APPENDIX 14B:

CLINICAL EVIDENCE – STUDY CHARACTERISTICS

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1.1 CHARACTERISTICS OF INCLUDED STUDIES

Study ID	**ALLISON2012**
Bibliographic reference	Allison, C., Auyeung, B. & Baron-Cohen, S. (2012) Towards brief 'red flags' for autism screening: the short autism spectrum quotient and the short quantitative checklist in 1000 cases and 3000 controls. *Journal of the American Academy of Child and Adolescent Psychiatry*, *51*, 202–212.
Clinical features and settings	**Recruitment:** adults with autism recruited as volunteers from www.autismresearchcentre.com. Control data collected at the Cambridge Psychology website for volunteers (www.cambridgepsychology.com). **Country:** UK.
Participants	**N =** 1,287 (autism N = 449; controls N = 838). **Age:** 32.93 years (standard deviation [SD] 12.20 years) to 35.62 years (SD 13.04 years) across groups. **Sex:** 569 male, 718 female. **Ethnicity:** not stated. **Intellectual ability:** not stated.
Study design	Case-control
Target condition and reference standard(s)	**Diagnosis:** Asperger's syndrome or high-functioning autism by DSM-IV. **Coexisting conditions:** none reported.
Index and comparator tests	**1. Instrument:** AQ – 10-item version. **2. Reference standard:** DSM-IV criteria. ***Assessors:*** **1. Instrument:** self-report. **2. Reference standard:** medic or clinical psychologist.
Follow-up	Not reported
Index cut-off	6+
Limitations	• Analysis was retrospective and data on AQ were produced post-diagnosis. This might mean the participants were more aware of symptoms and hence answered as expected. • Method of data collection varied between groups (for example by post, online and so on). • Diagnosis was not validated by the research team and only available data on diagnosis were utilised. • Case-control design with high risk of bias for patient selection, index test and flow and timing, and concerns about applicability with regards to patient selection and index test.
Sources of funding	Big Lottery Fund, the Medical Research Council (MRC), the Three Guineas Trust and the Collaboration for Leadership in Applied Health Research and Care
Notes	Ten most discriminating items of AQ were: Attention to Detail (Items 5 and 28); Attention Switching (Items 32 and 37); Communication (Items 27 and 31); Imagination (Items 20 and 41); and Social (Items 36 and 45).

Study ID	BARONCOHEN2001
Bibliographic reference	Baron-Cohen, S., Wheelwright, S., Skinner, R., *et al.* (2001a) The Autism-spectrum Quotient (AQ): evidence from Asperger syndrome/high functioning autism, males and females, scientists and mathematicians. *Journal of Autism and Developmental Disorders*, *31*, 5–17.
Clinical features and settings	**Recruitment:** Group 1 Recruited via NAS (UK), specialist clinics, and advertisements in news letters and on internet pages. Group 2 recruited from a random sample sent the AQ by post. Group 3 was a random sample of students sent the AQ. Group 4 were winners of a mathematics olympiad. **Country:** UK.
Participants	**N =** 1,088. Group 1: N = 58 adults with Asperger's syndrome/high-functioning autism. Group 2: N = 174 randomly selected adults. Group 3: N = 840 Cambridge University students. Group 4: N = 16 winners of UK Mathematics Olympiad. **Age:** Group 1: mean 31.6 years (SD 11.8 years, range 16.5 to 58.3 years). Group 2: mean 37 years (SD 7.7 years, range 18.1 to 60.0 years). Group 3: mean 21 years (SD 2.9 years, range 17.6 to 51.1 years). Group 4: mean 17.4 years (SD 1.0 year, range 15.3 to 18.7 years). **Sex:** Group 1: 45 male, 13 female. Group 2: 76 male, 98 female. Group 3: 454 male, 386 female. Group 4: 15 male, 1 female. **Ethnicity:** mixed (not specified). **Intellectual ability:** Group 1: normal range; N = 15 randomly selected for intellectual assessment using the WAIS-R (revised version); pro-rated IQ of >85 (normal range) (mean 106.5, SD 8.0). Group 2: 15 randomly selected for intellectual assessment using the WAIS-R (mean IQ 105.8, SD 6.3; not significantly different from Group 1, p > 0.5). Group 3: unclear. Group 4: unclear.
Study design	Case-control study. Cross-sectional (Group 1: unclear; Groups 2 and 3: randomly selected; Group 4: participants in a predefined group).
Target condition and reference standard(s)	**Diagnosis:** Asperger's syndrome or high-functioning autism by DSM-IV. **Coexisting conditions:** none reported.
Index and comparator tests	**1. Instrument:** AQ. **2. Reference standard:** DSM-IV criteria. ***Assessors:*** **1. Instrument:** self-report. **2. Reference standard:** clinicians.
Follow-up	Not reported
Index cut-off	32+
Limitations	• False negative in controls could not be determined as the majority of questionnaires were completed anonymously. • Case-control design with high risk of bias for patient selection, index test and flow and timing, and concerns about applicability with regards to patient selection and index test.
Source of funding	MRC, McDonnell-Pew Foundation and Three Guineas Trust
Notes	–

