



Screening for Autism in Childhood

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Collaborators



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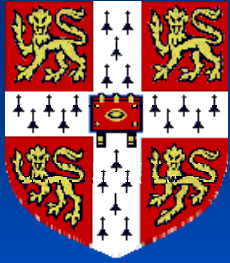
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This Talk



- Background to screening for ASC
- Childhood Screening Research at the ARC:
 1. Q-CHAT (Quantitative Checklist for Autism in Toddlers)
 2. CAST (Childhood Asperger Syndrome Test)



Background



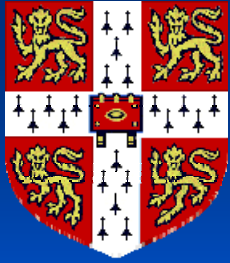
- Autism Spectrum Conditions (ASCs) difficult to detect in very young children
- Affects 1% population (Baird et al., 2006)
- Diagnosis often delayed although concerns often at 18 months:
 1. Core impairments vary from person to person
 2. Some 'symptoms' are subtle
- Delay of 20-60 months between parental concern and eventual diagnosis (Mandell et al., 2005)
- Yet clinical diagnosis stable from 2 years (Cox et al, 1999)



Benefits of early diagnosis



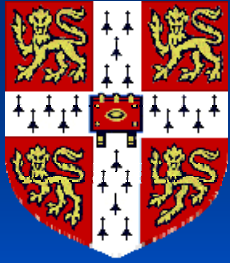
- Early detection – earlier intervention and better outcome (Lovaas & Smith, 1988)
- Prevention of secondary difficulties e.g. anxiety, depression, bullying (Tonge et al, 1999; Howlin, 2000)
- Parents
 - manage difficult behaviours and family stress
 - monitor later-born children/consider genetic risk for ASC



National Screening - UK



- UK – lack of standardised routine developmental screening
- National Screening Committee examine evidence for:
 - Condition in question
 - Screening test
 - Treatments available
 - Effectiveness of overall screening programme
- Present policy – *‘introduction of [ASC] screening cannot [currently] be recommended’*
(National Screening Committee Child Health Subgroup, 2005)



Context for Screening



- Ultimate goal – prospective identification of all children with ASC before difficulties apparent
- 3 questions
 1. Can we screen for ASC?
 2. Prospective identification of ASC from general population?
 3. How best can we do this?



Screening and Surveillance



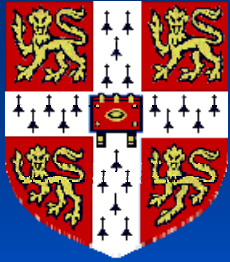
- **SCREENING** – prospective identification of disorder, applying specific tests
- **SURVEILLANCE** – collection of data relevant to identification of disorder by health system e.g. routine check-ups



Validation of a Screening Test



- Test administered to population
- All or sample of participants receive 'gold standard' diagnostic test
- Calculate indices of test accuracy:
 - Sensitivity (aim: few false negatives)
 - Specificity (aim: few false positives)
 - Positive Predictive Value (proportion of those screen positive who have disorder)



The CHAT



- Checklist for Autism in Toddlers (Baron-Cohen et al, 1992)
- Based on:
 - Health professional observation
 - Parental report
- Majority of typically developing children would manifest joint attention and pretend play
- Undiagnosed cases of ASC may be revealed by **absence** of these key behaviours

At 18 Months Does Your Child . . .

1. Look at you and point when he/she wants to show you something?



2. Look when you point to something?

3. Use imagination to pretend play?



If the answer is **NO**, your child may be at risk for **Autism**. Please alert your physician today.

HANS Help Autism Now Society
www.helpautismnow.com

Based on CHAT (Checklist for Autism in Toddlers)



The CHAT



(Baron-Cohen et al, 1992)

- CHAT examined 18 month old 'at risk' infants (n=41)
At 30 months, all 'high risk' infants were diagnosed with an ASC

(Baird et al, 2000)

- 16,235 children screened and followed up at age 7 -
PPV high (83%), sensitivity poor (18%)
- CHAT missed 4/5 children who later received
diagnosis
- Sensitivity improved (38%) when one-stage
screening procedure applied, still below acceptable
levels



Why did the CHAT miss cases?



