Development of clinical prediction rule for diagnosis of autistic spectrum disorder in children

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Abstract

Purpose – This study aims to develop a clinical prediction rule for the diagnosis of autistic spectrum disorder (ASD) in children.

Design/methodology/approach – This population-based study was carried out in children aged 2 to 5 years who were suspected of having ASD. Data regarding demographics, risk factors, histories taken from caregivers and clinical observation of ASD symptoms were recorded before specialists assessed patients using standardized diagnostic tools. The predictors were analyzed by multivariate logistic regression analysis and developed into a predictive model.

Findings – An ASD diagnosis was rendered in 74.8 per cent of 139 participants. The clinical prediction rule consisted of five predictors, namely, delayed speech for their age, history of rarely making eye contact or looking at faces, history of not showing off toys or favorite things, not following clinician’s eye direction and low frequency of social interaction with the clinician or the caregiver. At four or more predictors, sensitivity was 100 per cent for predicting a diagnosis of ASD, with a positive likelihood ratio of 16.62.

Originality/value – This practical clinical prediction rule would help general practitioners to initially diagnose ASD in routine clinical practice.

Keywords Autistic spectrum disorder, Autism, Autistic, Prediction, Diagnosis

Paper type Research paper

Introduction

Autistic spectrum disorder (ASD) is a neurodevelopmental disorder with a prevalence of 1:68 in children (Christensen, 2016; American Psychiatric Association, 2013). Early diagnosis with early intervention yield ameliorated long-term outcomes (Filipek et al., 2000; Granpeesheh et al., 2009; Landa, 2008). Because ASD is a disorder with a multitude of signs and symptoms, the diagnosis process requires massive history taking from the caregiver together with time-consuming clinical observation by experienced clinicians (Wing, 1988; Falkmer et al., 2013). Doctors working in countries with inadequate specialists and resources are challenged by the ASD diagnosis. These general practitioners, limited by time and experience, may underdiagnose ASD, resulting in delayed treatment. Having clear and concise predictors to facilitate the initial diagnosis of ASD in busy clinical practice would benefit both doctors and patients (Zwaigenbaum et al., 2015). This study aimed to develop a prediction rule for the diagnosis of ASD in children from baseline characteristic profiles, risk factors, history and clinical observation.

Materials and methods

We conducted a population-based study from January to December 2018 in consecutive children aged 2-5 years suspected of ASD who visited Thammasat University Hospital.

Eligibility was based upon the patients having any one of the following chief complaints: delayed speech (no discrete words by 18 months or no phrases by 24 months or no complete sentences speech by 36 months); social or play problems, e.g. preferred to be left alone; repetitive behaviors or restricted interests; behavioral or emotional regulation problems; or doctors/parents concerned that the child may have had ASD. Patients were excluded if they had any of the followings: severe chronic medical illness or physical disability, congenital anomalies/syndromes or hearing problems, had already been diagnosed with ASD, the main caregiver did not attend with the child and the caregiver was not able to communicate in Thai.

Assessment and data collection

The potential predictor variables included demographic data and risk factors, i.e. gender, age, chief complaint, level of communication, birthweight, maternal and paternal age, family history of autism or developmental delay, caregiver level of education, history of child’s ASD symptoms and symptoms from clinical observation (Appendix). All variables were selected based upon a review of the existing literature (Devlin and Scherer, 2012; Ozonoff et al., 2011; Gardener et al., 2009; Hultman et al., 2011; Ozonoff et al., 2009; McCoy et al., 2009;

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Received 29 January 2020
Revised 30 January 2020
Accepted 30 January 2020
Development of clinical prediction rule

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Clifford et al., 2013; Allison et al., 2012; Srisingshasongkram et al., 2016; Pornnoppadol et al., 2002; Panyayong, 2011; Krivichian, 2014; Maenner et al., 2013; Tsheringla et al., 2014; Dow et al., 2017; Ozonoff et al., 2008; Watt et al., 2008). While the caregiver filled out form on the demographic specifics, risk factors and history of child’s ASD symptoms, a general practitioner observed patients’ symptoms according to a prepared checklist. Both steps took less than 20 minutes per patient. All patients, then, were independently assessed by trained research assistants using ASD standardized diagnostic tools (Huerta and Lord, 2012). The Developmental, Dimensional and Diagnostic Interview short form and Autism Diagnostic Observation Schedule (Santosh et al., 2009; Chutthapisith et al., 2012; Lord et al., 2000). ASD diagnosis was made, in accordance with The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), by a child psychiatrist or developmental and behavioral pediatrician using clinical assessment and information from both tools. Other diagnosis and comorbidities were given following the DSM-5 criteria.

Data analysis

ASD and non-ASD groups were compared for evidence of differences (p-value) in clinical characteristics with t-test or exact probability test as appropriate. Prediction by each characteristic was calculated using univariable logistic regression and presented as an area under the receiver operating characteristic (AuROC) curve and its 95 per cent confidence interval (95% CI). Clinical predictors with a high AuROC curve and p value <0.01 were selected and processed with multivariable logistic regression with backward stepwise selection (p < 0.1) to aid the selection of the best variables. The discriminative performance of the model was calculated by an AuROC curve. The regression coefficient of each clinical predictor was divided by the smallest coefficient of the model and transform into an item risk score. Scores for each clinical predictor were added up to obtain a total risk score. Score prediction of ASD diagnosis was done by using a total score as the only summary predictor in the logistic model. Discrimination of the score was presented with an AuROC curve. Calibration of the prediction was analyzed with Hosmer-Lemeshow statistics. Scores predicting risk and observed risk were compared and presented in a graph. Internal validation of the score was done by logistic regression with the bootstrap method. Risk scores were categorized into risk levels. The predictive ability of each risk score level was calculated and presented as a likelihood ratio of different percentage distribution between ASD and non-ASD groups (Table I).

