DSM-5 criteria for autism spectrum disorder maximizes diagnostic sensitivity and specificity in preschool children

Lisa D. Wiggins[1], **Catherine E. Rice**[2], **Brian Barger**[3], **Gnakub N. Soke**[1], **Li-Ching Lee**[4], **Eric Moody**[5], **Rebecca Edmondson-Pretzel**[6], **Susan E. Levy**[7]

[1]National Center on Birth Defects and Developmental Disabilities, Centers for Disease Control and Prevention, 4770 Buford Highway NE MS S106-4, Atlanta, GA 30341, USA

[2]Emory Autism Resource Center, Emory University, Atlanta, GA, USA

[3]School of Public Health, Georgia State University, Atlanta, GA, USA

[4]Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA

[5]JFK Partners, University of Colorado-Anschutz Medical Campus, Aurora, CO, USA

[6]Carolina Institute for Developmental Disabilities, University of North Carolina, Chapel Hill, NC, USA

[7]Center for Autism Research, Children's Hospital of Philadelphia, Philadelphia, PA, USA

Abstract

Purpose—The criteria for autism spectrum disorder (ASD) were revised in the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM). The objective of this study was to compare the sensitivity and specificity of DSM-IV-Text Revision (DSM-IV-TR) and DSM-5 definitions of ASD in a community-based sample of preschool children.

Methods—Children between 2 and 5 years of age were enrolled in the Study to Explore Early Development-Phase 2 (SEED2) and received a comprehensive developmental evaluation. The clinician(s) who evaluated the child completed two diagnostic checklists that indicated the presence and severity of DSM-IV-TR and DSM-5 criteria. Definitions for DSM-5 ASD, DSM-IV-TR autistic disorder, and DSM-IV-TR Pervasive Developmental Disorder Not Otherwise Specified (PDD-NOS) were created from the diagnostic checklists.

Results—773 children met SEED2 criteria for ASD and 288 met criteria for another developmental disorder (DD). Agreement between DSM-5 and DSM-IV-TR definitions of ASD were good for autistic disorder (0.78) and moderate for PDD-NOS (0.57 and 0.59). Children who met DSM-IV-TR autistic disorder but not DSM-5 ASD ($n = 71$) were more likely to have mild ASD symptoms, or symptoms accounted for by another disorder. Children who met PDD-NOS but not DSM-5 ASD ($n = 66$), or vice versa ($n = 120$) were less likely to have intellectual disability

Lisa D. Wiggins lwiggins@cdc.gov.

and more likely to be female. Sensitivity and specificity were best balanced with DSM-5 ASD criteria (0.95 and 0.78, respectively).

Conclusions—The DSM-5 definition of ASD maximizes diagnostic sensitivity and specificity in the SEED2 sample. These findings support the DSM-5 conceptualization of ASD in preschool children.

Keywords

Autism; Autism spectrum disorder; Diagnostic and Statistical Manual of Mental Disorders (DSM); Diagnostic criteria

Introduction

Autism spectrum disorder (ASD) is a developmental disability that affects social communication and behavior development and is typically recognized in the first few years of life [1]. ASD is the fastest growing developmental disability and costs $236–262 billion per year in the USA [2]. More debilitating forms of ASD are associated with greater economic burden [2], parental stress [3], and more medical and behavior co-morbidities [4]. Early detection of ASD symptoms facilitates referral for early intervention services which are associated with improved developmental outcomes [5, 6]. The early detection of ASD is an important public health priority that may address immediate and long-term needs of children and families.

ASD is a behaviorally defined disorder that relies on child observation and parent report to differentiate from other childhood conditions [7]. The criteria used to diagnose ASD are outlined in the Diagnostic and Statistical Manual of Mental Disorders (DSM) published by the American Psychiatric Association (APA0). In DSM-IV-Text Revised (DSM-IV-TR), ASD included subtypes of autistic disorder, Asperger disorder, and Pervasive Developmental Disorder Not Otherwise Specified (PDD-NOS) [8]. A diagnosis of autistic disorder required the presence of at least six of 12 total symptoms from three domains (two social, at least one communication, and at least one behavioral), and onset before 36 months of age. A diagnosis of Asperger disorder specified qualitative impairments in social interaction and presence of restricted interests and repetitive behaviors, but no cognitive, language, or non-social adaptive delays noted in early development. Diagnoses of PDD-NOS were described as *a severe and pervasive impairment in the development of reciprocal social interaction* associated with impairment in either *verbal and nonverbal communication skills*, or *the presence of stereotyped behavior, interests, and activities*, but criteria not met for another ASD. Children with PDD-NOS, therefore, had to meet at least two diagnostic criteria with one from the social domain. These criteria differed from those offered in DSM-IV in that social deficits were required to meet the DSM-IV-TR definition of ASD, but were not required to meet the DSM-IV definition of ASD, and ultimately improved diagnostic specificity [9, 10].