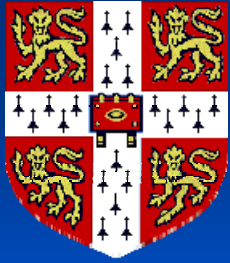
- Wording – ‘has your child *ever* pointed?’
- Focused on joint attention behaviours and pretend play
- CHAT screening only took place at 18 months – regressive autism?
- Criteria to determine high and medium risk groups may be too stringent



Development of the Q-CHAT



- Q-CHAT – ‘Quantitative’ and ‘Quick’
- Allows for a *reduced* rate of key behaviours
- Takes into account the continuum nature of ASC
- Retains all key items of CHAT
- Includes additional items - language development, repetitive and sensory behaviours



Design of the Q-CHAT



- 25 items
- Scored on 5-point scale (0-4), range of scores 0 – 100
- Parent-only report:
 1. reduction of burden
 2. Sensitivity higher for parent-only report (n=2541)
- Positive symptoms score more highly



Sample Question (I)



Does your child look at you when you call his/her name?

Always

Usually

Sometimes

Rarely

Never





Sample Question (II)



Does your child point *to share interest with you* (eg pointing at an interesting sight)?

many times a day
a few times a day
a few times a week
less than once a week
never





Study 1 – Q-CHAT Preliminary Study - Aim



Assess Q-CHAT ability to discriminate between:

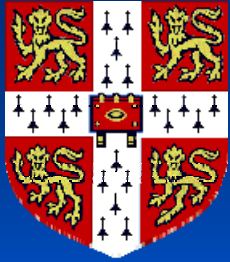
1. Typical development in toddlers at 18 to 24 months (Group 1)
 2. Toddlers with a diagnosis of an ASC (Group 2)
- Examine distribution of scores in population sample



Method



- Group 1: 2360 Q-CHATs distributed to parents of 18 – 24 month old infants in Cambridgeshire, via CHSD
- Group 2: parents completed online version of Q-CHAT at www.autismresearchcentre.com



Participants



Group	N	Mean Age (months)	SD
18 - 24 months	754 (382 M, 372 F)	21.2	2.1
ASC group	38 (29 M, 9 F)	31.2	4.9



ASC Group Diagnoses



	N
Asperger Syndrome	1
Atypical Autism	1
Autism	25
High Functioning Autism	7
Pervasive Developmental Disorder	4
Total	38



Response Rate



Typical Group:

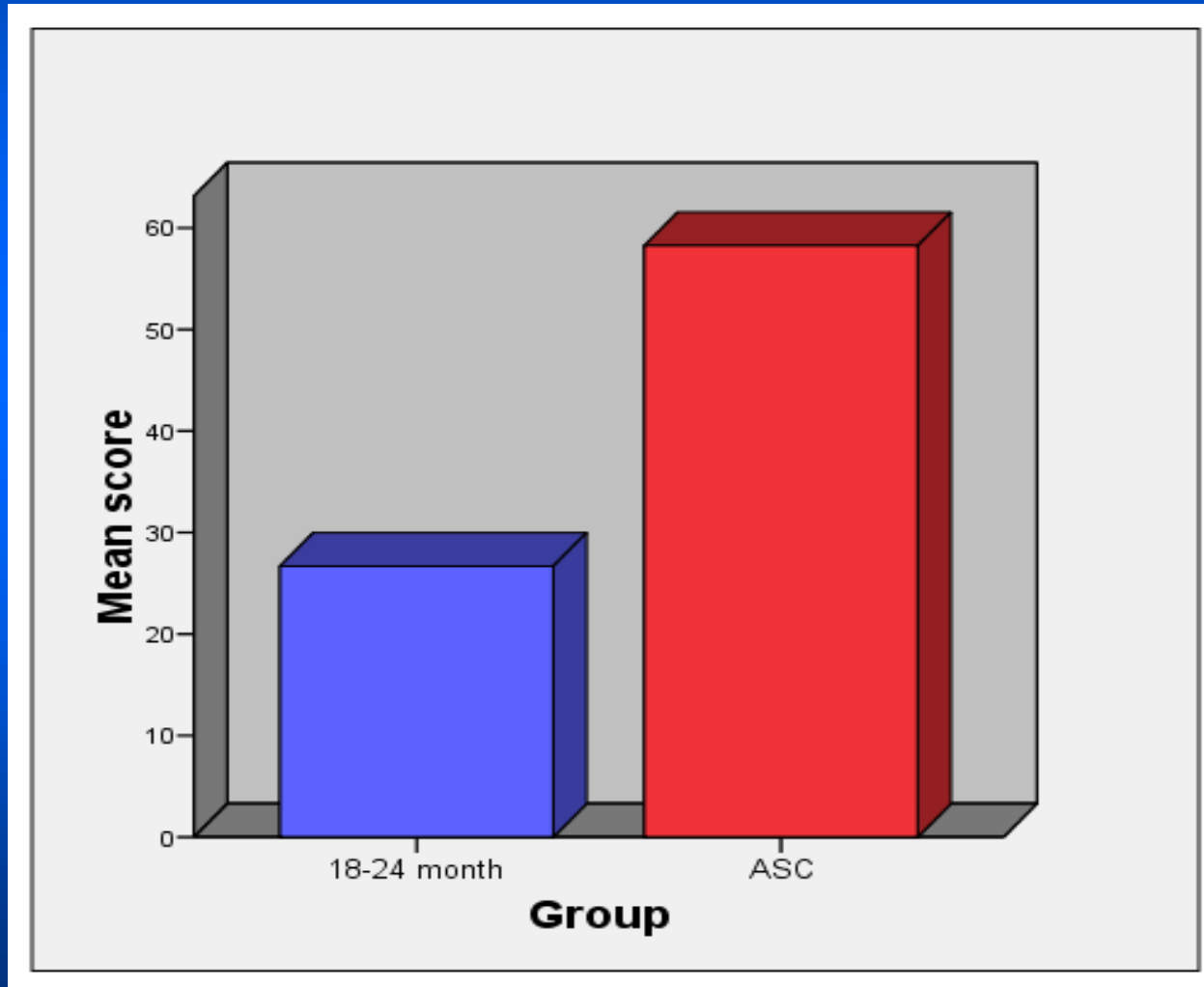
- 779 questionnaires returned (33% response)
- 25 questionnaires excluded – 754 for analysis
- 660 questionnaires had complete data