Results

One hundred and thirty-nine patients were enrolled (Table I). All patients had a complete assessment of ASD, and 104 (74.8 per cent) were diagnosed with ASD. In non-ASD group, diagnoses were language disorder (7.9 per cent), attention-deficit hyperactivity disorder (7.9 per cent), typical development (5.0 per cent), global developmental delay (2.9 per cent) and childhood-onset fluency disorder (stuttering) (1.5 per cent).

Eighty-five predictors from the patient profile, history taking and clinical observation were assessed. The association between all predictor variables and diagnosis of ASD determined using univariate analyses and the prediction ability measured by using AuROC were shown in the Appendix. Predictors that had p < 0.01 from univariable analyses were the level of communication, 11 symptoms from history taking and 16 symptoms observed by the clinician (Table II). These 28 variables were processed with multivariable logistic regression with backward stepwise selection (p < 0.1).

Prediction model

The best multivariable clinical predictors for the diagnosis of ASD from the multiple logistic regression were level of communication, history of rarely making eye contact or looking at faces, history of not showing off toys or favorite things, did not follow the clinician’s eye direction when called and signaled with eyes to look at things far away and had low frequency of social interaction with the clinician or the caregiver in the room. These five clinical predictors were each categorized into two levels. An item score of 1 was assigned to each predictor (Table III).

A summary risk score was obtained by adding up the item scores. The discriminative ability of the derived risk score, which ranged from 0 to 5, could directly be observed by the different percentage distribution between ASD and non-ASD groups (Figure 1).

The risk score predicted a diagnosis of ASD with an AuROC curve of 91.0 per cent (95% CI, 85.8-96.1) (Figure 2) and with the p-value for the Hosmer-Lemeshow goodness-of-fit test of 0.67. Internal validation by the bootstrapping method (1,000 replications) reduced the AuROC curve to 83.26 per cent (95% CI, 76.0-90.5).

When translating into absolute risks, the score predicted the risk of diagnosis of ASD increased when the risk score moved upward, with close calibration to the actual or observed risks (Figure 3).

The risk scores were categorized into three risk groups, low (0) when the slope of the risk curve was lowest, moderate (1-3), and high (4-5) to facilitate clinical interpretation. The positive
Table II Univariate correlation values of variables and area under receiver operating curve (AuROC) and 95% confidence interval (CI) from patients' profiles, caregiver report and clinical observation

| Predictors | ASD (%) | Non-ASD (%) | p-value | AuROC |
|------------|---------|-------------|---------|--------|
| **Patients' characteristic** | | | | |
| Level of communication | | | | |
| No meaningful word | 5 (4.8) | 2 (5.7) | | 0.77 (0.69-0.84) |
| Discrete words | 54 (51.9) | 2 (5.7) | | |
| Phrase | 26 (25.0) | 9 (25.7) | | |
| Complete sentence | 19 (18.2) | 22 (62.8) | <0.01 | |
| **Caregiver report** | | | | |
| Can do role-play, such as feeding dolls, acting as a goods vendor or other roles | 60 (57.69) | 30 (85.71) | <0.01 | 0.64 (0.55-0.72) |
| Nods or shakes his/her head to let you know that (s)he wants or does not want something | 71 (68.27) | 32 (91.43) | <0.01 | 0.62 (0.53-0.70) |
| Takes your hand to get what (s)he wants without looking at your face | 41 (39.42) | 25 (71.43) | <0.01 | 0.66 (0.58-0.74) |
| Knows to comfort other children when they are upset or injured | 34 (32.69) | 21 (60.00) | <0.01 | 0.64 (0.55-0.71) |
| Rarely makes eye contact or looks at faces, and usually looks another way when talked to | 62 (59.62) | 10 (28.57) | <0.01 | 0.66 (0.57-0.73) |
| Does not brag or persuade parents to be interested in what (s)he is doing | 36 (34.62) | 3 (8.57) | <0.01 | 0.63 (0.55-0.71) |
| Speaks a language of his/her own | 72 (69.23) | 14 (40.00) | <0.01 | 0.65 (0.56-0.73) |
| Shows off toys or favorite things | 60 (57.69) | 32 (91.43) | <0.01 | 0.67 (0.58-0.75) |
| Turns to look at you upon you calling his/her name | 81 (77.88) | 34 (97.14) | <0.01 | 0.60 (0.51-0.68) |
| Shows off or shows any items to you | 69 (66.35) | 32 (91.43) | <0.01 | 0.63 (0.54-0.71) |
| Looks at things you are looking at | 70 (67.31) | 32 (91.43) | <0.01 | 0.62 (0.53-0.70) |
| **Clinical observation** | | | | |
| The child's eye contact is abnormal | 69 (66.35) | 14 (40.00) | <0.01 | 0.63 (0.55-0.71) |
| Gestures and words the child uses to approach you look weird | 78 (75.00) | 16 (45.71) | <0.01 | 0.65 (0.56-0.73) |
| When the child's name is called (without touching), (s)he turns to look at you | 44 (42.31) | 28 (80.00) | <0.01 | 0.69 (0.61-0.77) |
| When you call to the child and signal with your eyes for him/her to look at things far away (without touching), (s)he looks in your eyes' direction to those things | 43 (40.38) | 30 (85.71) | <0.01 | 0.73 (0.65-0.80) |
| If you hold a toy the child wants in your hand, (s)he speaks or make gestures along with eye contact to ask for it | 39 (37.50) | 25 (71.43) | <0.01 | 0.67 (0.58-0.75) |
| Requesting eye contact, speech and gestures are simultaneous (natural) | 27 (25.96) | 19 (54.29) | <0.01 | 0.64 (0.56-0.72) |
| Upon getting toys, the child shows off/shows it to you or guardian | 28 (26.92) | 24 (68.57) | <0.01 | 0.71 (0.62-0.78) |
| While playing with toys, the child tries to get attention so that you or guardian become(s) interested in what (s)he is interested in (for mutual interest) | 28 (26.92) | 20 (57.14) | <0.01 | 0.65 (0.57-0.70) |
| The child often interacts with you or guardian in examination room, such as makes eye contact, smiles at you or the guardian, initiates conversations or asks questions | 24 (23.08) | 27 (77.14) | <0.01 | 0.77 (0.69-0.83) |
| Overall, you can build a natural relationship with the child | 27 (25.96) | 21 (60.00) | <0.01 | 0.67 (0.58-0.75) |
| The child has language development for age (can say short phrases by two years of age, can say short sentences by three, can say several consecutive sentences by four) | 16 (15.38) | 16 (45.71) | <0.01 | 0.63 (0.54-0.71) |
| The child has natural speaking/tone of voice (that does not sound weird) | 22 (21.15) | 16 (45.71) | <0.01 | 0.62 (0.54-0.71) |
| The child uses gestures in communication (such as makes gestures in story-telling, shakes his/her head, nods or waives his/her hand in rejection) | 37 (35.58) | 24 (68.57) | <0.01 | 0.67 (0.58-0.75) |
| If you hold one toy in each hand and ask the child which toy (s)he wants, (s)he can point index finger to the toy (s)he wants on his/her own without having to be told | 38 (36.54) | 26 (74.29) | <0.01 | 0.69 (0.61-0.77) |
| The child makes noises or strange speech (such as alien language, suddenly speaking out sounds from TV) | 65 (62.50) | 10 (28.57) | <0.01 | 0.67 (0.58-0.75) |
| The child is more interested in certain objects in examination room than people | 71 (68.27) | 12 (34.29) | <0.01 | 0.67 (0.58-0.75) |
A likelihood ratio for the diagnosis of ASD was 0.04 in the low risk, 0.45 (95% CI, 0.34-0.59) in the moderate and 16.62 (95% CI, 2.38, 116.05) in the high categories (Table IV).