Despite an improvement in diagnostic specificity, children with ASD defined by DSM-IV-TR criteria still presented with remarkable heterogeneity in symptom presentation defined by different levels of ASD severity and the presence of co-occurring conditions [11]. This

phenotypic diversity complicated diagnostic and treatment efforts, and the ability to synthesize findings from research studies [12]. In its publication of the DSM-5 in 2013, the APA made considerable changes to ASD diagnostic criteria in an effort to maintain diagnostic sensitivity and continue to improve diagnostic specificity. In DSM-5, ASD no longer includes subtypes but represents one singular condition defined by level of functional support required by the individual. DSM-5 also specifies that persons with ASD must meet all three social criteria (i.e., deficits in social-emotional reciprocity, deficits in nonverbal communicative behaviors, and deficits in developing, understanding, and maintaining relationships) and two of four behavioral criteria (i.e., repetitive speech or motor movements, insistence on sameness, restricted interests, or unusual response to sensory input) [1, 13].

The changes in DSM-5 diagnostic criteria have been thought to embody more restrictive requirements than the less stringent DSM-IV-TR PDD-NOS criteria with the potential to exclude very young children and those without intellectual disability (ID) [14–16]. Consequently, diagnostic sensitivity may suffer with improved diagnostic specificity and impact the early detection and treatment of children with ASD. Previous studies that compared the sensitivity and specificity of DSM-IV-TR to DSM-5 criteria utilized retrospective data collection methods and older populations of children (e.g., identifying DSM-5 symptoms in records of those evaluated with DSM-IV-TR criteria and employing a research algorithm applied to previously collected diagnostic instruments). To our knowledge, no study has examined concurrent coding of DSM-IV-TR and DSM-5 criteria for ASD by a clinician who evaluated the child at a developmental period when symptoms may be first recognized by a parent or healthcare professional.

The Study to Explore Early Development (SEED) is a multi-site case–control study designed to explore risk factors and behavioral phenotypes associated with ASD in children 2–5 years of age [17]. In its second phase of data collection (SEED2), study clinicians were asked to complete DSM checklists for both DSM-IV-TR and DSM-5 criteria utilizing all available information on the child. The objectives of this analysis were to (1) report the sensitivity and specificity of DSM-IV-TR and DSM-5 definitions of ASD compared to SEED2 final classification criteria, (2) examine agreement between DSM-IV-TR and DSM-5 definitions of ASD, and (3) evaluate differences between characteristics of children who met DSM-IV-TR but not DSM-5 definitions of ASD, and vice versa.

Methods

Participant ascertainment

SEED2 is a community-based case–control study conducted in six study sites across the United States: California, Colorado, Georgia, Maryland, North Carolina, and Pennsylvania. The SEED2 protocol was approved by Institutional Review Boards at each site and adhered to ethical standards. Children eligible for data collection were born between January 1, 2008 and December 31, 2011, enrolled between 2 and 5 years of age, resided in one of the study areas, and lived with a knowledgeable caregiver who was competent to communicate in English (or in California and Colorado, in English or Spanish). Three groups of children were recruited from each site: (1) those with known ASD, (2) those with known

developmental delays (DD) identified from multiple educational and health providers or family or physician referral, and (3) those from the general population identified from state vital records. Children in the DD group were later defined as those with ASD symptoms (i.e., those who had ASD risk noted on an ASD screen, received an ASD evaluation, and did not meet study criteria for ASD) and those without ASD symptoms (i.e., those who did not have ASD risk noted on an ASD screen and, therefore, received a more limited evaluation). Families were highly diverse, including non-white minorities and low socioeconomic status families, with distributions comparable to the racial and ethnic diversity in the United States [18]. Caregivers of enrolled children gave written consent to participate in the study. A detailed description of eligibility criteria, ascertainment methods, enrollment methods, and data collection procedures can be found in Schendel et al. [17].

Data collection procedures

The Social Communication Questionnaire (SCQ) [19] was administered to all families to provide an initial assessment of ASD risk and determine assessment procedures. All children were given the Mullen Scales of Early Learning (MSEL) [20]; the MSEL Early Learning Composite score was used as a measure of ID. Families of children who obtained a score of 11 or higher on the SCQ, had a previous ASD diagnosis, or demonstrated ASD behaviors during the MSEL administration were asked to complete the Autism Diagnostic Interview-Revised (a comprehensive parent interview) (ADI-R) [21], Autism Diagnostic Observation Schedule (a standardized observation of the child) (ADOS) [22, 23], and Vineland Adaptive Behavior Scales-Second Edition (VABS-II) [24]. The ADOS and ADI-R are considered gold-standard diagnostic instruments used to differentiate children with ASD from children with other DD [25].