ASC Group:

- No missing data



Results



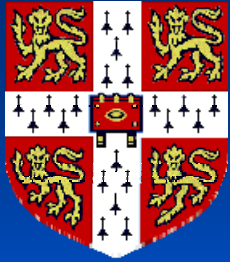


Results

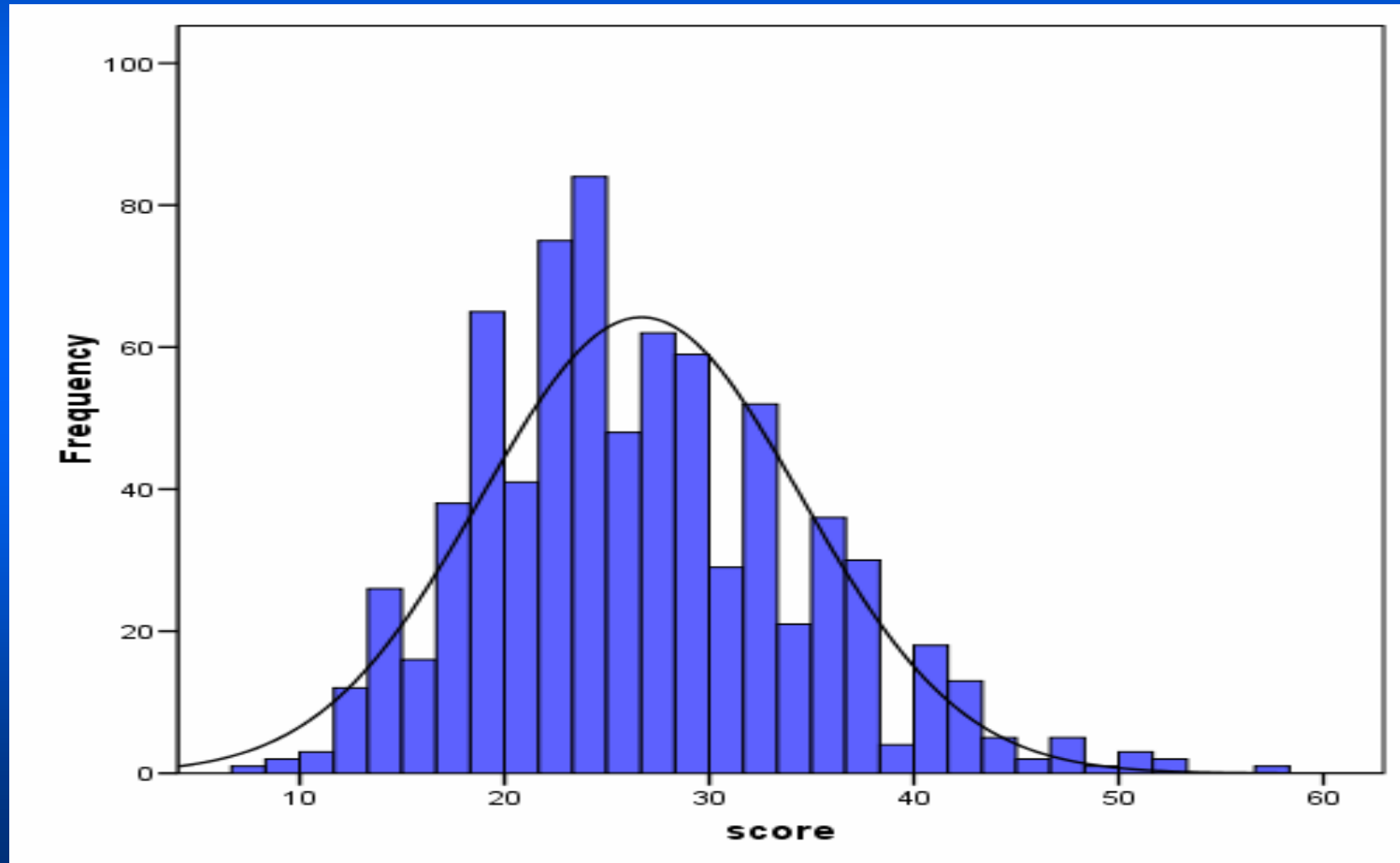


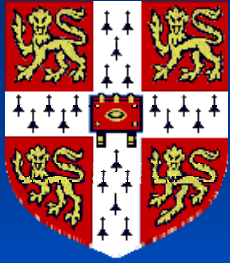
Group	Mean Score	Median Score	SD	Range
Typical	26.7	26.0	7.8	7, 57
ASC	58.3	59.5	12.6	26, 88

ASC group (Group 2) scored significantly higher than 18-24 month typically developing toddlers (Group 1) ($p < .001$)