**Discussion**

This clinical decision rule has been developed to help general practitioners for predicting the diagnosis of ASD in children aged 2-5 years old.

Research in the past from the UK found that parents of children with ASD brought them to hospital from age 2-6 1.92 years, but the average age of diagnosis was 5.7 years. In the first visit, usually with a general practitioner, less than 10 per cent of patients received diagnosis, and 26-30 per cent were told “no problem/no worry”. The other 50 per cent were referred to specialists (Howlin and Asgharian, 1999). This older study may convey the situation in Thailand and other developing countries today. Furthermore, in these countries where specialists are less than adequate, the referring process may take years. Caregivers who are not confident in the diagnosis may be lost to follow-ups, and the early intervention will be delayed. This clinical decision rule would allow the general practitioners to make the initial diagnosis of ASD based upon the clear and evidenced rule. Having more confidence regarding the initial diagnosis, they are able to provide disease-specific initial recommendations and management for caregivers and families.

Recently, several screening questionnaires for autism have been developed (Allison et al., 2012; Srisinghasongkram et al., 2016; Pornnoppadol et al., 2002; Panyayong, 2011; Krivichian, 2014). This decision rule would facilitate the initial diagnosis in patients with positive result from the screening process. This risk score is highly accurate in the predicted diagnosis of ASD (the AuROC being 91.0 per cent). We chose the cutoff score of 4 to classify patients into a very high-risk group. We chose a high cutoff score because we want this decision rule to be highly specific so the doctors would be confident in the initial diagnosis.

To apply this rule in practice, patients with four or more of these predictors, namely:

| Predictors                                                                 | OR          | 95% CI        | p-value   | B  | Score |
|----------------------------------------------------------------------------|-------------|---------------|-----------|----|-------|
| Delayed speech for their age                                              | 4.83        | 1.65-14.15    | 0.004     | 1.58 | 1     |
| History of rarely making eye contact or looks at faces, and usually looks another way when talked to | 4.81        | 1.58-14.65    | 0.006     | 1.57 | 1     |
| History of not showing off toys or favorite things                        | 5.69        | 1.18-27.36    | 0.030     | 1.74 | 1     |
| Did not follow clinician’s eye direction when called and signaled with eyes to look at things far away | 3.22        | 0.89-11.62    | 0.075     | 1.17 | 1     |
| Had low frequency of social interaction with clinician or caregiver in the room | 6.74        | 2.25-20.22    | 0.001     | 1.91 | 1     |

**Table III**  Clinical predictors, odds ratio (OR), 95% confidence interval (CI), logistic regression beta coefficient (β) and assigned item scores

**Figure 1**  Percentage distribution of clinical risk score of ASD (n = 104) and non-ASD (n = 35)

**Figure 2**  Area under receiver operating characteristic curve of clinical risk score and 95% confidence interval (CI) on prediction of ASD diagnosis

**Figure 3**  Observed risk (circle) vs score predicted risk (solid line) of ASD diagnosis
• delayed speech for their age;
• history of avoiding eye contact/meeting others’ gaze;
• history of a pattern of not showing objects to others;
• poor response when the clinician attempts to draw attention to something in a distance; and
• low frequency in reciprocal social interaction with the clinician or the caregiver in the room are at substantial risk of having ASD (positive likelihood ratio = 16.62).

