

APPENDIX 14C:

CLINICAL EVIDENCE - STUDY CHARACTERISTICS

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1.1 CHARACTERISTICS OF INCLUDED STUDIES

Study ID	BARONCOHEN2005
Bibliographic reference	Baron-Cohen, S., Wheelwright, S., Robinson, J., <i>et al.</i> (2005) The Adult Asperger Assessment (AAA): a diagnostic method. <i>Journal of Autism and Developmental Disorders</i> , 35, 807–819.
Clinical features and settings	Recruitment: patients attending the Cambridge Lifespan Asperger Syndrome Service. Country: UK.
Participants	N = 42. Age: mean 34.1 years (SD 10.6 years). Sex: ratio 9:1 male:female (28 male, 3 female). Ethnicity: not reported. Intellectual ability: normal range.
Study design	Cohort
Target condition and reference standard(s)	Diagnosis: DSM-IV Asperger’s syndrome and high-functioning autism. Coexisting conditions: none stated.
Index and comparator tests	1. Instrument: AAA. 2. Reference standard: DSM-IV criteria. Assessors: 1. Instrument: clinical psychologist or consultant psychiatrist and a clinician psychologist. 2. Reference standard: clinical psychologist or consultant psychiatrist and a clinician psychologist.
Follow-up	Not reported
Index cut-off	10+
Limitations	Same assessors completed the AAA and DSM-IV criteria.
Source of funding	Three Guineas Trust; MRC; Lifespan Healthcare NHS Trust; Cambridgeshire and Peterborough Mental Health Partnership NHS Trust
Notes	Each patient accompanied by at least one parent as an informant. Patients also completed the AQ and the EQ.

Study ID	BRUGHA2012
<i>Bibliographic reference</i>	Brugha, T. S., McManus, S., Smith, J., <i>et al.</i> (2012) Validating two survey methods for identifying cases of autism spectrum disorder among adults in the community. <i>Psychological Medicine</i> , 42, 647–656.
<i>Clinical features and settings</i>	Recruitment: Participants were recruited from a cohort general-population screening study using the AQ-20. Country: UK.
<i>Participants</i>	N = 199 participants had both an ADOS score and a vignette assessment. Age: not reported, but all participants >16 years. Sex: not reported. Ethnicity: not reported. Intellectual ability: not reported, but assumption that IQ >70 as screened using self-report postal questionnaire (AQ-20).
<i>Study design</i>	Cohort
<i>Target condition and reference standard(s)</i>	Diagnosis: autism (based on case vignette ratings). Coexisting conditions: not reported.
<i>Index and comparator tests</i>	1. Instrument: ADOS-4. 2. Reference standard: case vignette ratings. Assessors: 1. Instrument: research psychologists. 2. Reference standard: clinicians.
<i>Follow-up</i>	Not reported
<i>Index cut-off</i>	7+ and 10+
<i>Limitations</i>	Case vignette ratings are not gold standard for diagnosis.
<i>Source of funding</i>	The NHS Information Centre for Health and Social Care and the Department of Health, London, UK; NIHR and the Department of Health Policy Research Programme, London, UK
<i>Notes</i>	–

Study ID	DZIOBEK2006
<i>Bibliographic reference</i>	Dziobek, I., Fleck, S., Kalbe, E., <i>et al.</i> (2006) Introducing MASC: a Movie for the Assessment of Social Cognition. <i>Journal of Autism and Developmental Disorders</i> , 36, 623–636.
<i>Clinical features and settings</i>	Recruitment: Asperger’s syndrome group from local support groups or referred by specialist clinician. Matched control group from volunteers participating in ongoing studies of normal aging and dementia. Country: US.
<i>Participants</i>	N = Asperger’s syndrome N = 21 (two were excluded post-diagnosis); control N = 20. Age: Asperger’s syndrome group: mean 41.6 years (SD 10.4 years, range 25 to 62 years); matched control group: mean 39.9 years (SD 12.6 years). Sex: Asperger’s syndrome group: 19 male, 2 female; matched control group: 18 male, 2 female. Ethnicity: not stated. Intellectual ability: Asperger’s syndrome group WAIS IQ score of 122 (SD 6.1, range 111 to 134); matched control group WAIS IQ score of 124 (SD 6.3, range 108 to 139).
<i>Study design</i>	Cross-sectional
<i>Target condition and reference standard(s)</i>	Diagnosis: DSM-IV Asperger’s syndrome. Coexisting conditions: none stated.
<i>Index and comparator tests</i>	1. Instrument: MASC. 2. Reference standard: DSM-IV diagnosis; 16/19 also had the ADI-R as parental informants were available (assessed from taped interview). Assessors: 1. Instrument: trained tester. 2. Reference standard: one psychiatrist and two psychologists.
<i>Follow-up</i>	Not reported
<i>Limitations</i>	Sensitivity and specificity data could not be extracted.
<i>Source of funding</i>	Not stated
<i>Notes</i>	<ul style="list-style-type: none"> • Participants underwent medical, neurologic, psychiatric and neurological examinations to exclude any with conditions that could significantly impact of functional ability. • AQ, Reading the Mind in the Eyes Test and a basic emotion recognition task were also administered. • An extensive neurological test battery was administered to assess memory, attention and executive functions.