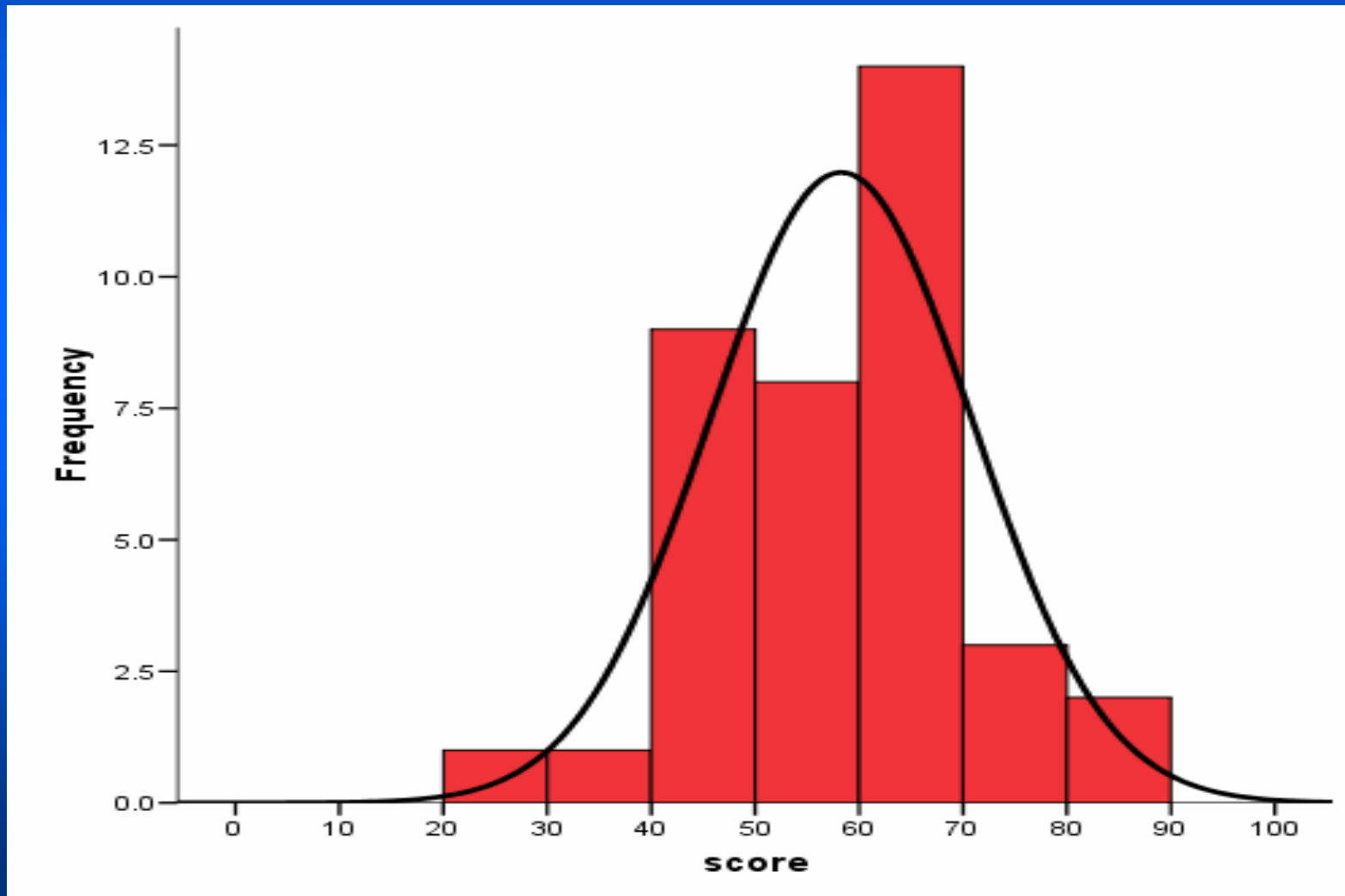


Typical Group Distribution



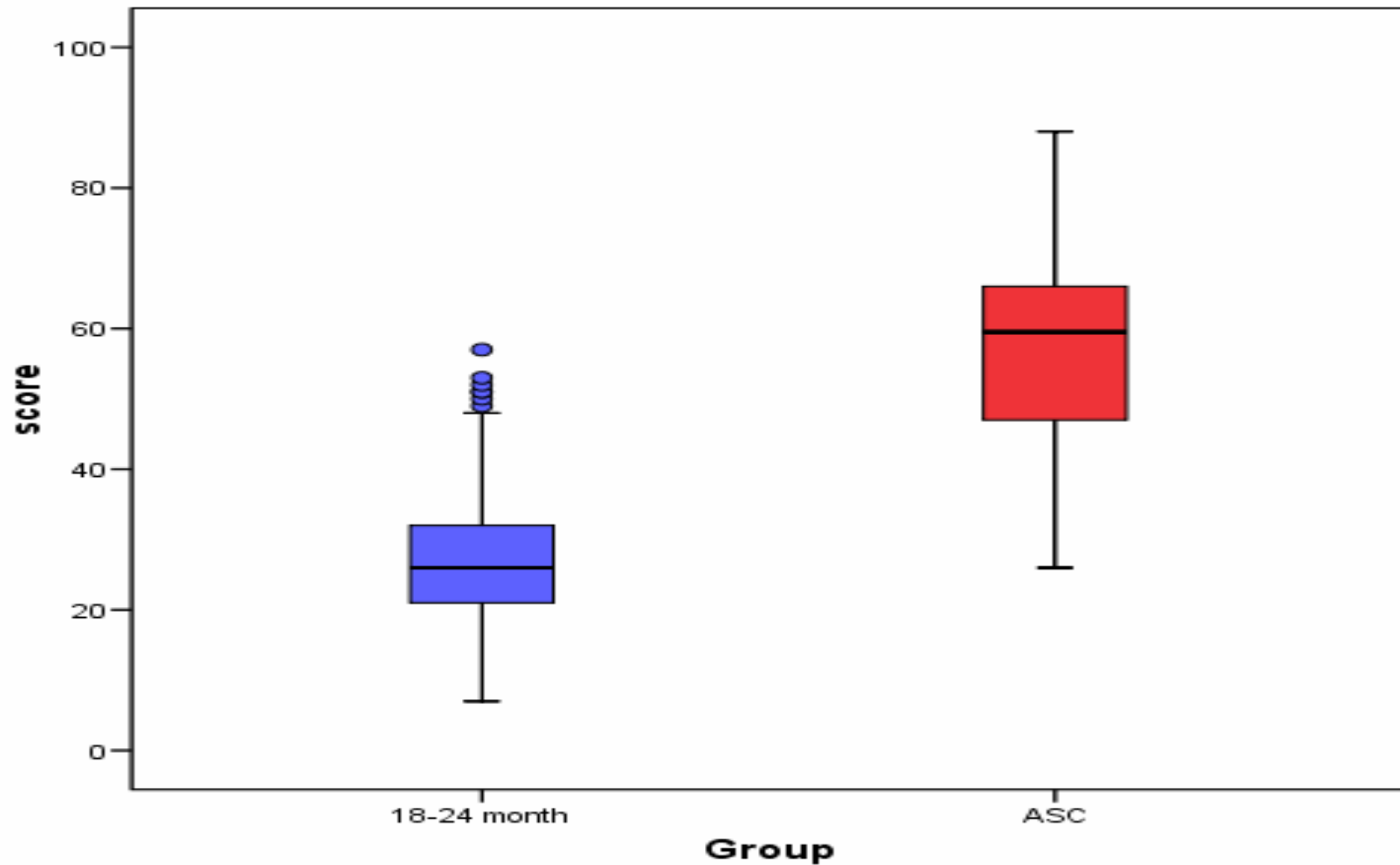


ASC Group Distribution





Score Distribution by Group

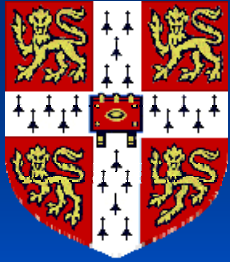




Results



- Typical Group Boys – Median 27 (IQR: 22 – 32, range: 11 – 57)
- Typical Group Girls – Median 25 (IQR: 21 – 30.75, range: 7 – 51)
- Score distributions significantly different from each other (Mann-Whitney, $p=0.03$)
- 4% scored 2 SD above mean



Discussion



- Q-CHAT can distinguish between ASC and typically developing children at 18-24 months
- BUT
 - age of ASC group older than 18-24 month toddler group
 - Parents of ASC group completed Q-CHAT AFTER diagnosis → bias?
 - no IQ data collected for ASC group – is Q-CHAT score associated with IQ?
 - To date, no validation data available on population sample
- Overall, results suggest majority of children with ASC score at least above 40
- Sampling across whole distribution



Discussion



- Q-CHAT scores followed near-normal distribution
→ continuum nature of ASC symptoms
(Constantino et al., 2006)