Clinicians who administered the ADOS and ADI-R had at least a Master's degree in psychology or related field and were deemed field ready once they established administration fidelity and research reliability with a supervising clinician at their site. These clinicians were monitored by the supervising clinician for administration fidelity at least once per year and for coding reliability at least once per quarter (or every 10th ASD assessment). First-pass coding reliability for field clinicians was 92% for the ADOS and 97% for the ADI-R. Supervising clinicians had a doctorate degree in psychology, medicine, or related field and established research reliability with a certified ADOS and ADI-R trainer. Supervising clinicians were monitored by each other for administration fidelity once during the study period and for coding reliability at least once per quarter. First-pass coding reliability for supervising clinicians also was 92% for the ADOS and 97% for the ADI-R.

DSM definitions

The clinician(s) who administered the ADOS and ADI-R completed two diagnostic checklists adapted for SEED2 from the Ohio State University (OSU) Autism Rating Scale [26]: one for DSM-IV-TR criteria and one for DSM-5 criteria. When completing the checklists, the clinician(s) was asked to rate each of the diagnostic criteria on the following scale: (0) never or rarely/not a problem, (1) sometimes/a little problem, (2) often/a pretty big problem, and (3) very often/a severe problem, given all available information on the child. Clinicians had access to information on ASD symptoms noted on the Social Responsiveness

Scale [27], behavior problems noted on the Child Behavior Checklist [28], and previously diagnosed conditions noted on a maternal interview, in addition to information collected with the ADI-R, ADOS, MSEL, VABS-II, and SCQ. Checklists were completed by both clinicians in collaboration when the ADOS and ADI-R were completed by two qualified staff members. Checklists were completed by one clinician when the ADOS and ADI-R were administered by the same person. The DSM-IV-TR checklist was administered before the DSM-5 checklist in the SEED2 study.

DSM-IV-TR autistic disorder was defined as the presence of at least six criteria (i.e., checklist ratings of 1) with two from the social domain, at least one from the communication domain, and at least one from the behavioral domain (Table 1). We considered a threshold of 1 for autistic disorder criteria because DSM-IV-TR denotes presence rather than severity of symptoms for diagnosis. A definition of Asperger disorder was not specified because only 30 children with ASD in the SEED2 sample did not have a cognitive or language delay noted on the MSEL and there were less than five of these children in some cells used to calculate sensitivity and specificity. Definitions of Childhood Disintegrative Disorder and Rett Syndrome were not created due to the low prevalence of these conditions. Two definitions of PDD-NOS were created for this analysis as indicated in the DSM-IV-TR:

- Impairment in any of the social criteria rated as (2) often/a pretty big problem or (3) very often/a severe problem AND impairment in any of the communication criteria rated as 1 (denoting "severe and pervasive impairment" in social skills and presence of communication deficits) (PDD-NOS(1)).

- Impairment in any of the social criteria rated as (2) often/a pretty big problem or (3) very often/a severe problem AND any of the behavioral criteria rated as 1 (denoting "severe and pervasive impairment" in social skills and presence of restricted behavior, interests, or activities) (PDD-NOS(2)).

We did not create DSM-IV-TR PDD-NOS definitions independent of DSM-IV autistic disorder (i.e., the same child could meet all definitions). This method allowed assessment of clinical definitions independent of others with maximal sample size.

DSM-5 ASD was defined as the presence of all three social symptoms (i.e., ratings of 1) and two of four behavioral symptoms (Table 2). The clinician(s) who completed DSM-IV-TR and DSM-5 checklists was also asked to rate severity of ASD symptoms (categorized for this analysis as mild, moderate, severe, or symptoms accounted for by another disorder), and certainty the child had ASD (categorized for this analysis as certain or uncertain).

ASD case status

SEED2 ASD case status was based on the results of the ADOS and ADI-R rather than a previous diagnosis or the diagnostic checklist. Briefly, children classified as ASD were those who met ASD criteria on both the ADI-R and ADOS, or who met ASD criteria on the ADOS and one of three alternate criteria on the ADI-R (i.e., met criteria on the social domain and was within two points on the communication domain, met criteria on the communication domain and was within two points on the social domain, or met criteria on

the social domain and had two points noted on the behavioral domain). Thus, if results of the ADOS and ADI-R were discrepant, the child could still be defined as an ASD case if ADOS criteria were met and one of the three alternate ADI-R criteria were met.

We recognize that diagnostic instruments alone cannot replace informed clinical judgment when diagnosing children with ASD. However, scores from the ADI-R and ADOS are both sensitive and specific in detecting children with ASD when used in combination, and offer several advantages to classify children with ASD in large epidemiologic studies. First, ADI-R and ADOS scores are assigned by experienced and reliable clinicians and offer a uniform method of characterizing ASD symptoms in large cohorts of children that can be replicated in other studies. Second, symptom profiles gleaned from the ADI-R and ADOS allow the opportunity to create ASD sub-groups based on observed and/or reported symptoms that could represent a range of behavioral trajectories and phenotypes. Consequently, using the ADI-R and ADOS to classify children with ASD may be advantageous when well-defined groups of children are an important clinical or research outcome.

Previous analyses found that SEED final classification criteria had a good balance of sensitivity and specificity when compared to clinical judgment of whether the child had ASD or another DD, and support the use of these instruments when defining ASD case status in SEED [29]. Moreover, kappa agreement between SEED2 final classification status and clinical judgment was 0.71, reflecting substantial agreement. Details on the SEED final classification algorithm can be found in Wiggins et al. [29].