Study ID	BERUMENT1999
Bibliographic reference	Berument, S. K., Rutter, M., Lord, C., *et al.* (1999) Autism screening questionnaire: diagnostic validity. *British Journal of Psychiatry*, *175*, 444–451.
Clinical features and settings	**Recruitment:** Postal questionnaire to individuals who had participated in previous studies. **Country:** UK.
Participants	**N =** 200 (PDD N = 160, non-PDD diagnosis N = 40). **Age:** ranged 4 to 40 years across diagnosis. Mean: autism 23.08 years (SD 8.7 years), atypical autism 7.03 years (SD 7.01 years), Asperger's syndrome 17.03 years (SD 4.09 years). **Sex:** ratios: autism 2.8:1 male:female; other PDD 6.7:1 male:female. **Ethnicity:** not stated. **Intellectual ability:** although learning disability was separated out, IQ ranged from 30 to >70 across the groups (see paper for more detail).
Study design	Case-control
Target condition and reference standard(s)	**Diagnosis:** ADI/ADI-R PDD: autism (N = 83), atypical autism (N = 49), Asperger's syndrome (N = 16), Fragile X (N = 7), Rett syndrome (N = 5). **Coexisting conditions:** none reported.
Index and comparator tests	**1. Instrument:** ASQ. **2. Reference standard:** ADI (N = 77), ADI-R (N = 123) measured several years before study. ***Assessors:*** **1. Instrument:** unclear – postal questionnaire, so might have been parental or self-report. **2. Reference standard:** clinicians.
Follow-up	Not reported
Index cut-off	Cut-off 15+ (autism versus other diagnosis). Also suggest 22+ (autism versus other PDDs)
Limitations	Case-control design with high risk of bias for patient selection, index test, reference standard, and flow and timing, and concerns about applicability with regards to patient selection.
Source of funding	MRC
Notes	Non-PDD comprised of conduct disorder (N = 10), specific developmental disorder (N = 7), learning disability (N = 15), other (N = 8) for example anxiety. ASQ now named Social Communications Questionnaire (SCQ).

Study ID	**BRUGHA2012**
Bibliographic reference	Brugha, T. S., McManus, S., Smith, J., *et al.* (2012) Validating two survey methods for identifying cases of autism spectrum disorder among adults in the community. *Psychological Medicine*, *42*, 647–656.
Clinical features and settings	**Recruitment:** Phase 1 data were obtained from a random probability sample of the general population; Phase 2 were selected based on high levels of probability of psychosis, ASD, borderline personality disorder and antisocial personality disorder. **Country:** UK.
Participants	**N =** Phase 1: N = 7,353; Phase 2: N = 618. **Age:** mean ages not reported, but all participants >16 years. **Sex:** not reported. **Ethnicity:** not reported. **Intellectual ability:** not reported.
Study design	Cohort
Target condition and reference standard(s)	**Diagnosis:** autism. **Coexisting conditions:** potential psychosis, borderline personality disorder and antisocial personality disorder.
Index and comparator tests	**1. Instrument:** AQ-20. **2. Reference standard:** ADOS – Module 4. ***Assessors:*** **1. Instrument:** self-reported postal questionnaire. **2. Reference standard:** research psychologists.
Follow-up	Not reported
Cut-off	10
Limitations	AQ-20 tested in general population not in sample where suspicion of autism has already been raised.
Source of funding	The NHS Information Centre for Health and Social Care and the Department of Health, London UK; The NIHR and the Department of Health Policy Research Programme, London, UK
Notes	–