- Boys score significantly higher on Q-CHAT than girls in population sample
- Sex difference consistent with other screening tests e.g. CAST (Williams et al, submitted) and AQ (Baron-Cohen et al, 2006; 2001)
- Consistent with higher prevalence of ASC in males (Wing et al, 1976), and EMB theory of autism (Baron-Cohen, 2002)



Strengths and Limitations



- Large population of typically developing 18–24 month old toddlers → robust results
- BUT low response rate – generalisable results?
- Need to assess test-retest reliability in sample enriched by individuals with high scores
- As whole scale, strong correlation between Q-CHAT1 and Q-CHAT2 - Q-CHAT stable over time



Potential of the Q-CHAT



- Epidemiological research **BUT** poor response rate and potential bias (concerns, SES?)
- High risk research – e.g. baby-sibling – may enable clinicians to diagnose ASC earlier → improved prognosis
- Genetic research – measure autistic traits in case-control design



Q-CHAT

Future Directions



- Validation of Group 1 – ADOS, ADI-R, Mullen Scales of Early Learning, Vineland – inform sampling strategy for main study
- Prospectively screen 20,000 toddlers (NAS & Big Lottery) in East Anglia
- Checklist for Referral (CR) at age 3 years to verify number of cases missed by the Q-CHAT
- Examination of the factor structure of the Q-CHAT using Classical Test Theory and Latent Trait Modelling
- Evaluate Q-CHAT in referred sample



The CAST



- Childhood Asperger Syndrome Test (CAST)
- 37 item parental self-completion questionnaire, range of scores 0 - 31
- Used predominantly in children with IQ in normal range, ages 4 - 11
- Designed on quantitative scale, assumes behaviour on continuous distribution
- Arbitrary cut-points – therefore compatible with a categorical conceptualization of autism



CAST Research

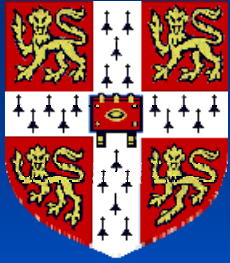


- Aims:

1. Develop test for use in general population
2. Sensitive to broader ASCs

(Scott et al., 2002)

- all children (n=13) with diagnosis of Asperger syndrome scored at 15 or above
- 98% specificity in mainstream school sample (n=1150)
- BUT response rate only 17% (n=199)
- Unable to calculate sensitivity – not possible to assess all who responded to CAST