A doctor can discuss the ASD diagnosis and give psychoeducation to the family. Also, initial management can be done promptly, i.e. referral to a speech therapist, occupational therapist or developmental stimulation program. Patients with one to three predictors may or may not have ASD and should be referred to specialists. Patients with no predictors are at low risk of having ASD. They can be managed as per other diagnoses or observed.

The strength of this study is that it was a population-based study conducted in routine clinical practice with limited observation time. Patients and doctors would represent target groups that results were intended to be used. The results also showed which ASD symptoms can be observed in the time-limited outpatient situation. The diagnosis process was based on the reference standard for the ASD diagnosis. As all variables were collected before the specialist assessed the patients, the bias of information would be reduced. Furthermore, as the format of the rule includes a simple list of history taking and clinical observations, it would make this rule clinically sensible for the busy general practitioner to apply it in routine practice.

However, the number of patients in this study was small, and the derived score is likely to be space domain specific. Also, as all data were collected in Thai, cultural and language effects should be considered. Clinical predictors in our setting may not be directly applicable to other settings. Model adjustment, either selection of different clinical predictors and/or different scoring weights, should always be considered for application to a new setting. Also, it is necessary for the model to have an external validation to provide sufficient evidence about its performance.

Conclusion

This simple and practical clinical decision rule may help non-specialists to make the initial diagnosis of ASD in children. Caregivers of the very high-risk patients may be informed about the disease and its caring process that will improve the quality of care.

References

Allison, C., Auyeung, B. and Baron-Cohen, S. (2012), “Toward brief ‘red flags’ for autism screening: the short autism spectrum quotient and the short quantitative checklist in 1,000 cases and 3,000 controls”, Journal of the American Academy of Child & Adolescent Psychiatry, Vol. 51, pp. 202-212, doi: 10.1016/j.jaac.2011.11.003.

American Psychiatric Association (2013), “Diagnostic and statistical manual of mental disorders, 5th ed., (DSM-5)”, doi: 10.1176/appi.books.9780890425596.

Christensen, D.L. (2016), “Prevalence and characteristics of autism spectrum disorder among children aged 8 years—autism and developmental disabilities monitoring network, 11 sites, United States, 2012”, MMWR Surveillance Summaries, Vol. 65 No. 3, pp. 1-23.

Chuthapisith, J., Taycharipranai, P., Ruangdaragonan, N., Warrington, R. and Skuse, D. (2012), “Translation and validation of the developmental, dimensional and diagnostic interview (3Di) for diagnosis of autism spectrum disorder in Thai children”, Autism, Vol. 16 No. 4, pp. 350-356, doi: 10.1177/1754488011433770.

Clifford, S.M., Hudry, K., Elsabbagh, M., Charman, T. and Johnson, M.H. and BASIS Team (2013), “Temperament in the first 2 years of life in infants at high-risk for autism spectrum disorders”, Journal of Autism and Developmental Disorders, Vol. 43 No. 3, pp. 673-686, doi: 10.1007/s10803-012-1612-y.

Devlin, B. and Scherer, S.W. (2012), “Genetic architecture in autism spectrum disorder”, Current Opinion in Genetics & Development, Vol. 22 No. 3, pp. 229-237, doi: 10.1016/j.gde.2012.03.002.

Dow, D., Guthrie, W., Stronach, S.T. and Wetherby, A.M. (2017), “Psychometric analysis of the systematic observation of red flags for autism spectrum disorder in toddlers”, Autism, Vol. 21 No. 3, pp. 301-309, doi: 10.1177/1754488016636760.

Falkmer, T., Anderson, K., Falkmer, M. and Horlin, C. (2013), “Diagnostic procedures in autism spectrum disorders: a systematic literature review”, European Child & Adolescent Psychiatry, Vol. 22 No. 6, pp. 329-340, doi: 10.1007/s00787-013-0375-0.

Filipek, P.A., Accardo, P.J., Ashwal, S., Baranek, G.T., Cook, E.H., Dawson, G., Gordon, B., Gravel, J.S., Johnson, C.P., Kallen, R.J. and Levy, S.E. (2000), “Practice parameter: screening and diagnosis of autism: report of the quality standards subcommittee of the American academy of neurology and the child neurology society”, Neurology, Vol. 55 No. 4, pp. 468-479, doi: 10.1212/WNL.55.4.468.

Gardener, H., Spiegelman, D. and Buka, S.L. (2009), “Prenatal risk factors for autism: comprehensive meta-analysis”, British Journal of Psychiatry, Vol. 195 No. 1, pp. 7-14, doi: 10.1192/bjp.bp.108.051672.
Granpeesheh, D., Tarbox, J. and Dixon, D.R. (2009), “Applied behavior analytic interventions for children with autism: a description and review of treatment research”, *Ann Clin Psychiatry*, Vol. 21 No. 3, pp. 162-173.

Howlin, P. and Asgharian, A. (1999), “The diagnosis of autism and Asperger syndrome: findings from a survey of 770 families”, *Developmental Medicine & Child Neurology*, Vol. 41 No. 12, pp. 834-839, doi: 10.1017/s0002162299001656.

Huerta, M. and Lord, C. (2012), “Diagnostic evaluation of autism spectrum disorders”, *Pediatric Clinics of North America*, Vol. 59 No. 1, pp. 103-111, doi: 10.1016/j.pcl.2011.10.018.

Hultman, C.M., Sandin, S., Levine, S.Z., Lichtenstein, P. and Reichenberg, A. (2011), “Advancing paternal age and risk of autism: new evidence from a population-based study and a meta-analysis of epidemiological studies”, *Molecular Psychiatry*, Vol. 16 No. 12, pp. 1203-1212, doi: 10.1038/mp.2010.121.

