follow-up duration, methods for detecting initially missed cases, child age at screening, versions of the M-CHAT used, racial and ethnic diversity, and ASD prevalence in the screened populations. Additionally, it's possible that the questionnaire's wording was unintentionally changed during translation into other languages. Local and cultural factors may also affect the way they are interpreted, which could alter the definition of a positive screen compared to screening in English [26].

Particularly in the initial screening, the PPV was low despite the excellent sensitivity and specificity. In order to decrease false positive results, the follow-up interview is therefore an essential methodological and ethical step. The M-CHAT(-R/F) is an effective tool for early detection overall, but in order to improve accuracy and minimize needless concerns, it should be used in conjunction with follow-up evaluations. A positive screening result led to earlier diagnosis and intervention, potentially improving outcomes. While the M-CHAT-R/F showed moderate sensitivity, incorporating additional strategies, such as focused ASD observation, could help reduce false negatives. However, ASD screening remains challenging, as no tool achieves perfect sensitivity and specificity. Therefore, providers should complement validated screening tools with ongoing developmental surveillance [16].

Conclusion

All children at elevated risk for ASD cannot be identified by a single measure, however, the M-CHAT(-R/F) demonstrates high overall sensitivity and specificity. According to studies, identifying children who are more likely to develop ASD and ensuring prompt access to early intervention treatments tailored to their needs depend on early and repeated screening. Furthermore, the parent-reported screening nature of the M-CHAT-R/F tool may lead to unreliable results if parents are unaware of the predicted social-communication stages, which may compromise the PPV of the tool. While sensitivity and specificity are not significantly impacted by the choice between the original and updated versions of the M-CHAT, screening accuracy increases substantially with subsequent follow-up. As the follow-up eval-

uation greatly reduces false-positive rates, fewer unnecessary referrals are made, and the burden on diagnostic and intervention systems is alleviated.

Author declarations

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