The CAST - Validation



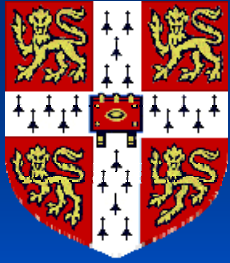
- 1925 CASTs distributed in schools in Cambridgeshire
- All 15+ and 12 – 14 scorers invited for detailed diagnostic assessment, and 5% low scorers
- ADI-R and ADOS assessments ‘gold standard’



Case Definition



- Assessment diagnosis (ADOS, ADI-R)
 - validated, reliable, standardised diagnostic tests
- Consensus diagnosis – ICD-10 criteria



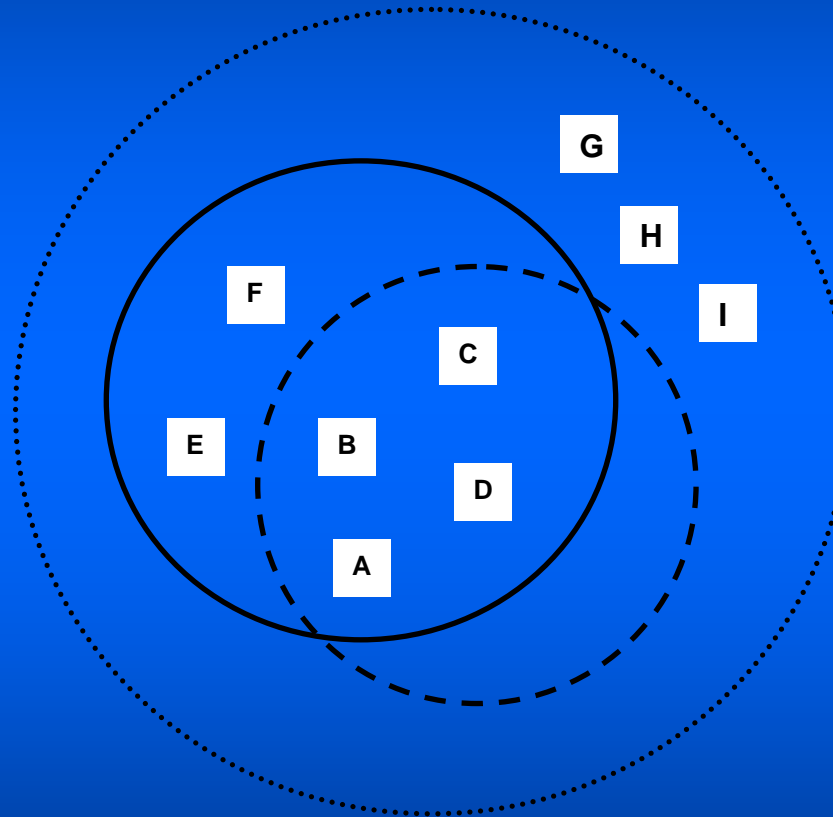
CAST Validation Study - Results



- 26% response rate for screen (n=500)
- 60% response rate for assessments
- 4 children had previous clinical diagnoses
- 2 children received a clinical diagnosis between CAST and the assessment
- 4 children were identified as cases using the assessment case definition, all of whom had a previous clinical diagnosis
- 3 children identified using the consensus case definition



Diagnoses at Assessment



- Previous diagnosis (stated to have diagnosis at start of ADI)
- - - Assessment diagnosis (above all cut-points on both ADOS and ADI)
- Consensus diagnosis