Study ID	GILLBERG2001
<i>Bibliographic reference</i>	Gillberg, C., Gillberg, C., Rastam, M., <i>et al.</i> (2001) The Asperger Syndrome (and High Functioning Autism) Diagnostic Interview (ASDI): a preliminary study of a new structured clinical interview. <i>Autism</i> , 5, 57-66.
<i>Clinical features and settings</i>	Recruitment: unclear. Country: Sweden.
<i>Participants</i>	N = 24. Age: 6 to 55 years. Sex: 18 male, 6 female. Ethnicity: not stated. Intellectual ability: not stated.
<i>Study design</i>	Cohort
<i>Target condition and reference standard(s)</i>	Diagnosis: DSM-IV Asperger's syndrome. Coexisting conditions: N = 17 with neuropsychiatric disorder.
<i>Index and comparator tests</i>	1. Instrument: ASDI. 2. Reference standard: DSM-IV diagnosis. Assessors: 1. Instrument: two expert neuropsychiatrists (one scoring ASDI and the other observing). 2. Reference standard: two neuropsychiatrists or one neuropsychiatrist and one neuropsychologist.
<i>Follow-up</i>	Not reported
<i>Index cut-off</i>	5/6 algorithm criteria
<i>Limitations</i>	High risk of bias in terms of index test, and concerns about applicability with regard to patient selection and index test.
<i>Source of funding</i>	Swedish MRC (grant no. K2000-21X-11251-06C). State grants under the LUA (Läkarutbildningsavtal) agreement
<i>Notes</i>	-

Study ID	LORD1997
<i>Bibliographic reference</i>	Lord, C., Pickles, A., McLennan, J., <i>et al.</i> (1997) Diagnosing autism: analyses of data from the Autism Diagnostic Interview. <i>Journal of Autism and Developmental Disorders</i> , 27, 501–517.
<i>Clinical features and settings</i>	Recruitment: data and referrals from eight sites (Institute of Psychiatry, University of London; Greensboro-High Point TEACH Centre, NC; Johns Hopkins University, MD; Glenrose Hospital, Edmonton, Alberta, Canada; INSERM Research Team, France; University of Pittsburgh Clinic for Social Dysfunction, PA; Emory University, DC. Country: Canada, US, UK and France
<i>Participants</i>	N = 330. Age: non-verbal participants' mean age 14.5 years (SD 7.2 years, range 3 to 37 years); verbal participants mean age 21.4 years (SD 6.9 years, range 12 to 40 years). Sex: not stated. Ethnicity: not stated. Intellectual ability: non-verbal group IQ 56 (SD 17.9, range 39 to 84) Verbal group IQ 94.8 (SD 14.3, range 80 to 144).
<i>Study design</i>	Cohort
<i>Target condition and reference standard(s)</i>	Diagnosis: DSM-III-R autism, PDD. Coexisting conditions: none stated.
<i>Index and comparator tests</i>	1. Instrument: ADI. 2. Reference standard: DSM-III-R diagnostic criteria. Assessors: 1. Instrument: unknown – scores on the instrument obtained from records. 2. Reference standard: clinical judgement of principle investigator/ senior research associates.
<i>Follow-up</i>	Not reported
<i>Index cut-off</i>	Communication: 8+ for verbal and 6+ for non-verbal. Social reciprocity: 10+. Restricted and repetitive behaviour: 4+.
<i>Limitations</i>	Scores on the ADI were obtained by unknown raters.
<i>Source of funding</i>	NIMH K05 MH01196, MH19726. Grant from the John D. And Catherine T. MacArthur Foundation in association with the DSM-IV Field Trials to the first author
<i>Notes</i>	–