Statistical methods

Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were assessed for the following ASD definitions compared to SEED2 final classification criteria as the gold-standard: DSM-5 ASD and DSM-IV-TR autistic disorder, PDD-NOS(1), PDD-NOS(2), and PDD-NOS(3). Sensitivity was the number of true positives (i.e., those defined as ASD by both the DSM checklist and SEED2 criteria) divided by the number of those defined as ASD by SEED2 criteria. Specificity was the number of true negatives (i.e., those defined as non-ASD by both the DSM checklist and SEED2 criteria) divided by the number of children defined as non-ASD based on SEED2 criteria. PPV was the number of true positives divided by the number of children who were defined as ASD by a DSM checklist definition; NPV was the number of true negatives divided by the number of children who were defined as non-ASD by a DSM checklist definition. The kappa statistic examined agreement between DSM-IV-TR and DSM-5 definitions of ASD, and chi square examined differences in characteristics of children who met DSM-IV-TR but not DSM-5 definitions of ASD, and vice versa. Due to multiple comparisons, significance for p was set at 0.01.

Results

A total of 773 children met SEED2 criteria for ASD and 288 met criteria for another DD after a comprehensive evaluation. The study sample, therefore, consisted of those defined as ASD ($n = 773$) and those previously described as DD with ASD symptoms ($n = 288$). Children classified as ASD were more likely to be male (81% versus 65%; $\chi^2 = 28.11$, $p <$

0.01) and have ID (63% versus 33%; $\chi^2 = 74.06$, $p < 0.01$) than those with DD and ASD symptoms. Children classified as ASD and those classified as DD with ASD symptoms did not differ in terms of maternal ethnicity, maternal race, or child age at the time of clinic visit: 15.8% of mothers identified as Hispanic, 51.8% of mothers identified as White, and the mean child age at the time of the clinic visit was 55 months (range 28–70 months).

Of the 1061 ASD and DD with ASD symptoms children in the sample, 802 met DSM-5 ASD, 864 met DSM-IV-TR autistic disorder, 744 met PDD-NOS(1) and 736 met PDD-NOS(2). Sensitivity, specificity, PPV, and NPV for each of these DSM definitions are shown in Table 3. DSM-5 ASD had a better balance of sensitivity and specificity compared to the SEED2 classification than DSM-IV-TR autistic disorder, PDD-NOS(1), or PDD-NOS(2).

There was substantial agreement between DSM-5 ASD and DSM-IV-TR autistic disorder [κ = 0.78 (95% CI 0.73–0.82)]. Agreement between DSM-5 ASD and DSM-IV-TR PDD-NOS(1) and PDD-NOS(2) was moderate [$\kappa = 0.57$ (95% CI 0.54–0.60) and $\kappa = 0.59$ (95% CI 0.56–0.62), respectively].

There were 71 children who met DSM-IV-TR autistic disorder but not DSM-5 ASD and 66 children who met DSM-IV-TR PDD-NOS(1) or DSM-IV-TR PDD-NOS(2) but not DSM-5 ASD. Characteristics of these children compared to those who did not have conflicting DSM-IV-TR and DSM-5 definitions are shown in Table 4.

Of note, there were 9 children who met DSM-5 ASD but not DSM-IV-TR autistic disorder, and 120 children who met DSM-5 ASD, but not PDD-NOS(1) or PDD-NOS(2). Children who met DSM-5 ASD but not PDD-NOS(1) or PDD-NOS(2) were less likely to have intellectual disability ($\chi^2 = 28.1$, $p < 0.01$) and more likely to be female ($\chi^2 = 8.5$, $p = 0.01$) and have mild ASD symptoms ($\chi^2 = 65.4$, $p < 0.01$). There were no differences between children who met DSM-5 ASD but not PDD-NOS(1) or PDD-NOS(2) in terms of maternal ethnicity, maternal race, or clinician certainty the child had ASD.

Discussion

To our knowledge, this is the first study to compare concurrent coding of DSM-IV-TR and DSM-5 criteria for ASD by a research-reliable clinician who evaluated preschool children in multiple US communities. Results suggest that the DSM-5 definition of ASD maximizes diagnostic sensitivity and specificity in the SEED2 sample of young children. Moreover, agreement between DSM-5 and DSM-IV-TR definitions of ASD were good for autistic disorder and moderate for PDD-NOS. Children who met DSM-IV-TR autistic disorder, but not DSM-5 ASD were more likely to have mild ASD symptoms, or their symptoms were accounted for by another disorder. Children who met PDD-NOS but not DSM-5 ASD, or vice versa, were less likely to have ID and more likely to be female. These findings support the DSM-5 conceptualization of ASD in preschool children [30], and highlight the need to learn more about the developmental profile and service needs of females with ASD and those with milder symptoms.