Study ID	**KRAIJER2005**
Bibliographic reference	Kraijer, D. & de Bildt A. (2005) The PDD-MRS: an instrument for identification of autism spectrum disorders in persons with mental retardation. *Journal of Autism and Developmental Disorders*, *35*, 499-513.
Clinical features and settings	**Recruitment:** residential institutions and day care centres. **Country:** Netherlands.
Participants	**N =** 1,230 (PDD N = 408, non-PDD N = 696, doubtful PDD N = 126). **Age:** range 2 to 80 years. **Sex:** 719 male, 511 female. **Ethnicity:** not stated. **Intellectual ability:** mild to profound learning disability.
Study design	Cohort
Target condition and reference standard(s)	**Diagnosis:** PDD with DSM-IV-TR. **Coexisting conditions:** learning disability (mild to profound), additional congenital impairments (Down's syndrome, Fragile X).
Index and comparator tests	**1. Instrument:** PDD-MRS. **2. Reference standard:** DSM-IV-TR clinical diagnosis (using ADOS and ADI-R). ***Assessors:*** **1. Instrument:** unclear. **2. Reference standard:** clinicians.
Follow-up	Not reported
Index cut-off	10+
Limitations	Subgroup analysis revealed poor sensitivity and specificity as well as misclassification rate for those with borderline intellectual functioning. Additionally, poor specificity and overall misclassification rate for those who are blind/severe visual impairments.
Source of funding	Not stated
Notes	–

Study ID	KURITA2005
Bibliographic reference	Kurita, H., Koyama, T. & Osada H. (2005) Autism-spectrum quotient – Japanese version and its short forms for screening normally intelligent persons with pervasive developmental disorders. *Psychiatry and Clinical Neurosciences*, *59*, 490–496.
Clinical features and settings	**Recruitment:** outpatients at the Child Guidance Clinic affiliated with the National Welfare Foundation for Disabled Children. **Country:** Japan.
Participants	**N =** 240 (high-functioning PDD N = 25, controls N = 215). **Age:** high-functioning PDD mean 24.2 years; control mean 30.4 years. **Sex:** 110 male, 130 female. **Ethnicity:** Japanese. **Intellectual ability:** normal intelligence.
Study design	Case-control
Target condition and reference standard(s)	**Diagnosis:** high-functioning PDD (N = 13 Asperger's syndrome, N = 5 autistic disorder, N = 7 PDD) with DSM-IV and ICD-10 (for PDD). **Coexisting conditions:** none stated.
Index and comparator tests	**1. Instrument:** AQ-J. **2. Reference standard:** DSM-IV clinical diagnosis. ***Assessors:*** **1. Instrument:** experienced psychologist. **2. Reference standard:** team of clinicians.
Follow-up	Not reported
Index cut-off	Different cut-offs evaluated: 50 item AQ cut-off = 26. 21 item AQ cut-off = 12. 10 item AQ cut-off = 7.
Limitations	Case-control design with high risk of bias for patient selection, index test and flow and timing, and concerns about applicability with regards to patient selection and index test.
Source of funding	Not stated
Notes	–

Study ID	VOLKMAR1988
Bibliographic reference	Volkmar, F. R., Cicchetti, D. V., Dykens, E., *et al.* (1988) An evaluation of the autism behavior checklist. *Journal of Autism and Developmental Disorders*, *8*, 81–97.
Clinical features and settings	**Recruitment** Participants recruited from university-affiliated school for autistic individuals, a residential facility for 'mentally retarded' children and a clinic for children with developmental disabilities. **Country:** US.
Participants	**N =** 157 (autistic N = 94, non-autistic N = 63). **Age:** mean age 19.72 years (SD 12.60 years). **Sex:** 121 male, 36 female. **Ethnicity:** not stated. **Intellectual ability:** mean IQ on Stanford Binet (for N = 147) 36.80 (SD 24.30). Sample included both profoundly 'retarded' (N = 47) and some with average scores (N = 14).
Study design	Case-control
Target condition and reference standard(s)	**Diagnosis:** infantile autism with DSM-III. Non-autistic Group included 'mental retardation', atypical pervasive developmental disorder, language disorder and schizophrenia of childhood onset. **Coexisting conditions:** none stated.
Index and comparator tests	**1. Instrument:** Autism Behavior Checklist. **2. Reference standard:** DSM-III clinical diagnosis (prior to scoring and analysis of ABC). ***Assessors:*** **1. Instrument:** teachers and parents. **2. Reference standard:** clinicians.
Follow-up	Not reported
Index cut-off	57+
Limitations	High risk of bias for patient selection, index test, and flow and timing, and concerns about applicability with regards to patient selection and index test.
Source of funding	In part by William T. Grant Foundation, the John Merck Fund, Mental Health Clincial Research Center Grant 30929, CCRC Grant RR00125, National Institute of Child and Human Development Grant HD-03008, NIMH Grant MH00418 and Mr Leonard Berger
Notes	–