Study ID	LORD2000
<i>Bibliographic reference</i>	Lord, C., Risi, S., Lambrecht, L., <i>et al.</i> (2000) The Autism Diagnostic Observation Schedule-Generic: a standard measure of social and communication deficits associated with the spectrum of autism. <i>Journal of Autism and Developmental Disorders</i> , 30, 205–223.
<i>Clinical features and settings</i>	Recruitment: referrals to the Developmental Disorders Clinic, University of Chicago. Country: US and UK.
<i>Participants</i>	N = 45 (20 participants used in reliability analyses). Age: autism group 18.65 years (SD 7.79 years); PDD-NOS group 21.59 years (SD 8.56 years); non-spectrum group 19.11 years (SD 6.27 years). Sex: 37 male, 8 female. Ethnicity: not stated. Intellectual ability: verbal IQ: autism group 99.94 (SD 22.29); PDD-NOS group 105.5 (SD 21.46); non-autism group 99.73 (SD 26.69) non-verbal IQ: autism group 94.06 (SD 28.22); PDD-NOS group 105.21 (SD 21.82); non-autism group 103.8 (SD 27.48).
<i>Study design</i>	Case-control
<i>Target condition and reference standard(s)</i>	Diagnosis: ADOS-G. Coexisting conditions: none stated.
<i>Index and comparator tests</i>	1. Instrument: ADOS-G-4. 2. Reference standard: clinical interview (included use of the ADI-R). Assessors: 1. Instrument: 12 experienced examiners. 2. Reference standard: clinical psychologist and clinical psychiatrist.
<i>Follow-up</i>	Not reported
<i>Index cut-off</i>	13+
<i>Limitations</i>	High risk of bias in terms of patient selection, reference standard and flow and timing, and concerns regarding applicability with regard to patient selection.
<i>Source of funding</i>	Not stated
<i>Notes</i>	Assessment conducted live and via videotape.

Study ID	MATSON2007A
<i>Bibliographic reference</i>	Matson, J. L., Boisjoli, J. A., Gonzalez, M. L., <i>et al.</i> (2007) Norms and cut off scores for the Autism Spectrum Disorders Diagnosis for Adults (ASD-DA) with intellectual disability. <i>Research in Autism Spectrum Disorders, 1</i> , 330–338.
<i>Clinical features and settings</i>	Recruitment: residents from two developmental centres located in the Southeastern region of the US. Country: US.
<i>Participants</i>	N = 232. Age: 20 to 80 years. Sex: not stated. Ethnicity: not stated. Intellectual ability: learning disability: profound N = 176; severe N = 33; moderate N = 12; mild N = 1; unspecified N = 10.
<i>Study design</i>	Case-control
<i>Target condition and reference standard(s)</i>	Diagnosis: DSM-IV/ICD-10 ASD. Coexisting conditions: with/ without a learning disability (profound to mild).
<i>Index and comparator tests</i>	1. Instrument: ASD-DA. 2. Reference standard: DSM-IV/ICD-10 diagnosis criteria list of symptoms. Assessors: 1. Instrument: clinical psychology doctorate students. 2. Reference standard: clinical psychology doctorate students.
<i>Follow-up</i>	Not reported
<i>Index cut-off</i>	24+ and 28+
<i>Limitations</i>	Case-control design with high risk of bias in terms of patient selection, index test and reference standard, and concerns about applicability with regard to patient selection and index test.
<i>Source of funding</i>	Not stated
<i>Notes</i>	–

Study ID	MATSON2007B
<i>Bibliographic reference</i>	Matson, J. L. & Wilkins, J. (2007) Reliability and factor structure of the Autism Spectrum Disorders – Diagnosis Scale for Intellectually Disabled Adults (ASD-DA). <i>Journal of Developmental and Physical Disabilities</i> , 19, 565–577.
<i>Clinical features and settings</i>	Recruitment: Residents from two developmental centres in central or south Louisiana. Country: US.
<i>Participants</i>	N = 192. Age: autism group mean age 48.4 years (SD 10.9 years, range 20 to 78 years); control group mean age 53.9 years (SD 13.5 years, range 27 to 88 years). Sex: 109 male, 83 female. Ethnicity: Caucasian: autism group 72%; control group 72.9%. Intellectual ability: learning disability: profound N = 142; severe N = 28; moderate N = 13; mild N = 1. Per group profound learning disability: autism group 88.8%; control group 52.9%.
<i>Study design</i>	Cross sectional
<i>Target condition and reference standard(s)</i>	Diagnosis: ASD (autism or PDD). Coexisting conditions: learning disability.
<i>Index and comparator tests</i>	1. Instrument: ASD-DA. 2. Reference standard: DSM-IV-TR and ICD-10 diagnostic criteria. Assessors: 1. Instrument: PhD students in clinical psychology. 2. Reference standard: PhD students in clinical psychology.
<i>Index cut-off</i>	Not applicable
<i>Follow-up</i>	Not reported
<i>Limitations</i>	Only reliability data reported in this paper.
<i>Source of funding</i>	Not stated
<i>Notes</i>	–