Although ASD traits cluster among those diagnosed with ASD, specific ASD behaviors are distributed across the general population [31]. Consequently, creating boundaries for clinical

diagnosis or research classification inherently includes some children with ASD symptoms and excludes others with milder symptoms or subthreshold presentation. The goal of categorical diagnostic systems is to maximize diagnostic sensitivity (accurate inclusion of true positives) as well as diagnostic specificity (accurate exclusion of true negatives). Results presented herein suggest that DSM-5 criteria for ASD achieves this goal within a large community-based sample of preschool children. These results should be replicated in other large and geographically diverse samples that incorporate concurrent coding of DSM-IV-TR and DSM-5 criteria in a clinic setting.

Some children in the SEED2 sample had a developmental profile defined by mild ASD symptoms and symptoms that were better accounted for by another disorder. These children were more likely to meet DSM-IV-TR autistic disorder, but not DSM-5 ASD, or either of the DSM-IV-TR PDD-NOS definitions but not DSM-5 ASD. Additionally, children who met PDD-NOS(1) or PDD-NOS(2) but not DSM-5 ASD, or vice versa, were less likely to have ID and more likely to be female. These findings are strikingly similar to an analysis of 439 children and adolescents enrolled in the Autism Treatment Network [30]. Previous SEED analyses have shown that children termed "DD with ASD symptoms" and used in these analyses have a phenotypic profile more similar to children with ASD than children with other DD [32]. These children may be those seen in clinic settings to differentiate from children with ASD, and likely face developmental challenges that warrant professional attention. Service delivery may, therefore, be more effective if based on the strengths and challenges of the individual child rather than inclusion in one categorical diagnosis. More research is needed on the developmental status of children with DD with ASD symptoms, and how they are recognized, diagnosed, and treated.

Less is known about the ASD phenotype of females compared to males with ASD [33]. Among females and males with similar ASD traits, females with more behavior problems or ID, or both, are more likely to be recognized and diagnosed [34, 35]. These results imply that higher-functioning females and those without ID may be missed by current diagnostic systems. Results of this study add to this dialogue by providing evidence that females who meet DSM-IV-TR autistic disorder are as likely as males to meet DSM-5 ASD; however, they are more likely than males to shift between DSM-IV-TR PDD-NOS and DSM-5 ASD.

DSM-IV-TR definitions of autistic disorder and PDD-NOS(1) and PDD-NOS(2) had an adequate balance of sensitivity and specificity. In fact, diagnostic specificity for PDD-NOS(1) and PDD-NOS(2) was higher in these analyses than previous reports. One possible reason for the improvement in PDD-NOS specificity seen in this paper is that we considered severity rather than mere presence of social deficits in our PDD-NOS definition. If only presence of any of the social deficits were required, in addition to presence of any of the communication or behavioral deficits, specificity would have dropped from 0.75 to 0.06 for PDD-NOS(1) and 0.78 to 0.16 for PDD-NOS(2) (data not shown). Consequently, considering the severity of social deficits among those with subthreshold DSM-5 ASD presentation may help guide decisions to monitor the ASD symptoms over time, especially among females and those without ID.

There are limitations associated with this study. First, evaluation instruments were administered in SEED2 as part of a research protocol so clinicians did not have a choice in the information collected to assess diagnostic symptoms. However, the instruments that were administered in SEED2 are considered gold-standard diagnostic instruments, and elicit valid and reliable information on ASD symptoms and other areas of development. Second, information collected during the child observation (ADOS) and parent interview (ADI-R) were considered in the diagnostic checklist, so the SEED final classification criteria and DSM definitions were not completely independent of one another. Nonetheless, this process reflects clinical practice and, therefore, may generalize to real-world clinic settings. Third, SEED2 did not systematically collect criteria for Social Communication Disorder (SCD), which was introduced in DSM-5 and thought to capture some children formerly defined as PDD-NOS. The closest definition of SCD in this study is PDD-NOS(1), which had an adequate balance of sensitivity and specificity for ASD classification. Fourth, the sample was limited to children 2–5 years of age who competed a comprehensive evaluation because of ASD risk noted on the SCQ. Sample characteristics undoubtedly influence measures of sensitivity and specificity so precaution must be taken when interpreting results. For instance, estimates of specificity (i.e., the number of true negatives) may have been reduced because only children with some social and communication difficulties—rather than children from the general population—were included the sample. Again, these sample characteristics may reflect clinical practice of distinguishing children with ASD from children with other DD, but must be considered nonetheless. In sum, these results are best generalized to samples with a similar age and developmental profile and may look different in sample of younger or older children or those with few social and communication concerns. Finally, this study was conducted many years after the publication of DSM-5 in 2013 although it is novel in the approach and sample used to compare the sensitivity and specificity of DSM-IV-TR and DSM-5 definitions of ASD. The strengths of our analyses outweigh these limitations. This is the first study to present concurrent coding of DSM-IV-TR and DSM-5 criteria for ASD by a clinician who evaluated preschool children with gold-standard diagnostic instruments. The sample was large and ascertained from clinic and non-clinic sources in multiple geographic areas throughout the United States. Results contribute to an important body of literature on how diagnostic criteria distinguish children with varied ASD symptoms, and highlights the need to learn more about those with mild ASD symptoms and the ASD phenotype in females. In conclusion, these findings support the DSM-5 conceptualization of ASD in preschool children and highlight areas for future research.