Krivichian, C. (2014), “Autism spectrum screening questionnaire for children under 2 years old”, *Journal of Mental Health of Thailand*, Vol. 22, pp. 1-10.

Landa, R.J. (2008), “Diagnosis of autism spectrum disorders in the first 3 years of life”, *Nature Clinical Practice Neurology*, Vol. 4 No. 3, pp. 138-147, doi: 10.1038/ncpneuro0731.

Lord, C., Risi, S., Lambrecht, L., Cook, E.H., Leventhal, B.L., DiLavore, P.C., Pickles, A. and Rutter, M. (2000), “The autism diagnostic observation schedule-generic: a standard measure of social and communication deficits associated with the spectrum of autism”, *Journal of Autism and Developmental Disorders*, Vol. 30 No. 3, pp. 205-223, doi: 10.1023/A:100592401947.

McCoy, A., Wetherby, A. and Woods, J. (2009), “Screening children between 18 and 24 months using the systematic observation of red flags (SORF) for autism spectrum disorders: a follow-up study”, *International Meeting for Autism Research*, Chicago, IL.

Maenner, M.J., Schieve, L.A., Rice, C.E., Cunniff, C., Giarelli, E., Kirby, R.S., Lee, L.C., Nicholas, J.S., Wingate, M.S. and Durkin, M.S. (2013), “Frequency and pattern of documented diagnostic features and the age of autism identification”, *Journal of the American Academy of Child & Adolescent Psychiatry*, Vol. 52 No. 4, pp. 401-413, doi: 10.1016/j.jaac.2013.01.014.

Ozonoff, S., Macari, S., Young, G.S., Goldring, S., Thompson, M. and Rogers, S.J. (2008), “Atypical object exploration at 12 months of age is associated with autism in a prospective sample”, *Autism*, Vol. 12 No. 5, pp. 457-472, doi: 10.1177/1362361308096402.

Ozonoff, S., Young, G.S., Steinfeld, M.B., Hill, M.M., Cook, I., Hutman, T., Macari, S., Rogers, S.J. and Sigman, M. (2009), “How early do parent concerns predict later autism diagnosis?”, *Journal of Developmental & Behavioral Pediatrics*, Vol. 30 No. 5, p. 367, doi: 10.1097/DBP.0b013e3181ba0f6c.

Ozonoff, S., Young, G.S., Carter, A., Messinger, D., Yirmiya, N., Zwaigenbaum, L., Bryson, S., Carver, L.J., Constantino, J.N., Dobkins, K. and Hutman, T. (2011), “Recurrence risk for autism spectrum disorders: a baby siblings research consortium study”, *Pediatrics*, Vol. 128, pp. 488-495, doi: 10.1542/peds.2010-2825.

Panyayong, B. (2011), “The validation of the pervasive developmental disorders screening instrument”, *Journal of Mental Health of Thailand*, Vol. 18, pp. 36-44.

Pornnoppadol, C., Thongngen, A., Gaevalin, A. and Sangratanayont, D. (2002), “Development of the pervasive developmental disorders screening questionnaires”, *Journal of Psychiatric Assoc Thailand*, Vol. 47, pp. 75-96.

Santosh, P.J., Mandy, W.P., Puura, K., Kaartinen, M., Warrington, R. and Skuse, D.H. (2009), “The construction and validation of a short form of the developmental, diagnostic and dimensional interview”, *European Child & Adolescent Psychiatry*, Vol. 18 No. 8, pp. 521-524, doi: 10.1007/s00787-009-0004-0.

Srisringhasongkram, P., Pruksananonda, C. and Chonchaiya, W. (2016), “Two-Step screening of the modified checklist for autism in toddlers in Thai children with language delay and typically developing children”, *Journal of Autism and Developmental Disorders*, pp. 1-13, doi: 10.1037/t67556-000.

Tsheringla, S., Minju, K.A., Russell, S., Mammen, P., Russell, P.S.S. and Nair, M.K.C. (2014), “A meta-analysis of the diagnostic accuracy of autism diagnostic observation schedule module-1 for autism spectrum disorders”, *Indian J Pediatr.*, Vol. 81, pp. 87-92, doi: 10.1007/s12098-014-1627-9.

Watt, N., Wetherby, A.M., Barber, A. and Morgan, L. (2008), “Repetitive and stereotyped behaviors in children with autism spectrum disorders in the second year of life”, *Journal of Autism and Developmental Disorders*, Vol. 38 No. 8, pp. 1518-1533, doi: 10.1007/s10803-007-0532-8.

Wing, L. (1988), *The Continuum of Autistic Characteristic*. Diagnosis and Assessment in Autism, Springer, pp. 91-110. doi: 10.1007/978-1-4899-0792-9_7.

Zwaigenbaum, L., Bauman, M.L., Stone, W.L., Yirmiya, N., Estes, A., Hansen, R.L., McPartland, J.C., Natowitz, M.R., Choueiri, R., Fein, D. and Kasari, C. (2015), “Early identification of autism spectrum disorder: Recommendations for practice and research”, *Pediatrics*, Vol. 136 No. Supplement, pp. S10-40, doi: 10.1542/peds.2014-3667C.