Study ID	MATSON2008
<i>Bibliographic reference</i>	Matson, J. L., Wilkins, J., Boisjoli, J. A., <i>et al.</i> (2008) The validity of the Autism Spectrum Disorders-Diagnosis for Intellectually Disabled Adults (ASD-DA). <i>Research in Developmental Disabilities</i> , 29, 537-546.
<i>Clinical features and settings</i>	Recruitment: residents of developmental centres. Country: US.
<i>Participants</i>	N = 307. Age: mean age 55 years, range 16 to 88 years. Sex: 168 male, 139 female. Ethnicity: percentage Caucasians: autism group 78.2%; control group 76% Intellectual ability: learning disabilities: profound N = 235; severe N = 40; moderate N = 16; mild N = 2; unspecified N = 14.
<i>Study design</i>	Cross sectional
<i>Target condition and reference standard(s)</i>	Diagnosis: DSM-IV-TR or ICD-10 ASD. Coexisting conditions: anxiety disorders, depressive disorder, pica and stereotypic movement disorder.
<i>Index and comparator tests</i>	1. Instrument: ASD-DA. 2. Reference standard: DSM-IV-TR or ICD-10 clinical diagnosis. Assessors: 1. Instrument: PhD level clinical psychology student. 2. Reference standard: PhD level clinical psychology student.
<i>Follow-up</i>	Not reported
<i>Index cut-off</i>	Not applicable
<i>Limitations</i>	Only convergent and discriminant validity reported in this paper.
<i>Source of funding</i>	Not stated
<i>Notes</i>	Direct care staff were interviewed not adults with autism.

Study ID	RITVO2008
<i>Bibliographic reference</i>	Ritvo, R. A., Ritvo, E. R., Guthrie, D., <i>et al.</i> (2008) A scale to assist the diagnosis of autism and Asperger's disorder in adults (RAADS): a pilot study. <i>Journal of Autism and Developmental Disorders</i> , 38, 213–223.
<i>Clinical features and settings</i>	Recruitment: patients known to clinicians, national autism and Asperger's syndrome support group, referrals from autism diagnostic clinics, volunteers for advertisements on websites for adults with Asperger's syndrome. Country: US.
<i>Participants</i>	N = 94. Age: mean age 38 years. Sex: 47 male, 47 female. Ethnicity: not stated. Intellectual ability: 17% high school education; 83% college education.
<i>Study design</i>	Case-control
<i>Target condition and reference standard(s)</i>	Diagnosis: Asperger's syndrome or autistic disorder. Coexisting conditions: none stated.
<i>Index and comparator tests</i>	1. Instrument: RAADS. 2. Reference standard: DSM-IV-TR clinical diagnosis. Assessors: 1. Instrument: self-completed. 2. Reference standard: two psychiatrists.
<i>Follow-up</i>	Not reported
<i>Index test cut-off</i>	77+
<i>Limitations</i>	<ul style="list-style-type: none"> • Clinicians not blind to participants prior diagnosis. • Case-control design with high risk of bias in terms of patient selection, index test and flow and timing, and concerns about applicability with regard to index test.
<i>Source of funding</i>	Not stated
<i>Notes</i>	–