Acknowledgements

References

1. American Psychiatric Association (2013) Diagnostic and statistical manual of mental disorders, 5th edn American Psychiatric Publishing, Arlington

2. Buescher A, Cidav Z, Knapp M, Mandell DS (2014) Cost of autism spectrum disorders in the United Kingdom and United States. JAMA Pediatrics 168:721–728 [PubMed: 24911948]

3. Hock R, Ahmedani B (2012) Parent perceptions of autism severity: exploring the social ecological context. Dis Heal J 5:298–304

4. Jang J, Matson JL (2015) Autism severity as a predictor of comorbid conditions. J Dev Phys Disabil 27:405–415

5. Boyd BA, Odom SL, Humphreys BP, Sam AM (2010) Infants and toddlers with autism spectrum disorder: early identification and early intervention. J Earl Intervent 32:75–98

6. Corsello C (2005) Early intervention in autism. Inf Youn Children 18:74–85

7. Johnson CP, Myers SM, American Academy of Pediatrics, Council on Children with Disabilities (2007) Identification and evaluation of children with autism spectrum disorders. Pediatrics 120:1183–1215 [PubMed: 17967920]

8. American Psychiatric Association (1994) Diagnostic and statistical manual of mental disorders, 4th edn American Psychiatric Association, text revision). Washington, DC

9. First MD, Pincus HA (2002) The DSM-IV text revision: rationale adn potential impact on clinical practice. Psych Serv 53:588–592

10. Volkmar FR, Shaffer D, First M (2000) PDDNOS in DSM-IV. J Autism Dev Disord 30:74–75 [PubMed: 10819126]

11. Levy SE, Giarelli E, Lee LC, Schieve L, Kirby R, Cunniff C et al. (2010) Autism spectrum disorder and co-occurring develop-mental, psychiatric, and medical conditions among children in multiple populations of the United States. J Dev Beh Pediatrics 31(4):267–275

12. Zwaigenbaum L, Bauman ML, Stone WL, Yirmiya N, Estes A, Harman R et al. (2015) Early identification of autism spectrum disorder: implications for practice and research. Pediatrics 136:S10–S40 [PubMed: 26430168]

13. Swedo SE, Baird G, Cook EH, Happé FG, Harris JC, Kaufmann WE et al. (2012) Commentary from the DSM-5 workgroup on neurodevelopmental disorders. J Amer Acad Child Adoles Psychiatry 51(4):347–349

14. Maenner MJ, Rice CE, Arneson CL, Cunniff C, Schieve LA, Carpenter LA et al. (2014) Potential impact of DSM-5 criteria on autism spectrum disorder prevalence estimates. JAMA Psychiatry 71(3):292–300 [PubMed: 24452504]

15. Mattila ML, Kielinen M, Linna SL, Jussila K, Ebeling H, Bloigu R et al. (2011) Autism spectrum disorder according to DSM-IV-TR and comparison with DSM-5 draft criteria: an epidemiological study. J Am Acad Child Adoles Psychiatry 50:583–592

16. Tsai LY (2014) Impact of DSM-5 on epidemiology of autism spectrum disorder. Res Aut Spec Disorders 8(11):1454–1470

17. Schendel D, DiGuiseppi C, Croen L, Fallin D, Reed P, Schieve L et al. (2012) The Study to Explore Early Development (SEED): a multi-site epidemiologic study of autism by the Centers for Autism and Developmental Disabilities Research and Epidemiology (CADDRE) Network. J Autism Dev Disord 42:2121–2140 [PubMed: 22350336]

18. DiGuiseppi C, Daniels J, Fallin D, Rosenberg S, Schieve L, Thomas K et al. (2016) Demographic profile of families and children in the Study to Explore Early Development (SEED): case–control study of autism spectrum disorder. Dis Heal J 9:544–551

19. Rutter MA, Bailey A, Lord C (2003) The social communication questionnaire. Western Psychological Services, Los Angeles

20. Mullen E (1995) Mullen Scales of early learning. Pearson, San Antonio

21. Lord C, Rutter M, Le Couteur AL (1994) Autism diagnostic interview-revised: a revised version of a diagnostic interview for caregivers of individuals with possible pervasive developmental disorders. J Aut Dev Disord 24:659–685

22. Gotham K, Risi S, Pickles A, Lord C (2007) The autism diagnostic observation schedule: revised algorithms for improved diagnostic validity. J Aut Dev Disord 37:613–627

23. Lord C, Rutter M, DiLavore PC, Risi S (1999) Autism diagnostic observation schedule. Western Psychological Services, Los Angeles