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### Appendix

**Table A1** Univariate correlation values of variables and area under receiver operating curve (AuROC) and 95% confidence interval (CI) from patients’ profiles

| Predictors                        | ASD   | Non-ASD | p-value | AuROC (95% CI) |
|-----------------------------------|-------|---------|---------|----------------|
| Male n (%)                        | 88 (84.6) | 31 (88.6) | 0.78 | 0.48 (0.40-0.57) |
| Age (months)                      | 43 (0.9) | 48 (1.7) | 0.01 | 0.35 (0.27-0.44) |
| Birthweight (g)                   | 3016.2 (61.5) | 3038.0 (83.9) | 0.85 | 0.50 (0.42-0.59) |
| Level of communication n (%)      | 5 (4.8) | 2 (5.7) | <0.01 | 0.77 (0.69-0.84) |
| No meaningful words               | 54 (51.9) | 2 (5.7) |       |                 |
| Discrete words                    | 26 (25.0) | 9 (25.7) |       |                 |
| Phrases                           | 19 (18.2) | 22 (62.8) |       |                 |
| Family history of ASD n (%)       | 38 (26.5) | 12 (34.3) | 0.84 | 0.51 (0.42-0.60) |
| Paternal age (years)              | 33.8 (0.9) | 33.7 (1.4) | 0.94 | 0.54 (0.45-0.62) |
| Maternal age (years)              | 30.9 (0.7) | 30.8 (1.1) | 0.94 | 0.50 (0.41-0.58) |
| Caregiver’s level of education (years) | 12.3 (4.6) | 11.9 (4.7) | 0.66 | 0.53 (0.42-0.64) |

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### Table AII
Univariate correlation values of variables and area under receiver operating curve (AuROC) with 95% confidence interval (CI) from caregiver reports

| No. | Caregiver report | ASD N (%) | Non-ASD N (%) | p-value | AuROC (95% CI) |
|-----|------------------|-----------|---------------|---------|----------------|
|     | **Deficits in social communication and social interaction** |           |               |         |                |
|     | **Interaction with parents** |           |               |         |                |
| 1   | Smiles at parents upon seeing them from a distance | 92 (88.46) | 32 (91.43) | 0.76    | 0.52 (0.43-0.60) |
| 2   | Smiles upon seeing you or in response to your smiles | 98 (94.23) | 32 (91.43) | 0.69    | 0.49 (0.40-0.58) |
| 3   | Likes to be held, hugged or kissed by parents | 95 (91.35) | 32 (91.43) | 1.00    | 0.50 (0.42-0.59) |
| 4   | Likes to show affections to parents by hugging, kissing or embracing | 93 (89.42) | 32 (91.43) | 1.00    | 0.51 (0.42-0.60) |
| 5   | Rushes to you to get help or to ask for comfort in times of injuries or accidents | 99 (95.19) | 31 (88.57) | 0.23    | 0.47 (0.38-0.55) |
| 6   | Seems not troubled or paying attention to having or not having your company | 40 (38.46) | 8 (22.86) | 0.10    | 0.58 (0.49-0.66) |
| 7   | Does not understand other people’s thoughts, facial expressions or emotions, such as does not realize when parents scold him/her | 21 (20.19) | 4 (11.43) | 0.31    | 0.54 (0.46-0.63) |
| 8   | Turns to look at you upon you calling his/her name | 81 (77.88) | 34 (97.14) | <0.01   | 0.60 (0.51-0.68) |
| 9   | Acts as if not listening when you speak to him/her | 73 (70.19) | 18 (51.43) | 0.06    | 0.59 (0.51-0.68) |
| 10  | When pointed to things, the child is interested and looks in corresponding directions | 85 (81.73) | 33 (94.29) | 0.10    | 0.56 (0.48-0.65) |
| 11  | Looks at things you are looking at | 70 (67.31) | 32 (91.43) | <0.01   | 0.62 (0.53-0.70) |
| 12  | Tries to make you interested in what (s)he is doing by calling to you or handing it to you | 82 (78.85) | 32 (91.43) | 0.13    | 0.56 (0.47-0.65) |
| 13  | Does not brag or persuade parents to be interested in what (s)he is doing | 36 (34.62) | 3 (8.57) | <0.01   | 0.63 (0.55-0.71) |
| 14  | Shows off toys or favorite things | 60 (57.69) | 32 (91.43) | <0.01   | 0.67 (0.58-0.75) |
| 15  | Shows off or shows any items to you | 69 (66.35) | 32 (91.43) | <0.01   | 0.63 (0.54-0.71) |
| 16  | **Interaction with other children** |           |               |         |                |
| 17  | Interested and wants to play with other children at school or playground | 74 (71.15) | 30 (85.71) | 0.12    | 0.57 (0.49-0.66) |
| 18  | Likes to play alone, to isolate himself/herself and is not interested in other children | 51 (49.04) | 8 (22.86) | 0.01    | 0.63 (0.55-0.71) |
| 19  | Knows to share snacks or toys with other children | 74 (71.15) | 27 (77.14) | 0.53    | 0.53 (0.45-0.62) |
| 20  | Knows to comfort other children when they are upset or injured | 68 (65.38) | 26 (74.29) | 0.41    | 0.55 (0.46-0.63) |
| 21  | **Non-verbal communication** |           |               |         |                |
| 22  | Often has glazed eyes or unfocused stares | 32 (30.77) | 6 (17.14) | 0.13    | 0.57 (0.48-0.65) |
| 23  | Rarely makes eye contact or looks at faces, and usually looks another way when talked to | 62 (59.62) | 10 (28.57) | <0.01   | 0.66 (0.57-0.73) |
| 24  | Stares with corners of eyes | 35 (33.65) | 5 (14.29) | 0.03    | 0.60 (0.51-0.68) |
| 25  | Points index finger to communicate interests | 82 (78.85) | 32 (91.43) | 0.13    | 0.56 (0.47-0.65) |
| 26  | Takes your hand to get what (s)he wants without looking at your face | 63 (60.58) | 10 (28.57) | <0.01   | 0.66 (0.58-0.74) |
| 27  | Nods or shakes his/her head to let you know that (s)he wants or does not want something | 71 (68.27) | 32 (91.43) | <0.01   | 0.62 (0.53-0.70) |
| 28  | Straight-faced child, rarely showing emotions | 21 (20.19) | 5 (14.29) | 0.62    | 0.53 (0.45-0.62) |
| 29  | **Language, play and imitation** |           |               |         |                |
| 30  | You used to wonder whether (s)he could be deaf | 24 (23.08) | 4 (11.43) | 0.15    | 0.56 (0.48-0.65) |