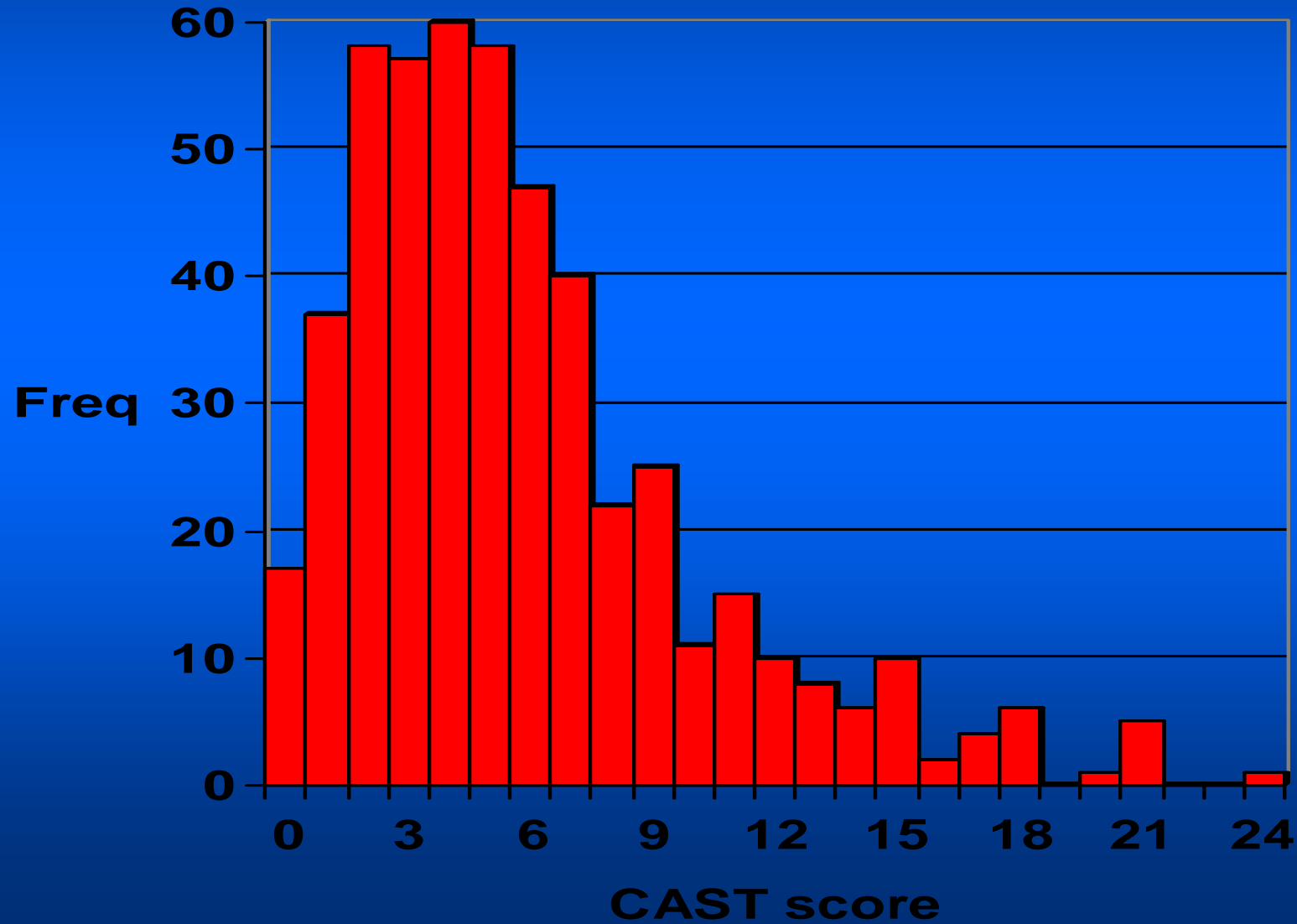
CAST Validation Study - Results



- Consensus diagnosis - cut-point 15, sensitivity=100%, specificity=97%
- Sensitivity dropped at higher cut-points
- Assessment diagnosis – cut point of 18 may be more appropriate to reach high levels of sensitivity and specificity



CAST Score Distribution





CAST Discussion



- CAST - good screen accuracy, high sensitivity and specificity
- BUT - low positive predictive value, a function of low prevalence of the condition in the general population
- resource implications of assessing a large number of children who are false positives
- Consensus diagnosis may be better 'gold standard' – ADI-R and ADOS less sensitive to subtler manifestations of ASC



CAST - Limitations



- Sampling bias?
 1. Few assessments in low scoring group
 2. Concerns over development higher in those who agreed to assessment
- Time lag between screen and assessment
- Small sample size – wide confidence intervals on indices of test accuracy
- Not possible to stay blind to diagnostic status
- No data on higher risk population
- Interventions at time of screen?
- Representative results?



Conclusions



- CAST can be recommended as screen in epidemiological research, not at population level – too many false positives, low response rate
- Performance of CAST depends on type of diagnosis used as gold standard
- False positives – manifesting other symptoms? e.g. ADHD, language delay



Overall Conclusions



- Screen is only 1st stage in diagnostic process
- Gaps in evidence for screening remain – case definition, natural history, interventions
- Sex difference in distribution of scores
- Outstanding Questions:
 1. What is acceptable sensitivity/specificity/PPV criteria for a screen?
 2. What is best age to screen for ASC?
 3. Should screens specifically target ASC?



Acknowledgements



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ANY QUESTIONS?

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