24. Sparrow S, Balla D, Cicchetti D (2005) Vineland adaptive behavior scales, 2nd edn Pearson, San Antonio

25. Gray K, Tonge B, Sweeney D (2008) Using the autism diagnostic interview-revised and the autism diagnostic observation schedule with young children with developmental delay: evaluating diagnostic validity. J Aut Dev Disord 38:657–667

26. The Ohio State University (OSU) Research Unit on Pediatric Psychopharmacology (2005) OSU Autism Rating Scale (OARS; adapted for SEED) and Clinical Global Impression (CGI; adapted for SEED). Retrieved August 30, 2010 from http://psychmed.osu.edu/resources.htm

27. Constantino J (2002) The social responsiveness scale. Western Psychological Services, Los Angeles

28. Achenbach T (1992) Child behavior checklist. Achenbach System of Empirically Based Assessment, Burlington

29. Wiggins LD, Reynolds A, Rice C, Moody EJ, Bernal P, Blaskey L et al. (2015) Using standardized diagnostic instruments to classify children with autism in the Study to Explore Early Development. J Aut Dev Disord 45:1271–1280

30. Mazurek MO, Lu F, Symecko H, Butter E, Bing NM, Hundley RJ et al. (2017) A prospective study of the concordance of DSM-IV and DSM-5 diagnostic criteria of autism spectrum disorder. J Aut Dev Disord 47:2783–2794

31. Constantino J, Todd R (2003) Autistic traits in the general population: a twin study. Arch Gen Psychiatry 60:524–530 [PubMed: 12742874]

32. Wiggins LD, Levy SE, Daniels J, Schieve L, Croen LA, DiGuiseppi C et al. (2015) Symptoms of autism spectrum disorder among children enrolled in the Study to Explore Early Development. J Aut Dev Disord 45:3183–3194

33. Rivet TT, Matson JL (2011) Review of gender differences in core symptomatology in autism spectrum disorders. Res Aut Spect Disord 5:957–976

34. Dworzynski K, Ronald A, Bolton R, Happe F (2012) How different are girls and boys above and below the diagnostic threshold for autism spectrum disorders? J Am Acad Chil Adoles Psychiatry 51:788–797

35. Frazier TW, Georgiades S, Bishop SL, Hardan AY (2014) Behavioral and cognitive characteristics of females and males with autism in the Simons Simplex Collection. J Am Acad Chil Adoles Psychiatry 53:329–340

Table 1

Checklist for autism spectrum disorder criteria outlined in the Diagnostic and Statistical Manual of Mental Disorders-Fourth edition-Text Revision

Never or rarely Not a problem (0)	Sometimes or a little A little problem (1)	Often A pretty big problem (2)	Very often A severe problem (3)
A. *Impairment in social interaction*			
1. Impairment in the use of multiple, nonverbal behaviors such as eye-to-eye gaze, facial expression, body postures, and gestures to regulate social interaction			
2. Impaired peer relations (compared to developmental level)			
3. Impairment in spontaneous seeking to share enjoyment, interests, or achievements with other people			
4. Impairment in social or emotional reciprocity (returning smiles or greetings, looking at speaker)			
B. *Impairment in communication*			
1. Does not attempt to speak or communicate; if nonverbal, fails to use gesture or mime to communicate			
2. If adequate speech: impairment in the ability to initiate or sustain a conversation (mark N/A in last column if nonverbal)			
3. Stereotyped and repetitive use of language or sounds or idiosyncratic language			
4. Lack of varied, spontaneous make-believe play or social imitative play appropriate to developmental level			
C. *Restricted repetitive and stereotyped patterns of behavior, interests, and activities*			
1. Excessive preoccupation with or stereotyped, restricted patterns of *interest* that are abnormal/odd either in intensity or focus			
2. Inflexible adherence to specific, nonfunctional *routines or rituals*			
3. Stereotyped, repetitive *motor mannerisms* (e.g., hand or finger flapping, or twisting, or complex whole-body movements or "self-stimming")			

Table 2

Checklist for autism spectrum disorder criteria outlined in the Diagnostic and Statistical Manual of Mental Disorders-Fifth edition

Never or rarely Not a problem (0)	Sometimes or a little A little problem (1)	Often A pretty big problem (2)	Very often A severe problem (3)
A. Impairment in social communication and social interaction			
1. Deficits in social-emotional reciprocity; ranging from abnormal social approach and lack of back and forth conversation through total lack of initiation of social interaction			
2. Deficits in nonverbal communicative behaviors used for social interaction; ranging from poorly integrated-verbal and nonverbal communication, through abnormalities in eye contact and total lack of facial expression or gestures			
3. Deficits in developing and maintaining relationships, appropriate to developmental level (beyond caregivers); ranging from difficulties adjusting behavior to suit different social contexts through absence of interest in people			
B. Restricted repetitive and stereotyped patterns of behavior, interests, and activities			
1. Stereotyped or repetitive speech, motor movements, or use of objects; (such as simple motor stereotypies, echolalia, repetitive use of objects, or idiosyncratic phrases)			
2. Excessive adherence to routines, ritualized patterns of verbal or nonverbal behavior, or excessive resistance to change; (such as motoric rituals, insistence on same route or food, repetitive questioning or extreme distress at small changes)			
3. Highly restricted, fixated interests abnormal in intensity or focus; (such as strong attachment to or preoccupation with unusual objects, excessively circumscribed or perseverative interests)			
4. Hyper-or hypo-reactivity to sensory input or unusual interest in sensory aspects of environment; (such as apparent indifference to pain/heat/cold, adverse response to specific sounds or textures, excessive smelling or touching of objects, fascination with lights)			