(continued)
| No. | Caregiver report                                                                 | ASD N (%) | Non-ASD N (%) | p-value | AuROC (95% CI) |
|-----|---------------------------------------------------------------------------------|-----------|---------------|---------|----------------|
| 31  | You used to feel that speech is delayed or to worry why your child does not start to speak | 89 (85.58) | 22 (62.86)    | <0.01  | 0.61 (0.53-0.69) |
| 32  | Cannot yet communicate what (s)he wants by speaking or pointing                 | 34 (32.69) | 5 (14.29)     | 0.05    | 0.59 (0.50-0.67) |
| 33  | Understands what others say                                                      | 74 (71.15) | 31 (88.57)    | 0.04    | 0.59 (0.50-0.67) |
| 34  | Does not know how to play with toys; taps, smells, throws or tosses them        | 36 (34.62) | 7 (20.00)     | 0.14    | 0.57 (0.49-0.66) |
| 35  | Can do role-play, such as feeding dolls, acting as a goods vendor or other roles | 60 (57.69) | 30 (85.71)    | <0.01  | 0.64 (0.55-0.72) |
| 36  | Can make gestures imitating adults, such as wearing makeups, combing hair, shaving or getting ready to go to work | 81 (77.88) | 29 (82.86)    | 0.64    | 0.53 (0.44-0.61) |
| 37  | Imitates your actions, such as sticks out tongue when you do so at him/her       | 74 (71.15) | 29 (82.86)    | 0.19    | 0.56 (0.48-0.65) |

Restricted, repetitive patterns of behavior, interests or activities

**Stereotyped or repetitive motor movements, use of objects or speech.**

| No. | Caregiver report                                      | ASD N (%) | Non-ASD N (%) | p-value | AuROC (95% CI) |
|-----|------------------------------------------------------|-----------|---------------|---------|----------------|
| 38  | Make repeated gestures (such as flick of the hand, tiptoeing, body rotation) | 46 (44.23) | 9 (25.71)     | 0.07    | 0.59 (0.50-0.67) |
| 39  | Likes doing or saying something repeatedly           | 65 (62.50) | 16 (45.71)    | 0.11    | 0.58 (0.50-0.67) |
| 40  | Likes to arrange toys in rows and will get very angry if someone re-arranges them | 54 (51.92) | 16 (45.71)    | 0.56    | 0.53 (0.45-0.62) |
| 41  | Speaks a language of his/her own                     | 72 (69.23) | 14 (40.00)    | <0.01  | 0.65 (0.56-0.73) |
| 42  | Says words (s)he hears or says on TV; repeats the last word | 59 (56.73) | 14 (40.00)    | 0.12    | 0.58 (0.50-0.67) |
| 43  | Often repeats what you just said                     | 47 (45.19) | 13 (37.14)    | 0.44    | 0.54 (0.45-0.62) |

**Insistence on sameness, inflexible adherence to routines or ritualized patterns of verbal or nonverbal behavior**

| No. | Caregiver report                                      | ASD N (%) | Non-ASD N (%) | p-value | AuROC (95% CI) |
|-----|------------------------------------------------------|-----------|---------------|---------|----------------|
| 44  | Hard to adapt to new things, such as refuses to try new dishes, cries when going to new places | 38 (36.54) | 10 (28.57)    | 0.42    | 0.54 (0.45-0.62) |
| 45  | Is hard to change what (s)he is used to doing; has own patterns | 31 (29.81) | 12 (34.29)    | 0.67    | 0.48 (0.40-0.57) |
| 46  | Seems like a more "organized" child than his/her peers | 19 (18.27) | 5 (14.29)     | 0.80    | 0.52 (0.43-0.60) |

**Highly restricted, fixated interests that are abnormal in intensity or focus**

| No. | Caregiver report                                      | ASD N (%) | Non-ASD N (%) | p-value | AuROC (95% CI) |
|-----|------------------------------------------------------|-----------|---------------|---------|----------------|
| 47  | Interested in few toys or matters                    | 52 (50.00) | 13 (37.14)    | 0.24    | 0.56 (0.48-0.65) |
| 48  | Is obsessed with something or always holds something, such as drinking straw or rope | 32 (30.77) | 7 (20.00)     | 0.28    | 0.55 (0.47-0.64) |
| 49  | Interested in playing a particular part of objects, such as car wheel | 44 (42.31) | 8 (22.86)     | 0.05    | 0.60 (0.51-0.68) |

Hyper- or hyporeactivity to sensory input or unusual interest in sensory aspects of the environment

| No. | Caregiver report                                      | ASD N (%) | Non-ASD N (%) | p-value | AuROC (95% CI) |
|-----|------------------------------------------------------|-----------|---------------|---------|----------------|
| 50  | Cries, covers ears or runs away upon hearing loud noises | 39 (37.50) | 17 (48.57)    | 0.32    | 0.45 (0.36-0.053) |
| 51  | Frustrating emotions                                 | 64 (61.54) | 22 (62.86)    | 1.00    | 0.49 (0.41-0.58) |
| 52  | Hard to soothe when upset                            | 47 (45.19) | 15 (42.86)    | 0.85    | 0.51 (0.42-0.60) |