Study ID	RITVO2011
<i>Bibliographic reference</i>	Ritvo, R. A., Ritvo, E. R., Guthrie, D., <i>et al.</i> (2011) The Ritvo Autism Asperger Diagnostic Scale-Revised (RAADS-R): a scale to assist the diagnosis of autism spectrum disorder in adults: an international validation study. <i>Journal of Autism and Developmental Disorders</i> , 41, 1076–1089.
<i>Clinical features and settings</i>	Recruitment: from nine English speaking centres on three continents. Country: English-speaking countries.
<i>Participants</i>	N = 779. Age: mean range 30.81 to 42.04 years across diagnostic groups. Sex: 394 male, 386 female. Ethnicity: not stated. Intellectual ability: IQ ≥80.
<i>Study design</i>	Case-control
<i>Target condition and reference standard(s)</i>	Diagnosis: DSM-IV-TR ASD (Asperger’s syndrome or autistic disorder). Coexisting conditions: none stated.
<i>Index and comparator tests</i>	1. Instrument: RAADS-R. 2. Reference standard: DSM-IV-TR clinical diagnosis. Assessors: 1. Instrument: self-completed. 2. Reference standard: psychiatrist or licensed psychologist.
<i>Follow-up</i>	Not reported
<i>Index test cut-off</i>	65+
<i>Limitations</i>	Case-control design with high risk of bias in terms of patient selection, index test and flow and timing, and concerns about applicability with regard to patient selection and index test.
<i>Source of funding</i>	Not stated
<i>Notes</i>	–

1.2 CHARACTERISTICS OF EXCLUDED STUDIES

BOLTE2008

Reason for exclusion	Validated in children.
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BUITELAAR1999

Reason for exclusion	8.7% of the sample were adults.
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CAPONE2005

Reason for exclusion	Validated in children.
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GARFIN1988

Reason for exclusion	Validated in children.
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HELLINGS2005

Reason for exclusion	Validated in children.
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LECAVALIER2006

Reason for exclusion	Validated in children.
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LECONTEUR1989

Reason for exclusion	Validated in children.
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PROSSER1998

Reason for exclusion	16% of the sample diagnosed with Autism, which was too low.
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READING2007

Reason for exclusion	Validated in children.
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ROJAHN2001

Reason for exclusion	4.4% with autism, which was too low.
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STURMEY1995

Reason for exclusion	Psychometric data not provided.
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1.2.1 References of excluded studies

Bolte, S., Poustka, F. & Constantino, J. N. (2008) Assessing autistic traits: cross-cultural validation of the Social Responsiveness Scale (SRS). *Autism Research*, 1, 354–363.

Buitelaar, J. K., Van der Gaag, R., Klin, A., *et al.* (1999) Exploring the boundaries of pervasive developmental disorder not otherwise specified: analyses of data from the DSM-IV autistic disorder field trial. *Journal of Autism and Developmental Disorders*, 29, 33–43.

Capone, G. T., Grados, M. A., Kaufmann, W. E., *et al.* (2005) Down syndrome and comorbid autism-spectrum disorder: characterization using the Aberrant Behavior Checklist. *American Journal of Medical Genetics*, 134A, 373–380.

Garfin, D. G. & McCallon, D. (1988) Validity and reliability of the Childhood Autism Rating Scale with autistic adolescents. *Journal of Autism and Developmental Disorders*, 18, 376–378.

Hellings, J. A., Nickel, E. J., Weckbaugh, M., *et al.* (2005) The Overt Aggression Scale for rating aggression in outpatient youth with autistic disorder: preliminary findings. *Journal of Neuropsychiatry and Clinical Neurosciences*, 17, 29–35.

Lecavalier, L. & Aman, M. G. (2006) Validity of the Autism Diagnostic Interview-Revised. *American Journal of Mental Retardation*, 111, 199–215.

Le Couteur, A. & Rutter, M. (1989) Autism Diagnostic Interview: a standardized investigator-based instrument. *Journal of Autism and Developmental Disorders*, 19, 363–387.

Prosser, H., Moss, S., Costello, H., *et al.* (1998) Reliability and validity of the mini PAS-ADD for assessing psychiatric disorders in adults with intellectual disability. *Journal of Intellectual Disability Research*, 42, 264–272.

Reading, S. & Richie, C. (2007) Documenting changes in communication behaviours using a structured observation system. *Child Language Teaching and Therapy*, 23, 181–200.

Rojahn, J., Matson, J. L., Lott, D., *et al.* (2001) The Behaviour Problems Inventory: an instrument for the assessment of self-injury, stereotyped behaviour, and aggression/destruction in individuals with developmental disabilities. *Journal of Autism and Developmental Disorders*, 31, 577–588.

Sturmey, P., Burcham, K. J. & Perkins, T. S. (1995) The Reiss Screen for Maladaptive Behaviour: its reliability and internal consistencies. *Journal of Intellectual Disability Research*, 39, 191–195.