Table 3

Psychometric properties of autism spectrum disorder criteria outlined in the Diagnostic and Statistical Manual of Mental Disorders (DSM) and defined in the Study to Explore Early Development-Phase 2 (SEED2)

	SEED2 final classification		
	ASD	DD	
Meets DSM-5 ASD[a]	738	64	Sens = 0.95
Does not meet DSM-5 ASD	35	224	Spec = 0.78 PPV = 0.92 NPV = 0.86
Meets DSM-IV autistic disorder[b]	761	103	Sens = 0.98
Does not meet DSM-IV autistic disorder	12	185	Spec = 0.64 PPV = 0.88 NPV = 0.94
Meets DSM-IV-TR PDD-NOS(1)[c]	673	71	Sens = 0.87
Does not meet DSM-IV-TR PDD-NOS (1)	100	217	Spec = 0.75 PPV = 0.90 NPV = 0.68
Meets DSM-IV-TR PDD-NOS(2)[d]	673	63	Sens = 0.87
Does not meet DSM-IV-TR PDD-NOS(2)	100	225	Spec = 0.78 PPV = 0.91 NPV = 0.69

[a]All three social symptoms and two of four behavioral symptoms in DSM-5

[b]At least six of 12 total criteria with two from the social domain, at least one from the communication domain, and at least one from the behavioral domain in DSM-IV-TR

[c]Impairment in any of the social criteria rated as a pretty big problem or severe problem AND presence of any of the communication criteria in DSM-IV-TR

[d]Impairment in any of the social criteria rated as a pretty big problem or severe problem AND presence of any of the behavioral criteria in DSM-IV-TR

Table 4

Characteristics of children with diagnostic agreement between autism spectrum disorder (ASD) definitions compared to those with diagnostic disagreement

	DSM-IV-TR autistic disorder			DSM-IV-TR PDD-NOS(1) or PDD-NOS(2)		
	Met DSM-IV-TR Autistic Disorder but not DSM-5 ASD N=71	Diagnostic agreement between DSM-IV-TR and DSM-5 N = 990	P for χ^2	Met DSM-IV-TR PDD-NOS but not DSM-5 ASD N = 66	Diagnostic agreement between DSM-IV-TR and DSM-5 N = 995	P for χ^2
	N (%)			N (%)		
ASD symptom severity						
Mild	24 (34%)	159 (16%)	< 0.01*	24 (35%)	159 (16%)	< 0.01*
Moderate	20 (28%)	460 (46%)		15 (24%)	465 (47%)	
Severe	2 (3%)	207 (21%)		3 (4%)	206 (21%)	
Symptoms accounted for by another disorder	25 (35%)	164 (17%)		24 (37%)	165 (16%)	
Child sex						
Male	47 (66%)	768 (77%)	0.03	38 (57%)	777 (78%)	< 0.01*
Female	24 (34%)	221 (22%)		28 (43%)	217 (21%)	
Missing data	-	1 (1%)		-	1 (1%)	
Child intellectual functioning						
Intellectual disability	32 (45%)	551 (56%)	0.09	26 (40%)	557 (56%)	0.01*
No intellectual disability	39 (55%)	430 (43%)		40 (60%)	429 (43%)	
Missing data	-	9 (1%)		-	9 (1%)	
Clinical impression						
Certain the child has ASD	29 (41%)	700 (71%)	< 0.01*	23 (35%)	706 (71%)	< 0.01*
Not certain the child has ASD	42 (59%)	290 (29%)		43 (65%)	289 (29%)	
Maternal ethnicity						
Hispanic	8 (11%)	160 (16%)	0.34	10 (15%)	158 (16%)	0.99
Not Hispanic	63 (89%)	826 (83%)		56 (85%)	833 (83%)	
Missing data	-	4 (1%)		0 (1%)	4 (1%)	
Maternal race						
White	36 (51%)	514 (51%)	0.53	40 (61%)	510 (51%)	0.35
Non-white	35 (49%)	460 (46%)		26 (39%)	469 (47%)	
Missing or refused data	-	16 (3%)		0	16 (2%)	

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

DSM-IV-TR diagnostic statistical manual of mental disorders-Fourth Edition-Text Fourth, *DSM-5* diagnostic statistical manual of mental disorders-fifth edition, *PDD-NOS* pervasive developmental disorders not otherwise