Study ID	WAKABAYASHI2006
Bibliographic reference	Wakabayashi, A., Baron-Cohen, S., Wheelwright, S., *et al.* (2006) The Autism-Spectrum Quotient (AQ) in Japan: a cross-cultural comparison. *Journal of Autism and Developmental Disorders*, *36*, 263–270.
Clinical features and settings	**Recruitment:** high-functioning autism sample recruited via the Japanese Autistic Society, specialist clinics and self-help groups. Control Group randomly selected from general population and sent a postal questionnaire. Students recruited from five universities in or near Tokyo. **Country:** Japan.
Participants	**N =** 1301 (Group 1: N = 57 high-functioning autism, Group 2: N = 194 control, Group 3: N = 1,050 students). **Age:** Group 1: mean age 26.9 years (SD 7.88 years, range 18 to 57 years). Group 2: mean age 33.6 years (SD 6.2 years, range 22 to 56 years). Group 3: mean age 20.3 years (SD 1.9 years, range 18 to 41 years). **Sex:** Group 1: 44 male, 13 female; Group 2: 103 male, 91 female; Group 3: 555 male, 495 female. **Ethnicity:** not stated. **Intellectual ability:** high-functioning autism Group assumed to have IQ in normal range as they had all completed high school and some had a university degree.
Study design	Cross-sectional (Group 1: unclear; Group 2: randomly: Group 3: unclear)
Target condition and reference standard(s)	**Diagnosis:** high-functioning autism or Asperger's syndrome with DSM-IV. **Coexisting conditions:** none stated.
Index and comparator tests	**1. Instrument:** AQ. **2. Reference standard:** DSM-IV clinical diagnosis. ***Assessors:*** **1. Instrument:** self-report. **2. Reference standard:** clinical reports.
Follow-up	Not reported
Index cut-off	33+
Limitations	Case-control design with high risk of bias for patient selection, index test and flow and timing, and concerns about applicability with regards to patient selection and index test.
Source of funding	MRC
Notes	–

Study ID	WOODBURYSMITH2005
Bibliographic reference	Woodbury-Smith, M. R., Robinson, J., Wheelwright, S., *et al.* (2005) Screening adults for Asperger syndrome using the AQ: a preliminary study of its diagnostic validity in clinical practice. *Journal of Autism and Developmental Disorders*, *35*, 331–335.
Clinical features and settings	**Recruitment:** Cambridge Lifespan Asperger Syndrome Service. **Country:** UK.
Participants	**N =** 100 patient referrals. **Age:** median age 32 years, range 18 to 69 years. **Sex:** ratio 4:1 male:female. **Ethnicity:** not stated. **Intellectual ability:** not stated, but people with a learning disability were excluded.
Study design	Cohort
Target condition and reference standard(s)	**Diagnosis:** Asperger's syndrome or autism with DSM-IV. **Coexisting conditions:** none stated.
Index and comparator tests	**1. Instrument:** AQ. **2. Reference standard:** DSM-IV clinical interview. ***Assessors:*** **1. Instrument:** self-report. **2. Reference standard:** two clinicians.
Follow-up	Not reported
Index cut-off	26+
Limitations	Clinicians not blind to AQ score because the AQ is used as part of clinical practice.
Source of funding	The Three Guineas Trust supports the Cambridge Lifespan Asperger Syndrome. Simon Baron-Cohen and Sally Wheelwright supported by MRC
Notes	–

1.2 CHARACTERISTICS OF EXCLUDED STUDIES

FERRITER2001

Reason for exclusion	No available data and the paper is a brief report with not enough information about the study. No access to full paper.

GARFIN1988

Reason for exclusion	No sensitivity and specificity data available.

MESIBOV1989

Reason for exclusion	No sensitivity and specificity data; reference standard is not adequate; age of sample (15.9 years) is outside the scope.

NYLANDER2001

Reason for exclusion	The sensitivity and specificity data were unreliable. Not all participants had a clear diagnosis.

1.2.1 References of excluded studies

Ferriter, M., Hare, D., Bendall, P., *et al.* (2001) Brief report: assessment of a screening tool for autistic spectrum disorders in adult population. *Journal of Autism and Developmental Disorders*, *3*, 351–353.

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.

Mesibov, G. B., Schopler, E., Schaffer, B., *et al.* (1989) Use of the childhood autism rating scale with autistic adolescents and adults. *Journal of American Academy of Child and Adolescent Psychiatry*, *28*, 538–541.

Nylander, L. & Gillberg, C. (2001) Screening for autism spectrum disorders in adult psychiatric out-patients: a preliminary report. *Acta Psychiatrica Scandinavica*, *103*, 428–434.