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Development of clinical prediction rule

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Mental Illness

Volume 12 · Number 1 · 2020 · 7–16
### Table AIII: Univariate correlation values of variables and area under receiver operating curve (AuROC) and 95% confidence interval (CI) from clinical observations

| No. | Clinical observations                                                                 | ASD N (%) | Non-ASD N (%) | p value | AuROC (95% CI)  |
|-----|-----------------------------------------------------------------------------------------|-----------|---------------|---------|-----------------|
| 1   | The child’s eye contact is abnormal                                                      | 69 (66.35) | 14 (40.00)    | <0.01  | 0.63 (0.55-0.71) |
| 2   | Gestures and words the child uses to approach you look weird                            | 78 (75.00) | 16 (45.71)    | <0.01  | 0.65 (0.56-0.73) |
| 3   | When the child’s name is called (without touching), (s)he turns to look at you         | 44 (42.31) | 28 (80.00)    | <0.01  | 0.69 (0.61-0.77) |
| 4   | When you call to the child and signal with your eyes for him/her to look at things far away (without touching), (s)he looks in your eyes’ direction to those things | 43 (40.38) | 30 (85.71)    | <0.01  | 0.73 (0.65-0.80) |
| 5   | If you hold a toy the child wants in your hand, (s)he speaks or make gestures along with eye contact to ask for it | 39 (37.50) | 25 (71.43)    | <0.01  | 0.67 (0.58-0.75) |
| 6   | Requesting eye contact, speech and gestures are simultaneous (natural)                  | 27 (25.96) | 19 (54.29)    | <0.01  | 0.64 (0.56-0.72) |
| 7   | Upon getting toys, the child shows off/shows it to you or guardian                      | 28 (26.92) | 24 (68.57)    | <0.01  | 0.71 (0.62-0.78) |
| 8   | While playing with toys, the child tries to get attention so that you or guardian become(s) interested in what (s)he is interested in (for mutual interest) | 28 (26.92) | 20 (57.14)    | <0.01  | 0.65 (0.57-0.70) |
| 9   | When you ask the child to play with toys (s)he likes, (s)he has fun with you            | 48 (46.15) | 24 (68.57)    | 0.03   | 0.61 (0.53-0.69) |
| 10  | The child often interacts with you or guardian in examination room, such as makes eye contact, smiles at you or the guardian, initiates conversations or asks questions | 24 (23.08) | 27 (77.14)    | <0.01  | 0.77 (0.69-0.83) |
| 11  | Overall, you can build a natural relationship with the child                            | 27 (25.96) | 21 (60.00)    | <0.01  | 0.67 (0.58-0.75) |
| 12  | The child has language development for age (can say short phrases by two years of age, can say short sentences by three, can say several consecutive sentences by four) | 16 (15.38) | 16 (45.71)    | <0.01  | 0.63 (0.54-0.71) |
| 13  | The child has natural speaking/tone of voice (that does not sound weird)               | 22 (21.15) | 16 (45.71)    | <0.0.01 | 0.62 (0.54-0.71) |
| 14  | The child shows emotions through facial expressions that look natural                   | 50 (48.08) | 25 (71.43)    | 0.02   | 0.62 (0.53-0.70) |
| 15  | The child uses gestures in communication (such as makes gestures in story-telling, shakes his/her head, nods or waves his/her hand in rejection) | 37 (35.58) | 24 (68.57)    | <0.01  | 0.67 (0.58-0.75) |
| 16  | If you hold one toy in each hand and ask the child which toy (s)he wants, (s)he can point index finger to the toy (s)he wants on his/her own without having to be told | 38 (36.54) | 26 (74.29)    | <0.01  | 0.69 (0.61-0.77) |
| 17  | The child often covers ears with hands                                                  | 7 (6.73)   | 0 (0.00)      | 0.19   | 0.53 (0.45-0.62) |
| 18  | The child stares at lights, illuminating objects or rotating objects for a long time    | 9 (8.65)   | 2 (5.71)      | 0.73   | 0.52 (0.43-0.60) |
| 19  | The child smells or licks objects/people                                               | 12 (11.54) | 1 (2.86)      | 0.18   | 0.54 (0.46-0.63) |
| 20  | The child makes certain repeated gestures (such as flick of the hand, tip-toeing, body rotation, moving fingers near face) | 20 (19.23) | 3 (8.57)      | 0.19   | 0.55 (0.47-0.64) |
| 21  | The child makes noises or strange speech (such as alien language, suddenly speaking out sounds from TV) | 65 (62.50) | 10 (28.57)    | <0.01  | 0.67 (0.58-0.75) |
| 22  | The child repeats the sentence you just finished saying                                  | 25 (24.04) | 7 (20.00)     | 0.82   | 0.52 (0.43-0.60) |
| 23  | The child does not know how to play with toys or to play with them as per their intended purposes (such as arranges, rotates or taps them repeatedly without role-play) | 33 (31.73) | 7 (20.00)     | 0.20   | 0.56 (0.48-0.65) |
| 24  | The child is interested in a particular part of objects (such as repeatedly spins car wheel without moving the car or is interested in repeatedly opening and closing doll’s eyes) | 26 (25.00) | 6 (17.14)     | 0.49   | 0.57 (0.48-0.66) |
| 25  | The child is more interested in certain objects in examination room than people         | 71 (68.27) | 12 (34.29)    | <0.01  | 0.67 (0.58-0.75) |